

Conjugated Azoalkenes. Part 8. Reaction of some Conjugated Azoalkenes with Activated Nitriles. Synthesis of New Pyrrolo[2,3-*b*]pyrroles and 1,2-Diaminopyrroles. X-Ray Molecular Structure of Diethyl 6-Amino-1,6-bis-(*t*-butoxycarbonylamino)-3a-cyano-2,5-dimethyl-1,3a,6,6a-tetrahydropyrrolo[2,3-*b*]pyrrole-3,4-dicarboxylate

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The reactions of some conjugated azoalkenes with nitriles containing active methylene groups have been studied and, depending on the nature and the molar ratios of the reagents, new 1,2-diamino-3-cyanopyrroles, and symmetric and asymmetric 1,3a,6,6a-tetrahydropyrrolo[2,3-*b*]pyrroles can be obtained in good yields and under mild reaction conditions. The stereochemistry of one of the 1,3a,6,6a-tetrahydropyrrolo[2,3-*b*]pyrrole derivatives was investigated in detail by X-ray diffraction.

Organic cyano compounds are versatile reagents which have been extensively utilized in heterocyclic synthesis,¹⁻³ especially in heterocyclization reactions involving addition of a nucleophile to the cyano group. The reactions of some arylozoalkenes with nitriles such as malononitrile or ethyl cyanoacetate have been studied,^{4,5} and it has been shown that 1,4-conjugate addition of the nitrile to the azo-ene system gives only the corresponding hydrazine derivative.

In previous papers⁶⁻⁸ we have described the reactions between conjugated azoalkenes and compounds containing active methylene groups, which give hydroxypyrroline derivatives, *via* the preliminary 1,4-conjugate addition followed by cyclization by intramolecular nucleophilic attack of the C=N nitrogen atom on the ketonic carbonyl group. Dehydration of the hydroxypyrrolines obtained gave the corresponding 1-aminopyrrole derivatives.^{7,8}

These results prompted us to extend these studies to the reactions between alkoxy- or amino-carbonyl azoalkenes (1) and nitriles with active methylene groups (2). It was envisaged that one or both of two reaction pathways would be followed: (i) initial 1,4-addition of compound (2) to azoalkene (1), followed by ring closure of the adduct (3) to give an

iminopyrroline intermediate which would readily tautomerize to a 1,2-diaminopyrrole (4) (path A, Scheme 1); and/or (ii) two sequential 1,4-addition reactions to the conjugated azoalkene to give a bis-adduct which, in principle, could undergo ring closure to give either a spiro-condensed or linearly condensed system (5). The latter process (path B, Scheme 1) was considered to be the more likely in view of the relative susceptibility of the imine group to nucleophilic addition.

Results and Discussion

We began our investigations by examining the reactions of the azoalkenes (1a-i) with varying amounts of malononitrile (2a) (Table 1). Addition of malononitrile (2a) to an equimolar amount of the alkoxy- (1a-e) or amino-carbonyl azoalkenes (1f-i) led, in all cases, to formation of two products, which were identified as the 1,2-diamino-3-cyanopyrroles (4a-i) and the pyrrolo[2,3-*b*]pyrroles (5a-i).

When a 2:1 ratio (1a-i):(2a) was employed, 1,2-diamino-3-cyanopyrroles were not detected and the reactions gave only the pyrrolo[2,3-*b*]pyrroles (5a-i) in very good yields (70-98%). In attempts to increase the yield of the 1,2-diamino-3-cyano-

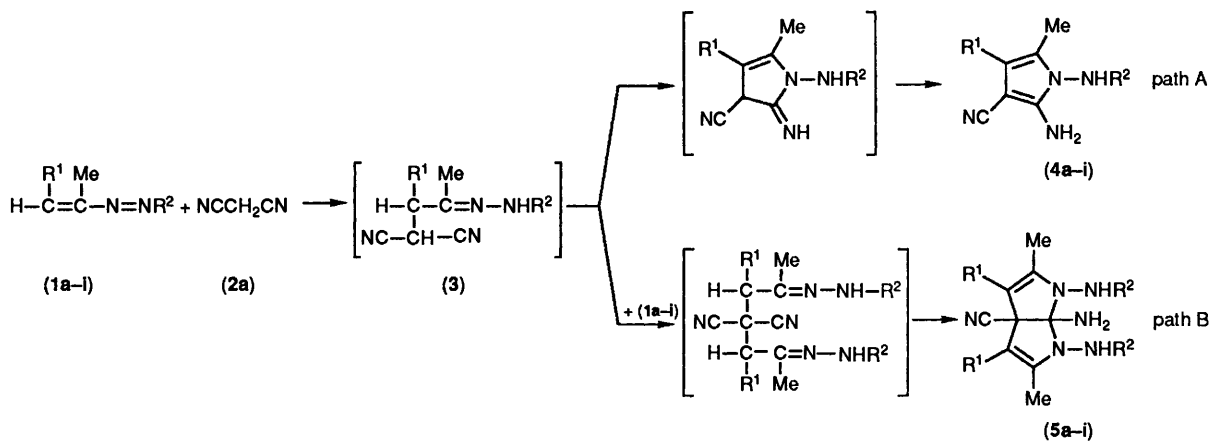
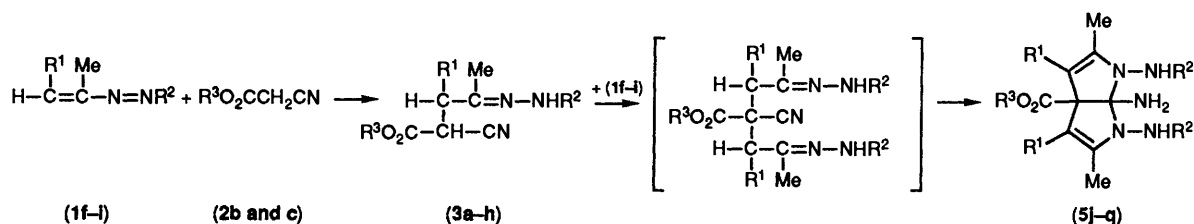
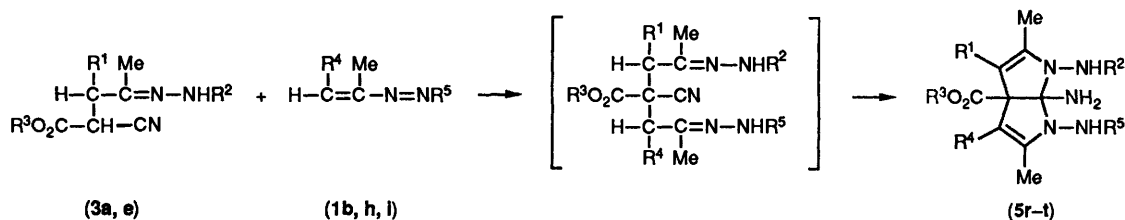


Table 1. Yields and reaction times for the synthesis of pyrroles (4a-i) and pyrrolo[2,3-b]pyrroles (5a-i) from conjugated azoalkenes (1a-i) and malononitrile (2a).

