Conjugated Azoalkenes. Part 12.[1] Synthesis of New 1-Amino-3-cyanopyrrole, 1,2-Diaminopyrrole and Pyrrolo[2,3-*b*]pyrrole Derivatives by Reaction of Some Conjugated Azoalkenes with Activated Nitriles

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The reactions of a variety of conjugated azoalkenes with β-cyano ketones or β-cyano amides have been studied and, depending on the nature and the molar ratios of the reagents, new 1-amino-3-cyanopyrroles, 1,2-diaminopyrroles and 1,3a,6,6a-tetrahydropyrrolo[2,3-*b*]pyrroles can be obtained in good yields and under mild reaction conditions.

We have previously shown that conjugated azoalkenes are excellent substrates for the synthesis of several 1-aminopyrrole, 1-amino-2-hydroxy-2,3-dihydropyrrole, and pyrrolo[2,3-*b*]pyrrole derivatives by reaction with compounds containing active methylene or methine groups.[2–4] These products are provided with versatile functional groups capable of further elaboration. In particular, in a previous part of this series,[4] we reported that reactions of certain conjugated azoalkenes with malononitrile gave 1,2-diamino-3-cyanopyrroles and 3a-cyanopyrrolo[2,3-*b*]pyrroles, while the reaction of the same reagents with β-cyanoesters gave mainly 3a-alkoxycarbonylpyrrolo[2,3-*b*]pyrroles. When nitriles with active methylene groups add to conjugated azoalkenes the unconjugated 1,4-adduct is formed. This can then react by one or both of two possible reaction pathways: ring closure of the 1,4-adduct to the iminopyrroline intermediate which readily tautomerizes to the 1,2-diaminopyrrole, and/or a further addition reaction of the 1,4-adduct to the conjugated azoalkene to give a bis-adduct which undergoes double ring closure to afford the linearly condensed system.

Result and Discussion

In connection with our continuing interest in the chemistry of conjugated azoalkenes and in the synthesis of new pyrrole and pyrrolo[2,3-*b*]pyrrole derivatives, we now describe the synthesis of new 1-amino-3-cyanopyrroles and 3a-carbonylpyrrolo[2,3-*b*]pyrroles by the reaction between conjugated azoalkenes and β-cyano ketones (Scheme 1) as well as the preparation of previously unknown 1,2-diamino-3-aminocarbonylpyrroles and 3a-aminocarbonylpyrrolo[2,3-*b*]pyrroles by the reaction of the same reagents with 1-cyanoacetylpiperidine (Scheme 2).[5]

The approach employed initially was based on the reaction of the azoalkenes **1a–f** with an equimolar amount of 4,4-dimethyl-3-oxopentanenitrile **2a** in THF (tetrahydrofuran) as a solvent. Under these conditions, the reactions led to two products, which were identified as the 1,4-adducts **3a–f**, and the pyrrolo[2,3-*b*]pyrroles **5a–d**. The 1,4-adducts **3a–f** can be isolated, purified, and characterized, and can be utilized for the preparation of 1-amino-3-cyanopyrroles **4a–f**, in the presence of $CuCl_2 \cdot 2H_2O$ (CCD), according to our previous investigations on this matter.[2,3a] When a 2:1 ratio **1a–d**:**2a** was employed, the yields of the pyrrolo[2,3-*b*]pyrroles **5a–d** were considerably increased.

The reactions between equimolar amounts of the azoalkenes **1a–f** and benzoylacetonitrile **2b** in the presence of CCD, in THF as a solvent, gave the 1-amino-3-cyanopyrroles **4g–l** directly in high yields, together with pyrrolo[2,3-*b*]pyrroles **5e–h** as minor secondary products. When the benzoylacetonitrile **2b** was added to the azoalkenes **1c–f** in the ratio of 1:2 an improvement in the yield of the pyrrolo[2,3-*b*]pyrroles **5e–h** was observed (Table 1).

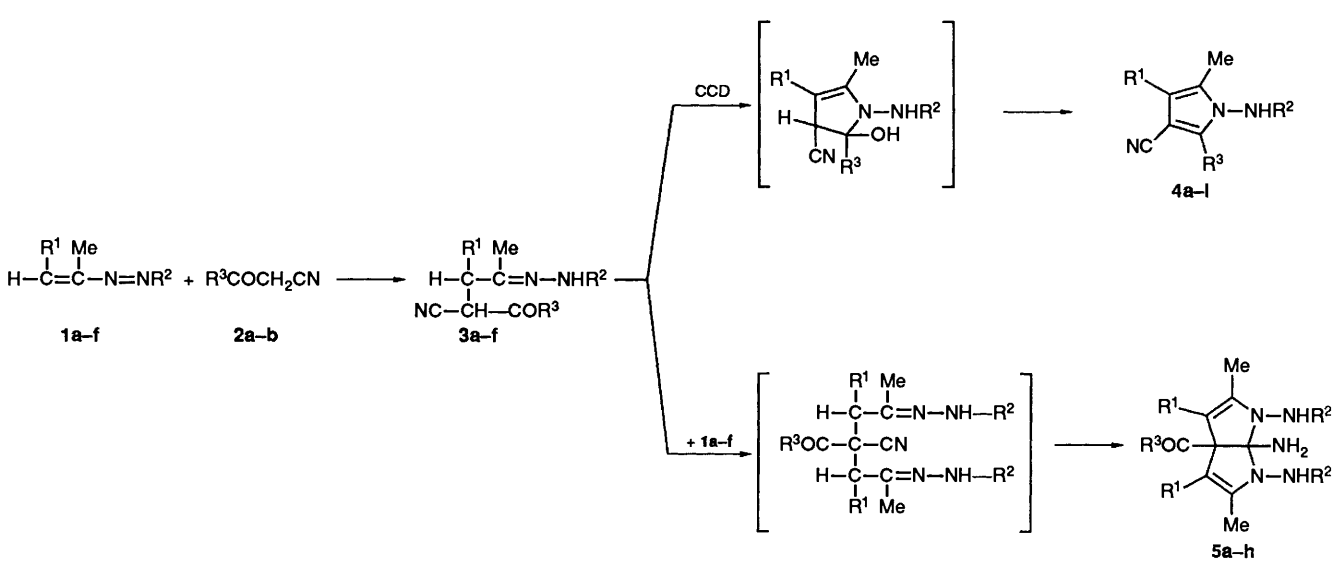
The reaction of azoalkenes **1a–f** with 1-cyanoacetylpiperidine **2c** in the ratio 1:1 was investigated next. This led to the 1,4-adducts **3g–l** in very good yields, together with traces of pyrrolo[2,3-*b*]pyrroles **5i–j**. The best yields in the subsequent cyclizations of the 1,4-adducts were obtained by treating them with NaH, which gave the 1,2-diamino-3-aminocarbonylpyrroles **4m–r** by ring closure to the cyano group. Use of a 2:1 ratio of **1c** or **1d** to **2c** increased considerably the yields of the pyrrolo[2,3-*b*]pyrroles **5i–j** (Table 2).