Starting materials (1)	R ¹	R ²	Molecular ratio (1):(2a)	Products		Yields (%)		Reaction time (h)
				(4)	(5)	(4)	(5)	
a	CO ₂ Me	CO ₂ Me	2:1	a	a	97	150	
a	CO ₂ Me	CO ₂ Me	1:1	a	a	12	72	150
a	CO ₂ Me	CO ₂ Me	1:5	a	a	35	50	150
b	CO ₂ Me	CO ₂ Et	2:1	b	b	80	150	
b	CO ₂ Me	CO ₂ Et	1:1	b	b	5	65	150
b	CO ₂ Me	CO ₂ Et	1:5	b	b	13	58	150
c	CO ₂ Me	CO ₂ Bu ^t	2:1	c	c	88	150	
c	CO ₂ Me	CO ₂ Bu ^t	1:1	c	c	10	78	150
c	CO ₂ Me	CO ₂ Bu ^t	1:5	c	c	27	73	150
d	CO ₂ Et	CO ₂ Me	2:1	d	d	75	150	
d	CO ₂ Et	CO ₂ Me	1:1	d	d	11	68	150
d	CO ₂ Et	CO ₂ Me	1:5	d	d	24	75	150
e	CO ₂ Et	CO ₂ Bu ^t	2:1	e	e	90	150	
e	CO ₂ Et	CO ₂ Bu ^t	1:1	e	e	12	72	150
e	CO ₂ Et	CO ₂ Bu ^t	1:5	e	e	23	47	150
f	CO ₂ Me	CONH ₂	2:1	f	f	98	0.5	
f	CO ₂ Me	CONH ₂	1:1	f	f	18	79	1
f	CO ₂ Me	CONH ₂	1:5	f	f	77	14	2
g	CO ₂ Me	CONHPh	2:1	g	g	91	0.5	
g	CO ₂ Me	CONHPh	1:1	g	g	35	65	1
g	CO ₂ Me	CONHPh	1:5	g	g	64	34	2
h	CO ₂ Et	CONH ₂	2:1	h	h	97	0.5	
h	CO ₂ Et	CONH ₂	1:1	h	h	14	71	1
h	CO ₂ Et	CONH ₂	1:5	h	h	73	13	2
i	CO ₂ Et	CONHPh	2:1	i	i	70	0.5	
i	CO ₂ Et	CONHPh	1:1	i	i	30	65	1
i	CO ₂ Et	CONHPh	1:5	i	i	86	10	2



Scheme 2.



Scheme 3.

pyrroles, a number of experiments were carried out in which the ratio (1a-i):(2a) was 1:5. In all cases, these reactions gave both compounds (4a-i) and (5a-i). The yields of the 1,2-diamino-3-cyanopyrroles were increased, but only in the case of the reactions of the aminocarbonyl azoalkenes did they exceed the yields of the pyrrolo[2,3-*b*]pyrrole derivatives.

Next, we investigated the reactions of alkoxy- (1a-e) and amino-carbonyl azoalkenes (1f-i) with alkyl cyanoacetates (2b and c), and the results are summarized in Table 2. In contrast to the results obtained using malononitrile (2a), treatment of the alkoxy-carbonyl azoalkenes (1a-e) with alkyl cyanoacetates gave complicated reaction mixtures. The reactions between equimolar amounts of the aminocarbonyl azoalkenes (1f-i) and alkyl cyanoacetates (2b and c), on the other hand, led to two products, which were identified as the 1,4-adducts (3a-h) and

the pyrrolo[2,3-*b*]pyrroles (5j-q) (Scheme 2). When the molar ratio (1f-i):(2b and c) was 2:1, only the pyrrolo[2,3-*b*]pyrrole derivatives (5j-q) were isolated, in very good yield (72-96%). When the alkyl cyanoacetates (2b and c) were added to the aminocarbonyl azoalkenes (1f-i) in the ratio of 5:1, an improvement in the yield of the 1,4-adducts (3a-h) was observed.

The 1,4-adducts (3a-h) could be readily isolated, purified, and characterized and can be utilized for the preparation of unsymmetrical pyrrolo[2,3-*b*]pyrroles (5r-t) as outlined in Scheme 3. Experimental data for the products thus prepared are summarized in Table 3.

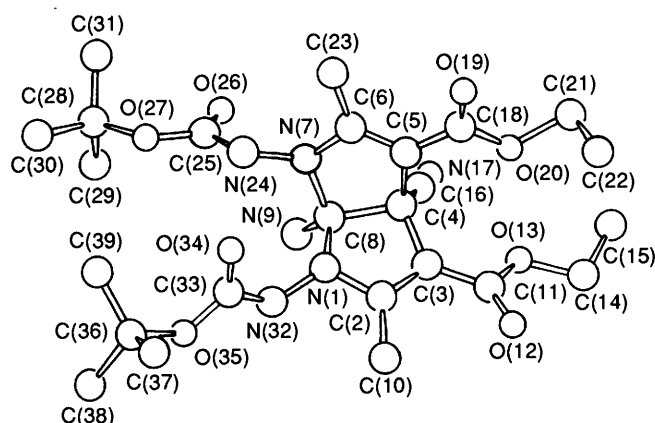
An X-ray diffraction study of diethyl 6a-amino-1,6-bis-(*t*-butoxycarbonylamino)-3a-cyano-2,5-dimethyl-1,3a,6,6a-tetrahydropyrrolo[2,3-*b*]pyrrole-3,4-dicarboxylate (5e) was carried out in order to confirm the structure unambiguously. The

Table 2. Yields and reaction times for the synthesis of semicarbazones (**3a–h**) and pyrrolo[2,3-*b*]pyrroles (**5j–q**) from conjugated azoalkenes (**1f–i**) and alkyl cyanoacetates (**2b** and **c**).

Starting Materials		R ¹	R ²	R ³	Molecular ratio (1):(2)	Products		Yield (%)		Reaction time (h)
(1)	(2)					(3)	(5)	(3)	(5)	
f	b	CO ₂ Me	CONH ₂	Me	2:1	a	j	94	0.5	
f	b	CO ₂ Me	CONH ₂	Me	1:1	a	j	39	56	1
f	b	CO ₂ Me	CONH ₂	Me	1:5	a	j	74	16	2
g	b	CO ₂ Me	CONHPh	Me	2:1	b	k		75	0.5
g	b	CO ₂ Me	CONHPh	Me	1:1	b	k	39	60	1
g	b	CO ₂ Me	CONHPh	Me	1:5	b	k	68	29	2
h	b	CO ₂ Et	CONH ₂	Me	2:1	c	l		96	0.5
h	b	CO ₂ Et	CONH ₂	Me	1:1	c	l	23	74	1
h	b	CO ₂ Et	CONH ₂	Me	1:5	c	l	84	15	2
i	b	CO ₂ Et	CONHPh	Me	2:1	d	m		90	0.5
i	b	CO ₂ Et	CONHPh	Me	1:1	d	m	45	55	1
i	b	CO ₂ Et	CONHPh	Me	1:5	d	m	78	20	2
f	c	CO ₂ Me	CONH ₂	Et	2:1	e	n		93	0.5
f	c	CO ₂ Me	CONH ₂	Et	1:1	e	n	26	73	1
f	c	CO ₂ Me	CONH ₂	Et	1:5	e	n	96	4	2
g	c	CO ₂ Me	CONHPh	Et	2:1	f	o		72	0.5
g	c	CO ₂ Me	CONHPh	Et	1:1	f	o	40	58	1
g	c	CO ₂ Me	CONHPh	Et	1:5	f	o	75	20	2
h	c	CO ₂ Et	CONH ₂	Et	2:1	g	p		94	0.5
h	c	CO ₂ Et	CONH ₂	Et	1:1	g	p	5	85	1
h	c	CO ₂ Et	CONH ₂	Et	1:5	g	p	78	19	2
i	c	CO ₂ Et	CONHPh	Et	2:1	h	q		82	0.5
i	c	CO ₂ Et	CONHPh	Et	1:1	h	q	20	69	1
i	c	CO ₂ Et	CPNHPh	Et	1:5	h	q	65	30	2

Table 3. Yields and reaction times for the synthesis of pyrrolo[2,3-*b*]pyrroles (**5r–t**) from semicarbazones (**3a** and **e**) and conjugated azoalkenes (**1b**, **i**, and **h**).

Starting materials		R ¹	R ²	R ³	R ⁴	R ⁵	Product (5)	Yield (%)	Reaction time (h)
(3)	(1)								
a	h	CO ₂ Me	CONH ₂	Me	CO ₂ Et	CONH ₂	r	95	1
a	i	CO ₂ Me	CONH ₂	Me	CO ₂ Et	CONHPh	s	98	1
e	b	CO ₂ Me	CONH ₂	Et	CO ₂ Me	CO ₂ Et	t	98	1

**Figure.** X-Ray molecular structure of compound (**5e**) with the atom numbering system used in the crystallographic analysis.

stereochemistry of this compound is shown in the Figure. Localized double bonds between C(2)–C(3) and C(5)–C(6) are identified by the atomic distances of 1.35 and 1.33 Å, respectively. The C≡N triple bond is shown by the atomic distance of 1.13 Å between C(16) and N(17). The C(4) and C(8) atoms represent two typical tetrahedral carbon atoms, and the

distance between them, 1.61 Å, indicates a pure single bond. The sum of the bond angles around the heteroatom N(1) is 346.6°, and that around N(7) is 351.8°, which shows non-perfect sp² hybridization for these two atoms. The sum of the bond angles involving the atoms of the five-membered heterocyclic rings is 533.9° for C(4),C(5),C(6),N(7),C(8), and 534.7° for C(4),C(3),C(2),N(1),C(8). Thus, the two rings are non-planar pentagons.

Experimental

Malononitrile and alkyl cyanoacetates were commercial materials and were used without further purification. Alkoxy- and amino-carbonyl azoalkenes were prepared as previously reported.⁶ M.p.s were determined with a Büchi apparatus, and are uncorrected. 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 (CD₃)₂SO solutions with SiMe₄ as internal standard. Merck precoated silica gel 60 F₂₅₄ plates were employed for analytical TLC, and silica gel Kieselgel 60 (0.063–0.200 mm) was used for column chromatography. All compounds prepared gave satisfactory elemental analyses (C ± 0.4, H ± 0.4, N ± 0.3%). Light petroleum refers to the fraction boiling in the range 40–60 °C.

Reactions of the 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 ml) 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 ml). The pale yellow reaction mixture was stirred magnetically at room temperature for the appropriate reaction time and was checked by TLC (ethyl acetate–cyclohexane or ethyl acetate–methanol mixtures). When the reaction was complete the solvent was evaporated under reduced pressure and the product (5), as a solid, was crystallized from THF–pentane or dichloromethane–light petroleum.

(b) *In the molecular ratio 1:1.* To a stirred solution of the azoalkene (1) (1 mmol) in THF (2 ml) was added a solution of nitrile (2) (1 mmol) and sodium methoxide (0.1 mmol) in THF (2 ml). The mixture was magnetically stirred at room temperature until the reaction was complete (TLC; only two spots as major components). The products were separated, after evaporation of the solvent under reduced pressure, by chromatography on a silica gel column (ethyl acetate–cyclohexane mixtures) and were shown to be the products (4) and (5), respectively, in the case of the reactions with malononitrile, or (3) and (5), respectively, in the case of the reactions with alkyl cyanoacetates.