From the above brief description it can be seen that conjugated azoalkenes react with β-cyano ketones by two different pathways. The simple 1,4-adduct initially formed may cyclize *via* the ketone to give a hydroxypyrroline derivative, which is readily dehydrated to the 1-amino-3-cyanopyrrole in the presence of CCD,[2,3a] while the bis-1,4-adduct gives the 3a-carbonylpyrrolo[2,3-*b*]pyrrole by the double ring closure process.[4]

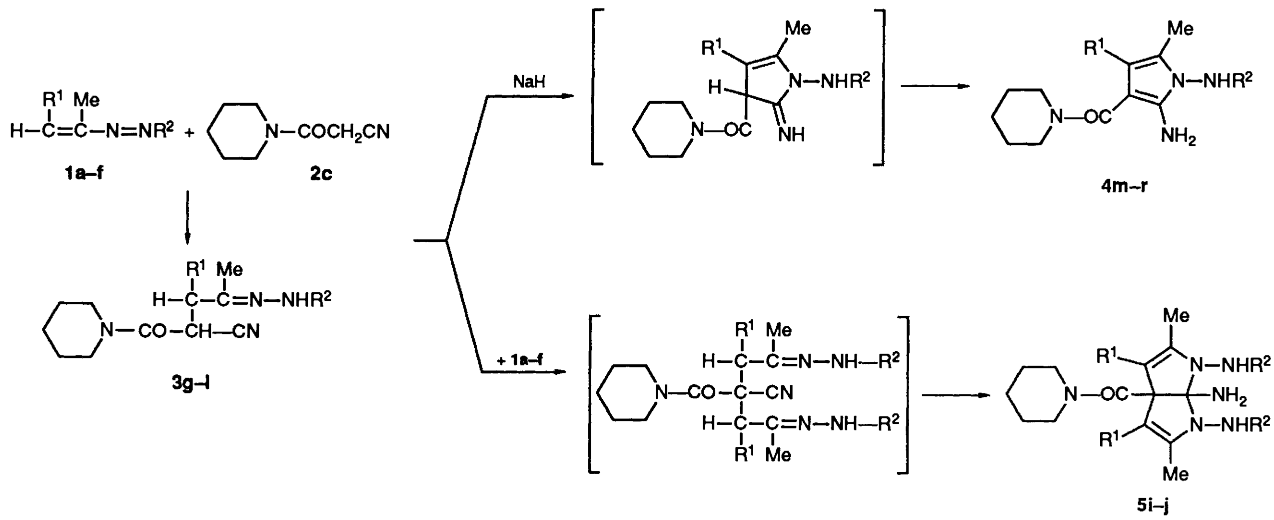
When the conjugated azoalkenes react with 1-cyanoacetylpiperidine, the simple 1,4-adduct is initially formed in THF, but attempts to carry out the ring closure under the same conditions as used for the β-cyano ketones failed to provide the 1,2-diamino-3-aminocarbonylpyrroles. Use of NaH in THF led to unacceptably slow reaction, but a solvent mixture of THF and MeOH in the ratio 1:1 was found to be more convenient, reproducibly giving the pyrroles in good yields in a few minutes. As was found with the simple cyano ketones, the 1,4-adducts **3g–l** readily react with a second azoalkene molecule to give the bis-1,4-adducts. Double ring closure to the cyano group leads to the 3a-aminocarbonylpyrrolo[2,3-*b*]pyrrole derivatives **5**. In neither case was cyclization to the amido group observed, according to our previous findings.[2]

Experimental

Amino- and alkoxy-carbonylazoalkenes were prepared as previously reported.[6] 4,4-Dimethyl-3-oxopentanenitrile, benzoylacetonitrile and 1-cyanoacetylpiperidine were commercial materials (Aldrich) and were used without further purification. M.p.s up to 200 °C were determined in capillary tubes with a Büchi (Tottoli) apparatus, and above 200 °C with a Reichert



Scheme 1



Scheme 2

(Kofler) apparatus. M.p.s were uncorrected. The products often decompose at melting point. All IR spectra were obtained for Nujol mulls and were recorded on a Perkin-Elmer 298 spectrophotometer. All ^1H NMR spectra were recorded on a Varian EM-360 L (60 MHz) spectrometer, for $(CD_3)_2SO$ solutions with $SiMe_4$ as internal standard, *J* values are given in Hz. The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; D_2O-exch., D_2O exchange. Merck precoated silica gel 60 F_{254} plates (0.25 mm) were used for analytical TLC, silica gel PF_{254} plates (2.0 mm) for preparative TLC, and silica gel Kieselgel 60 (0.063–0.200 mm) was used for column chromatography. All compounds prepared gave satisfactory elemental analyses (C $\pm$ 0.4, H $\pm$ 0.4, N $\pm$ 0.3%). Light petroleum refers to the fraction with b.p. 60–80 °C.

Reaction of Azoalkenes **1** *with Activated Nitriles* **2** *in Different Molecular Ratios: General Procedures.*—(*a*) *In the molecular ratio* 2:1. A solution of nitrile **2** (1 mmol) in tetrahydrofuran (THF) (2 cm^3) was stirred with sodium methoxide (0.1 mmol) for 15 min and added dropwise to a solution of azoalkene **1** (2 mmol) in THF (4 cm^3) at 0 °C. The reaction mixture was stirred magnetically at 0 °C for the appropriate reaction time and was checked by TLC (ethyl acetate–cyclohexane or ethyl acetate–methanol mixtures). In the case of the reactions with benzoylacetonitrile, the pyrrolo[2,3-*b*]pyrroles **5** crystallized directly from the reaction mixture. In the other cases the products were separated, after evaporation of the solvent under reduced pressure, by chromatography on silica gel column (ethyl acetate–cyclohexane mixtures) and were shown to be products **3** and **5**. All the products **3** were crystallized from dichloromethane–light petroleum, while all the products **5** were crystallized from THF.