(c) *In the molecular ratio 1:5.* A solution of azoalkene (1) (1 mmol) in THF (2 ml) was added dropwise to a solution of nitrile (2) (5 mmol) in THF (5 ml) which had previously been magnetically stirred for 15 min with sodium methoxide (0.1 mmol). The orange-red colour of the azoalkene disappeared immediately after the addition. The mixture was magnetically stirred for the appropriate reaction time and checked by TLC. After evaporation under reduced pressure, two products were separated by column chromatography. These were compounds (4) and (5), respectively, in the case of the reactions with malononitrile, or (3) and (5), respectively, in the case of the reactions with alkyl cyanoacetates. The following compounds were thus prepared.*

Methyl 5-amino-4-cyano-1-methoxycarbonylamino-2-methylpyrrole-3-carboxylate (4a). M.p. 168–170 °C (from dichloromethane–light petroleum); ν_{\max} 3 420, 3 330, 3 250, 2 210, 1 755, 1 740, and 1 670 cm^{-1} ; δ_{H} 2.2 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 6.3 (2 H, s, NH_2 , D_2O -exch.), and 10.3 (1 H, s, NH, D_2O -exch.) (Found: C, 47.2; H, 4.5; N, 22.3. $\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}_4$ requires C, 47.6; H, 4.8; N, 22.2%).

Dimethyl 6a-amino-3a-cyano-1,6-bis(methoxycarbonylamino)-2,5-dimethyl-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5a). M.p. 148–152 °C (from dichloromethane–light petroleum); ν_{\max} 3 325, 3 260, 3 185, 2 240, 1 745, and 1 720 cm^{-1} ; δ_{H} 2.1 (6 H, s, Me), 2.8 (2 H, s, NH_2 , D_2O -exch.), 3.7 (12 H, s, CO_2Me), and 9.2 (2 H, s, NH, D_2O -exch.) (Found: C, 46.3; H, 4.8; N, 19.4. $\text{C}_{17}\text{H}_{22}\text{N}_6\text{O}_8$ requires C, 46.6; H, 5.1; N, 19.2%).

Methyl 5-amino-4-cyano-1-ethoxycarbonylamino-2-methylpyrrole-3-carboxylate (4b). M.p. 198–203 °C (from dichloromethane–light petroleum) ν_{\max} 3 440, 3 330, 3 250, 2 210, 1 755, and 1 680 cm^{-1} ; δ_{H} 1.2 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.2 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 3.9–4.3 (2 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 6.3 (2 H, s, NH_2 , D_2O -exch.), and 10.3 (1 H, s, NH, D_2O -exch.) (Found: C, 49.8; H, 5.5; N, 20.8. $\text{C}_{11}\text{H}_{14}\text{N}_4\text{O}_4$ requires C, 49.6; H, 5.3; N, 21%).

Dimethyl 6a-amino-3a-cyano-1,6-bis(ethoxycarbonylamino)-2,5-dimethyl-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5b). M.p. 156–158 °C (from dichloromethane–light petroleum); ν_{\max} 3 320, 3 260, 3 180, 2 240, 1 740, and 1 705 cm^{-1} ; δ_{H} 1.4 (6 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.3 (6 H, s, Me), 3.0 (2 H, s, NH_2 , D_2O -exch.), 3.8 (6 H, s, CO_2Me), 4.1–4.5 (4 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), and 9.2 (2 H, s, NH, D_2O -exch.)

(Found: C, 48.5; H, 5.3; N, 18.2. $\text{C}_{19}\text{H}_{26}\text{N}_6\text{O}_8$ requires C, 48.9; H, 5.6; N, 18.0%).

Methyl 5-amino-1-(t-butoxycarbonylamino)-4-cyano-2-methylpyrrole-3-carboxylate (4c). M.p. 176–178 °C (from dichloromethane–light petroleum); ν_{\max} 3 390, 3 325, 3 280, 3 210, 2 210, 1 720, and 1 685 cm^{-1} ; δ_{H} 1.5 (9 H, s, Bu^t), 2.2 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 6.2 (2 H, s, NH_2 , D_2O -exch.), and 10.0 (1 H, s, NH, D_2O -exch.) (Found: C, 52.8; H, 6.0; N, 19.3. $\text{C}_{13}\text{H}_{18}\text{N}_4\text{O}_4$ requires C, 53.0; H, 6.2; N, 19.0%).

Dimethyl 6a-amino-1,6-bis-(t-butoxycarbonylamino)-3a-cyano-2,5-dimethyl-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5c). M.p. 180–185 °C (from dichloromethane–light petroleum); ν_{\max} 3 430, 3 310, 2 205, 1 735, and 1 690 cm^{-1} ; δ_{H} 1.4 (18 H, s, Bu^t), 2.0 (6 H, s, Me), 2.6 (2 H, s, NH_2 , D_2O -exch.), 3.5 (6 H, s, CO_2Me), and 8.7 (2 H, s, NH, D_2O -exch.) (Found: C, 52.9; H, 6.2; N, 15.9. $\text{C}_{23}\text{H}_{34}\text{N}_6\text{O}_8$ requires C, 52.8; H, 6.5; N, 16.05%).

Ethyl 5-amino-4-cyano-1-methoxycarbonylamino-2-methylpyrrole-3-carboxylate (4d). M.p. 169–174 °C (from dichloromethane–light petroleum); ν_{\max} 3 440, 3 310, 3 185, 2 205, 1 755, and 1 680 cm^{-1} ; δ_{H} 1.2 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.2 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 4.0–4.3 (2 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 6.3 (2 H, s, NH_2 , D_2O -exch.), and 10.5 (1 H, s, NH, D_2O -exch.) (Found: C, 49.3; H, 5.4; N, 21.2. $\text{C}_{11}\text{H}_{14}\text{N}_4\text{O}_4$ requires C, 49.6; H, 5.3; N, 21.0%).

Diethyl 6a-amino-3a-cyano-1,6-bis(methoxycarbonylamino)-2,5-dimethyl-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5d). M.p. 145–150 °C (from dichloromethane–light petroleum); ν_{\max} 3 320, 3 270, 3 180, 2 235, 1 740, and 1 715 cm^{-1} ; δ_{H} 1.2 (6 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.1 (6 H, s, Me), 2.8 (2 H, s, NH_2 , D_2O -exch.), 3.7 (6 H, s, CO_2Me), 3.9–4.3 (4 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), and 9.2 (2 H, s, NH, D_2O -exch.) (Found: C, 48.6; H, 5.8; N, 18.2. $\text{C}_{19}\text{H}_{26}\text{N}_6\text{O}_8$ requires C, 48.9; H, 5.6; N, 18.0%).

Ethyl 5-amino-1-(t-butoxycarbonylamino)-4-cyano-2-methylpyrrole-3-carboxylate (4e). M.p. 198–200 °C (from dichloromethane–light petroleum); ν_{\max} 3 380, 3 320, 3 210, 2 210, 1 725, and 1 680 cm^{-1} ; δ_{H} 1.4 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.5 (9 H, s, Bu^t), 2.2 (3 H, s, Me), 4.0–4.4 (2 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 6.2 (2 H, s, NH_2 , D_2O -exch.), and 10.0 (1 H, s, NH, D_2O -exch.) (Found: C, 54.1; H, 6.2; N, 17.9. $\text{C}_{14}\text{H}_{20}\text{N}_4\text{O}_4$ requires C, 54.3; H, 6.5; N, 18.2%).

Diethyl 6a-amino-1,6-bis-(t-butoxycarbonylamino)-3a-cyano-2,5-dimethyl-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5e). M.p. 159–165 °C (from dichloromethane–light petroleum); ν_{\max} 3 440, 3 350, 3 300, 2 240, 1 755, 1 715, and 1 695 cm^{-1} ; δ_{H} 1.2 (6 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.4 (18 H, s, Bu^t), 2.0 (6 H, s, Me), 2.6 (2 H, s, NH_2 , D_2O -exch.), 3.8–4.1 (4 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), and 8.7 (2 H, NH, D_2O -exch.) (Found: C, 53.7; H, 7.2; N, 15.4. $\text{C}_{25}\text{H}_{38}\text{N}_6\text{O}_8$ requires C, 53.5; H, 7.0; N, 15.3%).

Methyl 5-amino-4-cyano-2-methyl-1-ureidopyrrole-3-carboxylate (4f). M.p. 252–256 °C (decomp.) (from MeOH); ν_{\max} 3 430, 3 340, 3 200, 2 215, 1 740, and 1 680 cm^{-1} ; δ_{H} 2.5 (3 H, s, Me), 4.0 (3 H, s, CO_2Me), 6.3 (2 H, s, NH_2 , D_2O -exch.), 6.6 (2 H, s, NH_2 , D_2O -exch.), and 9.2 (1 H, s, NH, D_2O -exch.) (Found: C, 45.4; H, 4.8; N, 29.2. $\text{C}_9\text{H}_{11}\text{N}_5\text{O}_3$ requires C, 45.6; H, 4.8; N, 29.5%).

Dimethyl 6a-amino-3a-cyano-2,5-dimethyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5f). M.p. 204–210 °C (from THF–pentane); ν_{\max} 3 470, 3 340, 3 200, 2 210, 1 750, and 1 725 cm^{-1} ; δ_{H} 1.9 (6 H, s, Me), 3.7 (6 H, s, CO_2Me), 4.2 (2 H, s, NH_2 , D_2O -exch.), 6.2 (4 H, s, NH_2 , D_2O -exch.), and 9.5 (2 H, s, NH, D_2O -exch.) (Found: C, 43.8; H, 5.0; N, 23.2. $\text{C}_{15}\text{H}_{20}\text{N}_8\text{O}_6$ requires C, 44.1; H, 4.9; N, 23.5%).

Methyl 5-amino-4-cyano-2-methyl-1-(N'-phenylureido)pyrrole-3-carboxylate (4g). M.p. 230–233 °C (from MeOH); ν_{\max}

3 500, 3 300, 3 190, 2 210, 1 685, and 1 655 cm^{-1} ; δ_{H} 2.2 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 6.2 (2 H, s, NH_2 , D_2O -exch.), 6.9–7.6 (5 H, m, Ph), and 9.2 (2 H, s, NH, D_2O -exch.) (Found: C, 57.2; H, 4.9; N, 22.0. $\text{C}_{15}\text{H}_{15}\text{N}_5\text{O}_3$ requires C, 57.5; H, 4.8; N, 22.35%).

Dimethyl 6a-amino-3a-cyano-2,5-dimethyl-1,6-bis-(N'-phenylureido)-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5g). M.p. 181–183 °C (from THF–pentane); ν_{max} 3 390, 3 200, 3 100, 1 745, and 1 685 cm^{-1} ; δ_{H} 2.0 (3 H, s, Me), 2.3 (3 H, s, Me), 3.7 (6 H, s, CO_2Me), 4.6 (2 H, s, NH_2 , D_2O -exch.), 6.9–7.2 (10 H, m, Ph), 8.5 (2 H, s, NH, D_2O -exch.), and 10.2 (2 H, s, NH, D_2O -exch.) (Found: C, 57.7; H, 4.8; N, 19.8. $\text{C}_{27}\text{H}_{28}\text{N}_8\text{O}_6$ requires C, 57.85; H, 5.0; N, 20.0%).

Ethyl 5-amino-4-cyano-2-methyl-1-ureidopyrrole-3-carboxylate (4h). M.p. 238–240 °C (from MeOH); ν_{max} 3 460, 3 360, 3 310, 3 250, 3 200, 2 205, 1 725, and 1 680 cm^{-1} ; δ_{H} 1.2 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.2 (3 H, s, Me), 3.9–4.3 (2 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 6.0 (2 H, s, NH_2 , D_2O -exch.), 6.3 (2 H, s, NH_2 , D_2O -exch.), and 9.0 (1 H, s, NH, D_2O -exch.) (Found: C, 47.6; H, 5.0; N, 27.6. $\text{C}_{10}\text{H}_{13}\text{N}_5\text{O}_3$ requires C, 47.8; H, 5.2; N, 27.9%).