(*b*) *In the molecular ratio* 1:1. To a stirred solution of the azoalkene **1** (1 mmol) in THF (2 cm^3) was added dropwise a solution of nitrile **2** (1 mmol) and sodium methoxide (0.1 mmol) in THF (2 cm^3) at 0 °C. The mixture was magnetically stirred at 0 °C until the reaction was complete (TLC: only one spot as major component). In the case of 4,4-dimethyl-3-oxopentanenitrile, the products were purified on a silica gel column (ethyl acetate–cyclohexane mixtures) and identified as the 1,4-adducts **3**. This adduct **3** (1 mmol) in a mixture of THF–methanol 1:1 was stirred magnetically at room temp. and CCD ($CuCl_2 \cdot 2H_2O$) (0.1 mmol) added. The product formed rapidly (monitored by TLC). The reaction mixture was concentrated to a small volume under reduced pressure, mixed with aqueous sulfuric acid (1%) and extracted with ethyl acetate. The organic phase was separated, washed with water, dried ($MgSO_4$), and concentrated under reduced pressure to afford 1-amino-3-cyanopyrrole **4** in satisfactory purity. In the case of

Table 1 Experimental data for the synthesis of 1,4-adducts **3a–f**, 1-amino-3-cyanopyrroles **4a–l** and pyrrolo[2,3-*b*]pyrroles **5a–h** from conjugated azoalkenes **1a–f** and β-cyano ketones **2a–b**

Starting materials 1	2	R^1	R^2	R^3	Molecular ratio 1:2	Reaction time *t*/h	Products 3	4	5	Yield (%)[a] 3	4	5
a	**a**	CO_2Me	CO_2Me	Bu^t	1:1	0.4	**a**	**a**	**a**	90	74	5
a	**a**	CO_2Me	CO_2Me	Bu^t	2:1	2	**a**		**a**	7		68
b	**a**	CO_2Et	CO_2Bu^t	Bu^t	1:1	2.5	**b**	**b**	**b**	87	73	6
b	**a**	CO_2Et	CO_2Bu^t	Bu^t	2:1	4	**b**		**b**	14		65
c	**a**	CO_2Me	$CONH_2$	Bu^t	1:1	3	**c**	**c**	**c**	58	89	35
c	**a**	CO_2Me	$CONH_2$	Bu^t	2:1	96	**c**		**c**	35		48
d	**a**	CO_2Et	$CONH_2$	Bu^t	1:1	2	**d**	**d**	**d**	91	81	9
d	**a**	CO_2Et	$CONH_2$	Bu^t	2:1	48	**d**		**d**	6		80
e	**a**	CO_2Me	CONHPh	Bu^t	1:1	2	**e**	**e**		81	77	
f	**a**	CO_2Et	CONHPh	Bu^t	1:1	0.4	**f**	**f**		81	77	
a	**b**	CO_2Me	CO_2Me	Ph	1:1	0.3		**g**			65	
b	**b**	CO_2Et	CO_2Bu^t	Ph	1:1	2		**h**			80	
c	**b**	CO_2Me	$CONH_2$	Ph	1:1	24		**i**	**e**		93	5
c	**b**	CO_2Me	$CONH_2$	Ph	2:1	4		**i**	**e**		5	85
d	**b**	CO_2Et	$CONH_2$	Ph	1:1	24		**j**	**f**		70	18
d	**b**	CO_2Et	$CONH_2$	Ph	2:1	3		**j**	**f**		5	89
e	**b**	CO_2Me	CONHPh	Ph	1:1	0.3		**k**	**g**		82	11
e	**b**	CO_2Me	CONHPh	Ph	2:1	48		**k**	**g**		25	65
f	**b**	CO_2Et	CONHPh	Ph	1:1	0.4		**l**	**h**		66	5
f	**b**	CO_2Et	CONHPh	Ph	2:1	2		**l**	**h**		5	90

[a] Yields calculated with respect to the starting conjugated azoalkenes, except for 1-amino-3-cyanopyrroles **4a–f**, which were calculated with respect to the isolated 1,4-adducts **3a–f**.

Table 2 Experimental data for the synthesis of 1,2-diaminopyrroles **4m–r** and pyrrolo[2,3-*b*]pyrroles **5i–j** from conjugated azoalkenes **1a–f** and 1-cyanoacetylpiperidine **2c**

Starting materials 1	2	R^1	R^2	Molecular ratio 1:2	Reaction time, *t*/h	Products 3	4	5	Yield (%)[a] 3	4	5
a	**c**	CO_2Me	CO_2Me	1:1	0.1	**g**	**m**		79	66	
b	**c**	CO_2Et	CO_2Bu^t	1:1	0.1	**h**	**n**		80	82	
c	**c**	CO_2Me	$CONH_2$	1:1	0.1	**i**	**o**	**i**	89	77	10
c	**c**	CO_2Me	$CONH_2$	2:1	3	**i**		**i**	7		67
d	**c**	CO_2Et	$CONH_2$	1:1	0.1	**j**	**p**	**j**	95	75	5
d	**c**	CO_2Et	$CONH_2$	2:1	48	**j**		**j**	32		54
e	**c**	CO_2Me	CONHPh	1:1	0.1	**k**	**q**		90	78	
f	**c**	CO_2Et	CONHPh	1:1	0.1	**l**	**r**		78	82	

[a] Yields calculated with respect to the starting conjugated azoalkenes, except for the 1,2-diaminopyrroles **4m–r**, which were calculated with respect to the isolated 1,4-adducts **3g–l**.

benzoylacetonitrile, when the starting materials disappeared (monitored by TLC), CCD (0.1 mmol) was added to the reaction mixture to afford instantaneously the 1-amino-3-cyanopyrrole as a solid which crystallized directly from THF. In the case of 1-cyanoacetylpiperidine the products were purified on a silica gel column (ethyl acetate–cyclohexane mixtures) and identified as the 1,4-adducts. The adduct (1 mmol) was dissolved in a mixture of THF–MeOH (1:1) under magnetic stirring, and a catalytic amount of NaH added to afford rapidly the conversion product. The reaction mixture was concentrated to a small volume under reduced pressure, mixed with aqueous sulfuric acid (1%) and extracted with ethyl acetate. The organic phase was separated, washed with water, dried ($MgSO_4$), and concentrated under reduced pressure to give the 1,2-diaminopyrrole **4**. Use of a 2:1 ratio **1**:**2** increased considerably the yields of the pyrrolo[2,3-*b*]pyrroles. All the products **3** were crystallized as above, while the products **4** were crystallized as follows. The following compounds were thus prepared.*

* Tests on the anticancer and anti-AIDS activities of some of these compounds are performed under the auspices of the Developmental Therapeutics Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, Maryland, USA.

4-*Cyano*-3-*methoxycarbonyl*-6,6-*dimethylheptane*-2,5-*dione* 2-*methoxycarbonylhydrazone* **3a**. M.p. 102–105 °C; ν_{max}/cm^{-1} 3240, 3170, 3120, 2240, 1750, 1735, 1710 and 1635; δ_H 1.0 (9 H, s, Bu^t), 2.0 (3 H, s, Me), 3.6 (6 H, s, CO_2Me), 4.0–4.2 (1 H, m, CH), 6.5 (1 H, m, CH) and 8.7 (1 H, s, NH, D_2O-exch.) (Found: C, 54.3; H, 6.9; N, 13.2. $C_{14}H_{21}N_3O_5$ requires C, 54.0; H, 6.8; N, 13.5%).

4-*Cyano*-3-*ethoxycarbonyl*-6,6-*dimethylheptane*-2,5-*dione* 2-tert-*butoxycarbonylhydrazone* **3b**. M.p. 111–113 °C; ν_{max}/cm^{-1} 3238, 3165, 3115, 2238, 1753, 1737, 1710 and 1630; δ_H 1.0 (9 H, s, Bu^t), 1.2 (3 H, t, *J* 7, CO_2CH_2*Me*), 1.4 (9 H, s, Bu^t), 2.0 (3 H, s, Me), 3.8–4.3 (3 H, m, CO_2C*H_2*Me and CH), 6.4 (1 H, m, CH) and 8.2 (1 H, s, NH, D_2O-exch.) (Found: C, 58.7; H, 7.8; N, 11.3. $C_{18}H_{29}N_3O_5$ requires C, 58.8; H, 8.0; N, 11.4%).

4-*Cyano*-3-*methoxycarbonyl*-6,6-*dimethylheptane*-2,5-*dione* 2-*semicarbazone* **3c**. M.p. 139–143 °C; ν_{max}/cm^{-1} 3410, 3320, 3190, 2260, 1680, 1665, 1640, 1615 and 1520; δ_H 1.0 (9 H, s, Bu^t), 2.0 (3 H, s, Me), 3.6 (3 H, s, CO_2Me), 4.1 (1 H, m, CH), 6.3–6.5 (3 H, m, CH and NH_2, D_2O-exch.) and 8.8 (1 H, s, NH, D_2O-exch.) (Found: C, 52.9; H, 7.2; N, 19.8. $C_{13}H_{20}N_4O_4$ requires C, 52.7; H, 6.8; N, 18.9%).

4-Cyano-3-ethoxycarbonyl-6,6-dimethylheptane-2,5-dione 2-semicarbazone **3d**. M.p. 125–128 °C; ν_{max}/cm^{-1} 3420, 3300, 3200, 2260, 1680, 1660, 1630, 1610 and 1530; δ_H 1.0 (9 H, s, Bu^t), 1.2 (3 H, t, *J* 7, CO_2CH_2Me), 2.0 (3 H, s, Me), 3.7–4.2 (3 H, m, CH and CO_2CH_2Me), 6.1–6.3 (3 H, m, CH and NH_2, D_2O-exch.) and 8.6 (1 H, s, NH, D_2O-exch.) (Found: C, 54.1; H, 7.3; N, 18.3. $C_{14}H_{22}N_4O_4$ requires C, 54.2; H, 7.2; N, 18.1%).

4-Cyano-3-methoxycarbonyl-6,6-dimethylheptane-2,5-dione 2-phenylsemicarbazone **3e**. M.p. 143–145 °C; ν_{max}/cm^{-1} 3370, 3210, 3100, 2220, 1730, 1710, 1595 and 1535; δ_H 1.5 (9 H, s, Bu^t), 2.2 (3 H, s, Me), 3.9 (3 H, s, CO_2Me), 4.1–4.5 (1 H, m, CH), 5.3–5.6 (1 H, m, CH), 7.0–7.8 (5 H, m, Ph), 8.8 (1 H, s, NH, D_2O-exch.) and 9.8 (1 H, s, NH, D_2O-exch.) (Found: C, 61.0; H, 6.4; N, 15.2. $C_{19}H_{24}N_4O_4$ requires C, 61.3; H, 6.5; N, 15.0%).

4-Cyano-3-ethoxycarbonyl-6,6-dimethylheptane-2,5-dione 2-phenylsemicarbazone **3f**. M.p. 152–155 °C; ν_{max}/cm^{-1} 3370, 3200, 3100, 2220, 1720, 1680, 1595 and 1535; δ_H 1.0–1.3 (12 H, m, CO_2CH_2Me and Bu^t), 2.0 (3 H, s, Me), 3.9–4.3 (3 H, m, CO_2CH_2Me and CH), 5.1–5.3 (1 H, m, CH), 6.8–7.7 (5 H, m, Ph), 8.7 (1 H, s, NH, D_2O-exch.) and 9.8 (1 H, s, NH, D_2O-exch.) (Found: C, 62.6; H, 6.6; N, 14.7. $C_{20}H_{26}N_4O_4$ requires C, 62.2; H, 6.8; N, 14.5%).

*Methyl 5-*tert*-butyl-4-cyano-1-methoxycarbonylamino-2-methylpyrrole-3-carboxylate* **4a**. M.p. 192–195 °C; ν_{max}/cm^{-1} 3260, 2220, 1755, 1710, 1685 and 1590; δ_H 1.4 (9 H, s, Bu^t), 2.1 (3 H, s, Me), 3.7 (6 H, s, CO_2Me) and 11.0 (1 H, s, NH, D_2O-exch.) (Found: C, 57.6; H, 6.3; N, 14.6. $C_{14}H_{19}N_3O_4$ requires C, 57.3; H, 6.5; N, 14.3%).

*Ethyl 1-(*tert*-butoxycarbonylamino)-5-*tert*-butyl-4-cyano-2-methylpyrrole-3-carboxylate* **4b**. M.p. 203–205 °C; ν_{max}/cm^{-1} 3270, 2220, 1750, 1710, 1685 and 1590; δ_H 1.2–1.5 (21 H, m, CO_2CH_2Me and Bu^t), 2.2 (3 H, s, Me), 4.2 (2 H, q, *J* 7, CO_2CH_2Me) and 10.6 (1 H, s, NH, D_2O-exch.) (Found: C, 62.1; H, 7.7; N, 11.8. $C_{18}H_{27}N_3O_4$ requires C, 61.9; H, 7.8; N, 12.0%).

*Methyl 5-*tert*-butyl-4-cyano-2-methyl-1-ureidopyrrole-3-carboxylate* **4c**. M.p. 230–234 °C (from methanol); ν_{max}/cm^{-1} 3380, 3240, 3170, 2225, 1690 overlap and 1580; δ_H 1.4 (9 H, s, Bu^t), 2.2 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 6.4 (2 H, s, NH_2, D_2O-exch.) and 9.4 (1 H, s, NH, D_2O-exch.) (Found: C, 55.9; H, 6.4; N, 20.2. $C_{13}H_{18}N_4O_3$ requires C, 56.1; H, 6.5; N, 20.1%).

*Ethyl 5-*tert*-butyl-4-cyano-2-methyl-1-ureidopyrrole-3-carboxylate* **4d**. M.p. 228–233 °C (from methanol); ν_{max}/cm^{-1} 3430, 3250, 3190, 2225, 1690 overlap and 1580; δ_H 1.2 (3 H, t, *J* 7, CO_2CH_2Me), 1.4 (9 H, s, Bu^t), 2.1 (3 H, s, Me), 4.1 (2 H, q, *J* 7, CO_2CH_2Me), 6.2 (2 H, s, NH_2, D_2O-exch.) and 9.1 (1 H, s, NH, D_2O-exch.) (Found: C, 57.7; H, 6.8; N, 18.9. $C_{14}H_{20}N_4O_3$ requires C, 57.5; H, 6.9; N, 19.2%).