Diethyl 6a-amino-3a-cyano-2,5-dimethyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5h). M.p. 170–175 °C (from THF–pentane); ν_{max} 3 480, 3 220, 2 210, 1 740, and 1 720 cm^{-1} ; δ_{H} 1.2 (6 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.9 (6 H, s, Me), 3.9–4.3 (6 H, m, $2 \times \text{CO}_2\text{CH}_2\text{Me}$ and NH_2 , D_2O -exch.), 6.2 (4 H, s, NH_2 , D_2O -exch.), and 9.4 (2 H, s, NH, D_2O -exch.) (Found: C, 47.0; H, 5.3; N, 25.5. $\text{C}_{17}\text{H}_{24}\text{N}_8\text{O}_6$ requires C, 46.8; H, 5.5; N, 25.7%).

Ethyl 5-amino-4-cyano-2-methyl-1-(N'-phenylureido)pyrrole-3-carboxylate (4i). M.p. 216–218 °C (from MeOH); ν_{max} 3 450, 3 300, 3 260, 2 215, 1 715, and 1 650 cm^{-1} ; δ_{H} 1.3 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.3 (3 H, s, Me), 4.0–4.4 (2 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 6.2 (2 H, s, NH_2 , D_2O -exch.), 7.0–7.6 (5 H, m, Ph), 9.2 (1 H, s, NH, D_2O -exch.), and 9.3 (1 H, s, NH, D_2O -exch.) (Found: C, 58.9; H, 5.4; N, 21.2. $\text{C}_{16}\text{H}_{17}\text{N}_5\text{O}_3$ requires C, 58.7; H, 5.2; N, 21.4%).

Diethyl 6a-amino-3a-cyano-2,5-dimethyl-1,6-bis-(N'-phenylureido)-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,4-dicarboxylate (5i). M.p. 184–186 °C (from THF–pentane); ν_{max} 3 380, 3 200, 3 090, 2 210, 1 790, and 1 685 cm^{-1} ; δ_{H} 1.2 (6 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.1 (6 H, s, Me), 4.0–4.5 (4 H, q, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 4.6 (2 H, s, NH_2 , D_2O -exch.), 6.9–7.6 (10 H, m, Ph), 8.5 (2 H, s, NH, D_2O -exch.), and 10.2 (2 H, s, NH, D_2O -exch.) (Found: C, 59.0; H, 5.3; N, 18.7. $\text{C}_{29}\text{H}_{32}\text{N}_8\text{O}_6$ requires C, 59.2; H, 5.5; N, 19.0%).

Dimethyl 2-acetyl-3-cyanobutanedioate semicarbazone (3a). M.p. 128–135 °C (from dichloromethane–light petroleum); ν_{max} 3 450, 3 300, 3 210, 2 250, 1 755, 1 735, 1 705, and 1 595 cm^{-1} ; δ_{H} 1.9 (3 H, s, Me), 3.7 (6 H, s, CO_2Me), 3.9–4.1 (1 H, m, CH), 4.7–4.9 (1 H, m, CH, D_2O -exch.), 6.2 (2 H, s, NH_2 , D_2O -exch.), and 9.2 (1 H, s, NH, D_2O -exch.) (Found: C, 44.2; H, 5.3; N, 20.9. $\text{C}_{10}\text{H}_{14}\text{N}_4\text{O}_5$ requires C, 44.4; H, 5.2; N, 20.7%).

Trimethyl 6a-amino-2,5-dimethyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5j). M.p. 156–162 °C (from THF–pentane); ν_{max} 3 470, 3 290, 3 225, 1 790, 1 760, 1 685, and 1 590 cm^{-1} ; δ_{H} 1.8 (6 H, s, Me), 3.5 (3 H, s, CO_2Me), 3.6 (6 H, s, CO_2Me), 4.0 (2 H, s, NH_2 , D_2O -exch.), 6.1 (4 H, s, NH_2 , D_2O -exch.), and 9.3 (2 H, s, NH, D_2O -exch.) (Found: C, 43.2; H, 5.0; N, 21.9. $\text{C}_{16}\text{H}_{23}\text{N}_7\text{O}_8$ requires C, 43.5; H, 5.2; N, 22.2%).

Dimethyl 2-acetyl-3-cyanobutanedioate phenylsemicarbazone (3b). M.p. 164–166 °C (from dichloromethane–light petroleum); ν_{max} 3 360, 3 200, 2 250, 1 745, 1 680, and 1 595 cm^{-1} ; δ_{H} 2.0 (3 H, s, Me), 3.7 (6 H, s, CO_2Me), 4.2–4.4 (1 H, m, CH), 5.0–5.2 (1 H, m, CH, D_2O -exch.), 7.0–7.8 (5 H, m, Ph), 8.5 (1 H, s, NH, D_2O -exch.), and 10.0 (1 H, s, NH, D_2O -exch.) (Found: C, 55.7; H, 5.5; N, 16.4. $\text{C}_{16}\text{H}_{18}\text{N}_4\text{O}_5$ requires C, 55.5; H, 5.2; N, 16.2%).

Trimethyl 6a-amino-2,5-dimethyl-1,6-bis-(N'-phenylureido)-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5k). M.p. 170–172 °C (from THF–pentane); ν_{max} 3 360, 3 200, 3 100, 1 745, 1 725, 1 685, and 1 595 cm^{-1} ; δ_{H} 2.0 (6 H, s, Me), 3.6 (3 H, s, CO_2Me), 3.7 (6 H, s, CO_2Me), 4.4 (2 H, s, NH_2 , D_2O -exch.), 7.0–7.8 (10 H, m, Ph), 8.7 (1 H, s, NH, D_2O -exch.), 8.8 (1 H, s, NH, D_2O -exch.), 10.0 (2 H, s, NH, D_2O -exch.) (Found: C, 56.4; H, 5.1; N, 16.7. $\text{C}_{28}\text{H}_{31}\text{N}_7\text{O}_8$ requires C, 56.7; H, 5.3; N, 16.5%).