*Methyl 5-*tert*-butyl-4-cyano-2-methyl-(N′-phenylureido)pyrrole-3-carboxylate* **4e**. M.p. 179–181 °C (from methanol); ν_{max}/cm^{-1} 3310, 3150, 3090, 2220, 1730, 1690, 1610 and 1550; δ_H 1.4 (9 H, s, Bu^t), 2.2 (3 H, s, Me), 3.6 (3 H, s, CO_2Me), 6.7–7.3 (5 H, m, Ph), 9.2 (1 H, s, NH, D_2O-exch.) and 9.4 (1 H, s, NH, D_2O-exch.) (Found: C, 64.8; H, 6.0; N, 15.7. $C_{19}H_{22}N_4O_3$ requires C, 64.4; H, 6.3; N, 15.8%).

*Ethyl 5-*tert*-butyl-4-cyano-2-methyl-1-(N′-phenylureido)pyrrole-3-carboxylate* **4f**. M.p. 228–232 °C (from methanol); ν_{max}/cm^{-1} 3310, 3150, 3100, 2220, 1730, 1680, 1610 and 1550; δ_H 1.3 (3 H, t, *J* 7, CO_2CH_2Me), 1.5 (9 H, s, Bu^t), 2.3 (3 H, s, Me), 4.2 (2 H, q, *J* 7, CO_2CH_2Me), 6.9–7.6 (5 H, m, Ph), 9.4 (1 H, s, NH, D_2O-exch.) and 9.6 (1 H, s, NH, D_2O-exch.) (Found: C, 65.0; H, 6.2; N, 14.9. $C_{20}H_{24}N_4O_3$ requires C, 65.2; H, 6.6; N, 15.2%).

Methyl 4-cyano-1-methoxycarbonylamino-2-methyl-5-phenylpyrrole-3-carboxylate **4g**. M.p. 175–177 °C (from tetrahydrofuran); ν_{max}/cm^{-1} 3315, 2225, 1755, 1700, 1575 and 1545; δ_H 2.4 (3 H, s, Me), 3.6 (3 H, s, CO_2Me), 3.8 (3 H, s, CO_2Me), 7.5 (5 H, s, Ph) and 11.1 (1 H, s, NH, D_2O-exch.) (Found: C, 61.2; H, 4.7; N, 13.6. $C_{16}H_{15}N_3O_4$ requires C, 61.3; H, 4.8; N, 13.4%).

*Ethyl 1-(*tert*-butoxycarbonylamino)-4-cyano-2-methyl-5-phenylpyrrole-3-carboxylate* **4h**. M.p. 193–196 °C (from tetrahydrofuran); ν_{max}/cm^{-1} 3280, 2225, 1750, 1710, 1680, 1570 and 1550; δ_H 1.1–1.4 (12 H, m, CO_2CH_2Me and Bu^t), 2.4 (3 H, s, Me), 4.3 (2 H, q, *J* 7, CO_2CH_2Me), 7.5 (5 H, s, Ph) and 10.7 (1 H, s, NH, D_2O-exch.) (Found: C, 65.2; H, 6.6; N, 11.6. $C_{20}H_{23}N_3O_4$ requires C, 65.0; H, 6.3; N, 11.4%).

Methyl 4-cyano-2-methyl-5-phenyl-1-ureidopyrrole-3-carboxylate **4i**. M.p. 242–245 °C (from tetrahydrofuran); ν_{max}/cm^{-1} 3425, 3320, 3245, 3195, 2225, 1725, 1675, 1575 and 1535; δ_H 2.3 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 6.2 (2 H, s, NH_2, D_2O-exch.), 7.3 (5 H, s, Ph) and 9.2 (1 H, s, NH, D_2O-exch.) (Found: C, 60.5; H, 4.2; N, 19.0. $C_{15}H_{14}N_4O_3$ requires C, 60.4; H, 4.7; N, 18.8%).

Ethyl 4-cyano-2-methyl-5-phenyl-1-ureidopyrrole-3-carboxylate **4j**. M.p. 270–273 °C (from tetrahydrofuran); ν_{max}/cm^{-1} 3425, 3320, 3250, 3200, 2225, 1720, 1680, 1575 and 1540; δ_H 1.2 (3 H, t, *J* 7, CO_2CH_2Me), 2.3 (3 H, s, Me), 4.1 (2 H, q, *J* 7, CO_2CH_2Me), 6.2 (2 H, s, NH_2, D_2O-exch.), 7.3 (5 H, s, Ph) and 9.2 (1 H, s, NH, D_2O-exch.) (Found: C, 61.7; H, 5.0; N, 17.7. $C_{16}H_{16}N_4O_3$ requires C, 61.5; H, 5.2; N, 17.9%).

Methyl 4-cyano-2-methyl-5-phenyl-1-(N′-phenylureido)pyrrole-3-carboxylate **4k**. M.p. 230–234 °C (from tetrahydrofuran); ν_{max}/cm^{-1} 3340, 3295, 2225, 1715, 1695, 1600 and 1540; δ_H 2.3 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 6.6–7.2 (5 H, m, Ph), 7.3 (5 H, s, Ph), 9.1 (1 H, s, NH, D_2O-exch.) and 9.4 (1 H, s, NH, D_2O-exch.) (Found: C, 67.8; H, 4.7; N, 15.3. $C_{21}H_{18}N_4O_3$ requires C, 67.4; H, 4.9; N, 15.0%).

*Ethyl 4-cyano-2-methyl-5-phenyl-1-(N′-phenylureido)pyrrole-*3-carboxylate **4l**. M.p. 221–225 °C (from tetrahydrofuran); ν_{max}/cm^{-1} 3340, 3320, 2225, 1720, 1690, 1610 and 1550; δ_H 1.3 (3 H, t, *J* 7, CO_2CH_2Me), 2.4 (3 H, s, Me), 4.2 (2 H, q, *J* 7, CO_2CH_2Me), 6.7–7.6 (10 H, m, Ph), 9.3 (1 H, s, NH, D_2O-exch.) and 9.7 (1 H, s, NH, D_2O-exch.) (Found: C, 67.8; H, 5.1; N, 14.7. $C_{22}H_{20}N_4O_3$ requires C, 68.0; H, 5.2; N, 14.4%).

Dimethyl 6a-amino-1,6-bis-(methoxycarbonylamino)-2,5-dimethyl-3a-trimethylacetyl-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate **5a**. M.p. 138–140 °C; ν_{max}/cm^{-1} 3240, 3160, 3120, 1760, 1710 and 1640; δ_H 1.5 (9 H, s, Bu^t), 2.1 (6 H, s, Me), 3.7–3.9 (12 H, m, CO_2Me), 4.0 and 4.4 (2 H, 2 s, NH_2, D_2O-exch.) and 10.1 (2 H, s, NH, D_2O-exch.) (Found: C, 50.8; H, 6.1; N, 14.3. $C_{21}H_{31}N_5O_9$ requires C, 50.7; H, 6.3; N, 14.1%).

*Diethyl 6a-amino-1,6-bis-(*tert*-butoxycarbonylamino)-2,5-dimethyl-3a-trimethylacetyl-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate* **5b**. M.p. 103–105 °C; ν_{max}/cm^{-1} 3240, 3160, 3120, 1755, 1690 and 1620; δ_H 1.0–1.5 (33 H, m, CO_2CH_2Me and Bu^t), 1.8 (6 H, s, Me), 3.5–4.2 (6 H, m, CO_2CH_2Me and NH_2, D_2O-exch.) and 9.7 (2 H, s, NH, D_2O-exch.) (Found: C, 56.8; H, 7.9; N, 11.6. $C_{29}H_{47}N_5O_9$ requires C, 57.1; H, 7.8; N, 11.5%).

Dimethyl 6a-amino-2,5-dimethyl-3a-trimethylacetyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3,b]pyrrole-3,4-dicarboxylate **5c**. M.p. 165–169 °C; ν_{max}/cm^{-1} 3480, 3450, 3200, 1755, 1745, 1700, 1670 and 1580; δ_H 1.2 (9 H, s, Bu^t), 1.8 (6 H, s, Me), 3.5 (3 H, s, CO_2Me), 3.6 (3 H, s, CO_2Me), 3.9 and 4.2 (2 H, 2 s, NH_2, D_2O-exch.), 6.3 (2 H, s, NH_2, D_2O-exch.), 6.4 (2 H, s, NH_2, D_2O-exch.), 9.3 (1 H, s, NH, D_2O-exch.) and 9.6 (1 H, s, NH, D_2O-exch.) (Found: C, 48.5; H, 6.7; N, 21.1. $C_{19}H_{29}N_7O_7$ requires C, 48.8; H, 6.3; N, 21.0%).

Diethyl 6a-amino-2,5-dimethyl-3a-trimethylacetyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate **5d**. M.p. 182–184 °C; ν_{max}/cm^{-1} 3520, 3460, 3200, 1745, 1695, 1640 and 1580; δ_H 0.9–1.3 (15 H, m, CO_2CH_2Me and Bu^t), 1.8 (6 H, s, Me), 3.8–4.2 (6 H, m, CO_2CH_2Me and NH_2, D_2O-exch.), 6.1 (2 H, s, NH_2, D_2O-exch.), 6.2 (2 H, s, NH_2, D_2O-

exch.), 9.1 (1 H, s, NH, D_2O-exch.) and 9.3 (1 H, s, NH, D_2O-exch.) (Found: C, 50.7; H, 7.0; N, 19.7. $C_{21}H_{33}N_7O_7$ requires C, 50.9; H, 6.7; N, 19.8%).

Dimethyl 6a-*amino*-3a-*benzoyl*-2,5-*dimethyl*-1,6-*diureido*-1,-3a,6,6a-*tetrahydropyrrolo*[2,3-b]*pyrrole*-3,4-*dicarboxylate* **5e**. M.p. 180–182 °C; ν_{max}/cm^{-1} 3475, 3380, 3300, 3190, 1750, 1690 and 1580; δ_H 1.6 (3 H, s, Me), 1.8 (3 H, s, Me), 3.4 (3 H, s, CO_2Me), 3.5 (3 H, s, CO_2Me), 3.9 and 4.3 (2 H, 2 s, NH_2, D_2O-exch.), 5.7 (2 H, s, NH_2, D_2O-exch.), 6.2 (2 H, s, NH_2, D_2O-exch.), 7.0–7.9 (5 H, m, Ph), 9.0 (1 H, s, NH, D_2O-exch.) and 9.1 (1 H, s, NH, D_2O-exch.) (Found: C, 51.9; H, 4.8; N, 19.9. $C_{21}H_{25}N_7O_7$ requires C, 51.7; H, 5.2; N, 20.1%).

Diethyl 6a-*amino*-3a-*benzoyl*-2,5-*dimethyl*-1,6-*diureido*-1,3a,-6,6a-*tetrahydropyrrolo*[2,3-b]*pyrrole*-3,4-*dicarboxylate* **5f**. M.p. 180–183 °C; ν_{max}/cm^{-1} 3475, 3400, 3310, 3190, 1740, 1690 and 1580; δ_H 0.8–1.3 (6 H, m, CO_2CH_2Me), 1.6 (3 H, s, Me), 1.8 (3 H, s, Me), 3.4–4.3 (6 H, m, CO_2CH_2Me and NH_2, D_2O-exch.), 5.7 (2 H, s, NH_2, D_2O-exch.), 6.2 (2 H, s, NH_2, D_2O-exch.), 7.0–7.9 (5 H, m, Ph), 9.0 (1 H, s, NH, D_2O-exch.) and 9.1 (1 H, s, NH, D_2O-exch.) (Found: C, 52.1; H, 5.5; N, 19.9. $C_{21}H_{25}N_7O_7$ requires C, 51.7; H, 5.2; N, 20.1%).

Dimethyl 6a-*amino*-3a-*benzoyl*-2,5-*dimethyl*-1,6-*bis*-(N′-*phenylureido*)-1,3a,6,6a-*tetrahydropyrrolo*[2,3-b]*pyrrole*-3,4-*dicarboxylate* **5g**. M.p. 178–181 °C; ν_{max}/cm^{-1} 3340, 3200, 3100, 1745, 1690 and 1595; δ_H 1.8 (3 H, s, Me), 1.9 (3 H, s, Me), 3.3 (3 H, s, CO_2Me), 3.6 (3 H, s, CO_2Me), 4.2 and 4.6 (2 H, 2 s, NH_2, D_2O-exch.), 6.6–7.9 (15 H, m, Ph), 8.5 (1 H, s, NH, D_2O-exch.), 8.7 (1 H, s, NH, D_2O-exch.), 9.5 (1 H, s, NH, D_2O-exch.) and 9.7 (1 H, s, NH, D_2O-exch.) (Found: C, 61.7; H, 5.1; N, 15.1. $C_{33}H_{33}N_7O_7$ requires C, 62.0; H, 5.2; N, 15.3%).

Diethyl 6a-*amino*-3a-*benzoyl*-2,5-*dimethyl*-1,6-*bis*-(N′-*phenylureido*)-1,3a,6,6a-*tetrahydropyrrolo*[2,3-b]*pyrrole*-3,4-*dicarboxylate* **5h**. M.p. 196–198 °C; ν_{max}/cm^{-1} 3345, 3315, 3205, 3100, 1750, 1740, 1680 and 1595; δ_H 0.8–1.3 (6 H, m, CO_2CH_2Me), 1.8 (3 H, s, Me), 2.0 (3 H, s, Me), 3.7–4.2 (4 H, m, CO_2CH_2Me), 4.3 and 4.7 (2 H, 2 s, NH_2, D_2O-exch.), 6.8–8.0 (15 H, m, Ph), 8.8 (1 H, s, NH, D_2O-exch.), 9.0 (1 H, s, NH, D_2O-exch.), 9.7 (1 H, s, NH, D_2O-exch.) and 9.9 (1 H, s, NH, D_2O-exch.) (Found: C, 63.0; H, 5.8; N, 14.6. $C_{35}H_{37}N_7O_7$ requires C, 63.0; H, 5.6; N, 14.7%).