1-Ethyl 4-methyl 2-acetyl-3-cyanobutanedioate semicarbazone (3c). M.p. 130–133 °C (from dichloromethane–light petroleum); ν_{max} 3 460, 3 290, 3 190, 2 250, 1 750, 1 710, and 1 595 cm^{-1} ; δ_{H} 1.1 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.8 (3 H, s, Me), 3.6 (3 H, s, CO_2Me), 3.8–4.2 (3 H, m, CH and $\text{CO}_2\text{CH}_2\text{Me}$), 4.7–4.8 (1 H, m, CH, D_2O -exch.), 6.1 (2 H, s, NH_2 , D_2O -exch.), and 9.1 (1 H, s, NH, D_2O -exch.) (Found: C, 46.7; H, 5.4; N, 19.9. $\text{C}_{11}\text{H}_{16}\text{N}_4\text{O}_5$ requires C, 46.5; H, 5.7; N, 19.7%).

3,4-Diethyl 3a-methyl 6a-amino-2,5-dimethyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5l). M.p. 154–156 °C (from THF–pentane); ν_{max} 3 470, 3 390, 3 210, 1 740, 1 690, and 1 570 cm^{-1} ; δ_{H} 1.1 (6 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.8 (6 H, s, Me), 3.5 (3 H, s, CO_2Me), 3.8–4.2 (6 H, m, $2 \times \text{CO}_2\text{CH}_2\text{Me}$ and NH_2 , D_2O -exch.), 6.1 (4 H, s, NH_2 , D_2O -exch.), and 9.1 (2 H, s, NH, D_2O -exch.) (Found: C, 45.8; H, 5.6; N, 20.6. $\text{C}_{18}\text{H}_{27}\text{N}_7\text{O}_8$ requires C, 46.05; H, 5.8; N, 20.9%).

1-Ethyl 4-methyl 2-acetyl-3-cyanobutanedioate phenylsemicarbazone (3d). M.p. 141–144 °C (from dichloromethane–light petroleum); ν_{max} 3 480, 3 200, 2 250, 1 755, 1 730, 1 680, and 1 595 cm^{-1} ; δ_{H} 1.2 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.0 (3 H, s, Me), 3.6 (3 H, s, CO_2Me), 3.8–4.3 (3 H, m, $\text{CO}_2\text{CH}_2\text{Me}$ and CH), 4.8–5.0 (1 H, m, CH, D_2O -exch.), 6.8–7.5 (5 H, m, Ph), 8.2, (1 H, s, NH, D_2O -exch.), and 9.7 (1 H, s, NH, D_2O -exch.) (Found: C, 56.4; H, 5.5; N, 15.6. $\text{C}_{17}\text{H}_{20}\text{N}_4\text{O}_5$ requires C, 56.7; H, 5.6; N, 15.5%).

3,4-Diethyl 3a-methyl 6a-amino-2,5-dimethyl-1,6-bis-(N'-phenylureido)-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5m). M.p. 180–183 °C (from THF–pentane); ν_{max} 3 360, 3 300, 3 200, 1 740, 1 685, 1 675, and 1 596 cm^{-1} ; δ_{H} 1.0 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.2 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.9 (6 H, s, Me), 3.6 (3 H, s, CO_2Me), 3.8–4.4 (6 H, m, $2 \times \text{CO}_2\text{CH}_2\text{Me}$ and NH_2 , D_2O -exch.), 6.7–7.5 (10 H, m, Ph), 8.4 (1 H, s, NH, D_2O -exch.), 8.6 (1 H, s, NH, D_2O -exch.), and 9.7 (2 H, s, NH, D_2O -exch.) (Found: C, 57.8; H, 5.8; N, 15.6. $\text{C}_{30}\text{H}_{35}\text{N}_7\text{O}_8$ requires C, 58.0; H, 5.7; N, 15.8%).

4-Ethyl 1-methyl 2-acetyl-3-cyanobutanedioate semicarbazone (3e). M.p. 88–90 °C (from dichloromethane–light petroleum); ν_{max} 3 460, 3 300, 3 200, 2 250, 1 740, 1 705, and 1 595 cm^{-1} ; δ_{H} 1.2 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 1.9 (3 H, s, Me), 3.6 (3 H, s, CO_2Me), 3.8–4.3 (3 H, m, $\text{CO}_2\text{CH}_2\text{Me}$ and CH), 4.7–4.9 (1 H, m, CH, D_2O -exch.), 6.2 (2 H, s, NH_2 , D_2O -exch.), and 9.2 (1 H, s, NH, D_2O -exch.) (Found: C, 46.7; H, 5.5; N, 19.9. $\text{C}_{11}\text{H}_{16}\text{N}_4\text{O}_5$ requires C, 46.5; H, 5.7; N, 19.7%).

3a-Ethyl 3,4-dimethyl 6a-amino-2,5-dimethyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5n). M.p. 147–154 °C (from THF–pentane); ν_{max} 3 450, 3 290, 3 200, 1 745, 1 735, 1 700, and 1 596 cm^{-1} ; δ_{H} 1.4 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.2 (6 H, s, Me), 3.7 (6 H, s, CO_2Me), 4.0–4.5 (4 H, m, $\text{CO}_2\text{CH}_2\text{Me}$ and NH_2 , D_2O -exch.), 6.5 (4 H, s, NH_2 , D_2O -exch.), and 9.4 (2 H, s, NH, D_2O -exch.) (Found: C, 44.6; H, 5.2; N, 21.6. $\text{C}_{17}\text{H}_{25}\text{N}_7\text{O}_8$ requires C, 44.8; H, 5.5; N, 21.5%).

4-Ethyl 1-methyl 2-acetyl-3-cyanobutanedioate phenylsemicarbazone (3f). M.p. 147–151 °C (from dichloromethane–light petroleum); ν_{max} 3 370, 2 250, 1 745, 1 730, 1 695, and 1 595 cm^{-1} ; δ_{H} 1.1 (3 H, t, J 7 Hz, $\text{CO}_2\text{CH}_2\text{Me}$), 2.0 (3 H, s, Me), 3.7 (3 H, s, CO_2Me), 4.0–4.4 (3 H, m, $\text{CO}_2\text{CH}_2\text{Me}$ and CH), 5.0–5.1 (1 H, m, CH, D_2O -exch.), 7.0–7.8 (5 H, m, Ph), 8.4 (1 H, s,

NH, D₂O-exch.), and 10.0 (1 H, s, NH, D₂O-exch.) (Found: C, 56.8; H, 5.4; N, 15.7. C₁₇H₂₀N₄O₅ requires C, 56.6; H, 5.6; N, 15.5%).