4-*Cyano*-2-*methoxycarbonyl*-3-*piperidin*-1-*ylcarbonylbutan*-2-*one methoxycarbonylhydrazone* **3g**. M.p. 141–144 °C; ν_{max}/cm^{-1} 3230, 3180, 2220, 1747, 1730 and 1650; δ_H 1.2–1.7 (6 H, m, Pip), 1.8 (3 H, s, Me), 3.2–3.7 (7 H, m, Pip and CO_2Me), 3.8 (1 H, d, *J* 10, CH), 4.5 (1 H, d, *J* 10, CH) and 9.8 (1 H, s, NH, D_2O-exch.) (Found: C, 53.6; H, 6.8; N, 16.4. $C_{15}H_{22}N_4O_5$ requires C, 53.3; H, 6.6; N, 16.6%).

4-*Cyano*-2-*ethoxycarbonyl*-3-*piperidin*-1-*ylcarbonylbutan*-2-*one* tert-*butoxycarbonylhydrazone* **3h**. M.p 158–159 °C; ν_{max}/cm^{-1} 3245, 3175, 2245, 1740, 1720 and 1650; δ_H 1.2 (3 H, t, *J* 7, CO_2CH_2Me), 1.3–1.7 (15 H, m, Bu^t and Pip), 1.8 (3 H, s, Me), 3.2–3.5 (4 H, m, Pip), 3.7 (1 H, d, *J* 10, CH), 4.0 (2 H, q, *J* 7, CO_2CH_2Me), 4.5 (1 H, d, *J* 10, CH) and 9.4 (1 H, s, NH, D_2O-exch.) (Found: C, 57.7; H, 7.4; N, 13.9. $C_{19}H_{30}N_4O_5$ requires C, 57.9; H, 7.7; N, 14.2%).

4-*Cyano*-2-*methoxycarbonyl*-3-*piperidin*-1-*ylcarbonylbutan*-2-*one semicarbazone* **3i**. M.p. 175–176 °C; ν_{max}/cm^{-1} 3500, 3380, 3190, 2245, 1735, 1725, 1685, 1655 and 1580; δ_H 1.3–1.6 (6 H, m, Pip), 1.8 (3 H, s, Me), 3.2–3.6 (7 H, m, Pip and CO_2Me), 3.8 (1 H, d, *J* 10, CH), 4.8 (1 H, d, *J* 10, CH), 6.2 (2 H, s, NH_2, D_2O-exch.) and 9.0 (1 H, s, NH, D_2O-exch.) (Found: C, 52.3; H, 6.4; N, 21.6. $C_{14}H_{21}N_5O_4$ requires C, 52.0; H, 6.6; N, 21.7%).

4-*Cyano*-2-*ethoxycarbonyl*-3-*piperidin*-1-*ylcarbonylbutan*-2-*one semicarbazone* **3j**. M.p. 170–171 °C; ν_{max}/cm^{-1} 3445, 3290, 3180, 2240, 1740, 1725, 1695, 1635 and 1590; δ_H 1.1 (3 H, t, *J* 7, CO_2CH_2Me), 1.3–1.6 (6 H, m, Pip), 1.8 (3 H, s, Me), 3.3–4.1 (7 H, m, Pip, CH and CO_2CH_2Me), 4.8 (1 H, d, *J* 10, CH), 6.2 (2 H, s, NH_2, D_2O-exch.) and 9.0 (1 H, s, NH, D_2O-exch.) (Found: C, 53.2; H, 6.8; N, 21.1. $C_{15}H_{23}N_5O_4$ requires C, 53.4; H, 6.9; N, 20.8%).

4-*Cyano*-2-*methoxycarbonyl*-3-*piperidin*-1-*ylcarbonylbutan*-2-*one* 4-*phenylsemicarbazone* **3k**. M.p. 164–167 °C; ν_{max}/cm^{-1} 3360, 3200, 2220, 1740, 1685, 1655 and 1595; δ_H 1.2–1.7 (6 H, m, Pip), 1.9 (3 H, s, Me), 3.2–3.6 (7 H, m, Pip and CO_2Me), 4.0 (1 H, d, *J* 10, CH), 4.9 (1 H, d, *J* 10, CH), 6.7–7.6 (5 H, m, Ph), 8.5 (1 H, s, NH, D_2O-exch.) and 9.5 (1 H, s, NH, D_2O-exch.) (Found: 59.8; H, 6.5; N, 17.2 $C_{20}H_{25}N_5O_4$ requires C, 60.1; H, 6.3; N, 17.5%).

4-*Cyano*-2-*ethoxycarbonyl*-3-*piperidin*-1-*ylcarbonylbutan*-2-*one phenylsemicarbazone* **3l**. M.p. 187–191 °C; ν_{max}/cm^{-1} 3345, 3200, 2230, 1735, 1685, 1655 and 1595; δ_H 1.1 (3 H, t, *J* 7, CO_2CH_2Me), 1.2–1.7 (6 H, m, Pip), 2.0 (3 H, s, Me), 3.3–4.3 (7 H, m, Pip, CO_2CH_2Me, and CH), 5.1 (1 H, d, *J* 10, CH), 6.8–7.7 (5 H, m, Ph), 8.7 (1 H, s, NH, D_2O-exch.) and 9.8 (1 H, s, NH, D_2O-exch.) (Found: C, 61.3; H, 6.3; N, 17.1. $C_{21}H_{27}N_5O_4$ requires C, 61.0; H, 6.6; N, 16.9%).

Methyl 5-*amino*-1-*methoxycarbonylamino*-2-*methyl*-4-*piperidin*-1-*ylcarbonylpyrrole*-3-*carboxylate* **4m**. M.p. 202–204 °C (from ethyl acetate); ν_{max}/cm^{-1} 3385, 3300, 3180, 1750, 1700, 1640 and 1610; δ_H 1.3–1.6 (6 H, m, Pip), 2.1 (3 H, s, Me), 3.2–3.5 (4 H, m, Pip), 3.6 (6 H, s, CO_2Me), 4.7 (2 H, s, NH_2, D_2O-exch.) and 10.5 (1 H, s, NH, D_2O-exch.) (Found: C, 53.6; H, 6.4; N, 16.9. $C_{15}H_{22}N_4O_5$ requires C, 53.3; H, 6.6; N, 16.6%).

Ethyl 5-*amino*-1-tert-*butoxycarbonylamino*-2-*methyl*-4-*piperidin*-1-*ylcarbonylpyrrole*-3-*carboxylate* **4n**. M.p. 254–257 °C (from ethyl acetate); ν_{max}/cm^{-1} 3440, 3390, 3310, 3140, 1720, 1700, 1620 and 1595; δ_H 1.1 (3 H, t, *J* 7, CO_2CH_2Me), 1.3–1.5 (15 H, m, Bu^t and Pip), 2.1 (3 H, s, Me), 3.3–3.5 (4 H, m, Pip), 4.2 (2 H, q, *J* 7, CO_2CH_2Me), 4.6 (2 H, s, NH_2, D_2O-exch.) and 9.7 (1 H, s, NH, D_2O-exch.) (Found: C, 58.3; H, 7.6; N, 14.5. $C_{19}H_{30}N_4O_5$ requires C, 57.9; H, 7.7; N, 14.2%).

Methyl 5-*amino*-2-*methyl*-4-*piperidin*-1-*ylcarbonyl*-1-*ureidopyrrole*-3-*carboxylate* **4o**. M.p. 218–220 °C (from ethyl acetate); ν_{max}/cm^{-1} 3420, 3330, 3180, 1715, 1685, 1625, 1590 and 1565; δ_H 1.3–1.6 (6 H, m, Pip), 2.2 (3 H, s, Me), 3.2–3.5 (4 H, m, Pip), 3.6 (3 H, s, CO_2Me), 4.5 (2 H, s, NH_2, D_2O-exch.), 6.2 (2 H, s, NH_2, D_2O-exch.) and 8.9 (1 H, s, NH, D_2O-exch.) (Found: C, 52.1; H, 6.9; N, 21.6. $C_{14}H_{21}N_5O_4$ requires C, 52.0; H, 6.6; N, 21.7%).

Ethyl 5-*amino*-2-*methyl*-4-*piperidin*-1-*ylcarbonyl*-1-*ureidopyrrole*-3-*carboxylate* **4p**. M.p. 185–188 °C (from ethyl acetate); ν_{max}/cm^{-1} 3425, 3320, 3210, 1700, 1620, 1595 and 1560; δ_H 1.2 (3 H, t, *J* 7, CO_2CH_2Me), 1.3–1.7 (6 H, m, Pip), 2.2 (3 H, s, Me), 3.2–3.5 (4 H, m, Pip), 4.0 (2 H, q, *J* 7, CO_2CH_2Me), 4.5 (2 H, s, NH_2, D_2O-exch.), 6.2 (2 H, s, NH_2, D_2O-exch.) and 8.9 (1 H, s, NH, D_2O-exch.) (Found: C, 53.6; H, 6.6; N, 20.7. $C_{15}H_{23}N_5O_4$ requires C, 53.4; H, 6.9; N, 20.8%).

Methyl 5-*amino*-2-*methyl*-4-*piperidin*-1-*ylcarbonyl*-1-(N′-*phenylureido*)*pyrrole*-3-*carboxylate* **4q**. M.p. 172–174 °C (from ethyl acetate); ν_{max}/cm^{-1} 3280, 3200, 3140, 3100, 1710, 1625, 1605, 1580 and 1560; δ_H 1.3–1.6 (6 H, m, Pip), 2.2 (3 H, s, Me), 3.2–3.5 (4 H, m, Pip), 3.6 (3 H, s, CO_2Me), 4.7 (2 H, s, NH_2, D_2O-exch.), 6.8–7.6 (5 H, m, Ph), 9.0 (1 H, s, NH, D_2O-exch.) and 9.2 (1 H, s, NH, D_2O-exch.) (Found: C, 60.0; H, 6.5; N, 17.4. $C_{20}H_{25}N_5O_4$ requires C, 60.1; H, 6.3; N, 17.5%).

Ethyl 5-*amino*-2-*methyl*-4-*piperidin*-1-*ylcarbonyl*-1-(N′-*phenylureido*)*pyrrole*-3-*carboxylate* **4r**. M.p. 139–142 °C (from ethyl acetate); ν_{max}/cm^{-1} 3275, 3200, 3140, 3090, 1695, 1615, 1585 and 1550; δ_H 1.2 (3 H, t, *J* 7, CO_2CH_2Me), 1.3–1.6 (6 H, m, Pip), 2.2 (3 H, s, Me), 3.2–3.5 (4 H, m, Pip), 4.0 (2 H, q, *J* 7, CO_2CH_2Me), 4.6 (2 H, s, NH_2, D_2O-exch.), 6.8–7.6 (5 H, m, Ph), 9.0 (1 H, s, NH, D_2O-exch.) and 9.1 (1 H, s, NH, D_2O-exch.) (Found: C, 61.3; H, 6.3; N, 16.7. $C_{21}H_{27}N_5O_4$ requires C, 61.0; H, 6.6; N, 16.9%).

Dimethyl 6a-*amino*-2,5-*dimethyl*-3a-*piperidin*-1-*ylcarbonyl*-1,-6-*diureido*-1,3a,6,6a-*tetrahydropyrrolo*[2,3-b]*pyrrole*-3,4-*dicar*-

boxylate **5i**. M.p. 185–189 °C; ν_{max}/cm^{-1} 3475, 3300, 1745, 1640, 1632 and 1580; δ_H 1.3–1.9 (12 H, m, Pip and Me), 3.2–3.7 (10 H, m, Pip and CO_2Me), 3.9 and 4.2 (2 H, 2 s, NH_2, D_2O-exch.), 6.0 (2 H, s, NH_2, D_2O-exch.), 6.2 (2 H, s, NH_2, D_2O-exch.), 9.0 (1 H, s, NH, D_2O-exch.) and 9.2 (1 H, s, NH, D_2O-exch.) (Found: C, 48.3; H, 6.0; N, 22.9. $C_{20}H_{30}N_8O_7$ requires C, 48.6; H, 6.1; N, 22.7%).

Diethyl 6a-*amino*-2,5-*dimethyl*-3a-*piperidin*-1-*ylcarbonyl*-1,6-*diureido*-1,3a,6,6a-*tetrahydropyrrolo*[2,3-b]*pyrrole*-3,4-*dicarboxylate* **5j**. M.p. 168–170 °C; ν_{max}/cm^{-1} 3480, 3330, 3180, 1745, 1685, 1645 and 1580; δ_H 0.9–1.2 (6 H, m, CO_2CH_2Me), 1.3–1.6 (6 H, m, Pip), 1.8 (6 H, s, Me), 3.2–4.3 (10 H, m, Pip, CO_2CH_2Me and NH_2, D_2O-exch.), 6.1 (2 H, s, NH_2, D_2O-exch.), 6.2 (2 H, s, NH_2, D_2O-exch.), 9.0 (1 H, s, NH, D_2O-exch.) and 9.2 (1 H, s, NH, D_2O-exch.) (Found: C, 50.4; H, 6.3; N, 21.3. $C_{22}H_{34}N_8O_7$ requires C, 50.6; H, 6.6; N, 21.4%).

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