3a-Ethyl 3,4-dimethyl 6a-amino-2,5-dimethyl-1,6-bis-(N'-phenylureido)-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5o). M.p. 191–193 °C (from THF–pentane); ν_{\max} 3 370, 3 310, 3 200, 1 740, 1 690, 1 675, and 1 595 cm⁻¹; δ_{H} 1.1 (3 H, t, *J* 7 Hz, CO₂CH₂Me), 2.0 (6 H, s, Me), 3.6 (3 H, s, CO₂Me), 3.7 (3 H, s, CO₂Me), 3.9–4.5 (4 H, m, CO₂CH₂Me and NH₂, D₂O-exch.), 7.0–7.7 (10 H, m, Ph), 8.6 (1 H, s, NH, D₂O-exch.), 8.7 (1 H, s, NH, D₂O-exch.), and 10.0 (2 H, s, NH, D₂O-exch.) (Found: C, 57.0; H, 5.7; N, 16.2. C₂₉H₃₃N₇O₈ requires C, 57.3; H, 5.5; N, 16.1%).

Diethyl 2-acetyl-3-cyanobutanedioate semicarbazone (3g). M.p. 109–112 °C (from dichloromethane–light petroleum); ν_{\max} 3 450, 3 290, 3 170, 2 250, 1 745, 1 725, 1 695, and 1 595 cm⁻¹; δ_{H} 1.2 (6 H, t, *J* 7 Hz, CO₂CH₂Me), 2.0 (3 H, s, Me), 4.0–4.4 (5 H, m, 2 × CO₂CH₂Me and CH), 4.8–5.0 (1 H, m, CH, D₂O-exch.), 6.3 (2 H, s, NH₂, D₂O-exch.), and 9.5 (1 H, s, NH, D₂O-exch.) (Found: C, 48.5; H, 6.0; N, 18.6. C₁₂H₁₈N₄O₅ requires C, 48.3; H, 6.1; N, 18.8%).

Triethyl 6a-amino-2,5-dimethyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5p). M.p. 143–151 °C (from THF–pentane); ν_{\max} 3 470, 3 290, 3 210, 1 740, 1 695, and 1 585 cm⁻¹; δ_{H} 1.1 (9 H, t, *J* 7 Hz, CO₂CH₂Me), 1.8 (6 H, s, Me), 3.7–4.2 (8 H, m, 3 × CO₂CH₂Me and NH₂, D₂O-exch.), 6.1 (4 H, s, NH₂, D₂O-exch.), and 9.1 (2 H, s, NH, D₂O-exch.) (Found: C, 47.4; H, 6.2; N, 20.0. C₁₉H₂₉N₇O₈ requires C, 47.2; H, 6.0; N, 20.3%).

Diethyl 2-acetyl-3-cyanobutanedioate phenylsemicarbazone (3h). M.p. 110–115 °C (from dichloromethane–light petroleum); ν_{\max} 3 380, 2 250, 1 750, 1 710, and 1 595 cm⁻¹; δ_{H} 1.2–1.7 (6 H, m, CO₂CH₂Me), 2.3 (3 H, s, Me), 4.2–4.7 (5 H, m, 2 × CO₂CH₂Me and CH), 5.3 (1 H, s, CH, D₂O-exch.), 7.2–8.0 (5 H, m, Ph), 8.8 (1 H, s, NH, D₂O-exch.), and 10.3 (1 H, s, NH, D₂O-exch.) (Found: C, 58.0; H, 5.7; N, 14.7. C₁₈H₂₂N₄O₅ requires C, 57.7; H, 5.9; N, 15.0%).

Triethyl 6a-amino-2,5-dimethyl-1,6-bis-(N'-phenylureido)-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5q). M.p. 185–188 °C (from THF–pentane); ν_{\max} 3 360, 3 300, 3 200, 1 735, 1 675, and 1 590 cm⁻¹; δ_{H} 0.9–1.3 (9 H, m, CO₂CH₂Me), 2.0 (6 H, s, Me), 3.9–4.5 (8 H, m, 3 × CO₂CH₂Me and NH₂, D₂O-exch.), 6.9–7.7 (10 H, m, Ph), 8.6 (1 H, s, NH, D₂O-exch.), 8.8 (1 H, s, NH, D₂O-exch.), and 10.0 (2 H, s, NH, D₂O-exch.) (Found: C, 58.4; H, 6.0; N, 15.7. C₃₁H₃₇N₇O₈ requires C, 58.6; H, 5.9; N, 15.4%).

Reactions of the Azoalkenes (1) with Semicarbazones (3).—A solution of an azoalkene (1) (1 mmol) in THF (2 ml) was added dropwise to a solution of a semicarbazone (3) (1 mmol) in THF (2 ml) which had previously been stirred for 15 min with sodium methoxide (0.1 mmol). After the appropriate time, evaporation of the solvent gave the crude product (5), which was purified by crystallization from THF–pentane. The following compounds were prepared.

3-Ethyl 3a,4-dimethyl 6a-amino-2,5-dimethyl-1,6-diureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5r). M.p. 180–184 °C; ν_{\max} 3 470, 3 290, 3 220, 1 740, 1 700, and 1 575 cm⁻¹; δ_{H} 1.5 (3 H, t, *J* 7 Hz, CO₂CH₂Me), 2.2 (6 H, s, Me), 3.9 (6 H, s, CO₂Me), 4.2–4.5 (4 H, m, CO₂CH₂Me and NH₂, D₂O-exch.), 6.5 (4 H, s, NH₂, D₂O-exch.), and 9.5 (2 H, s, NH, D₂O-exch.) (Found: C, 44.4; H, 5.7; N, 21.3. C₁₇H₂₅N₇O₈ requires C, 44.8; H, 5.5; N, 21.5%).

3-Ethyl 3a,4-dimethyl 6a-amino-2,5-dimethyl-1-(N'-phenylureido)-6-ureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5s). M.p. 179–185 °C; ν_{\max} 3 470, 3 360, 3 200, 1 740, 1 710, 1 640, and 1 595 cm⁻¹; δ_{H} 1.2 (3 H, t, *J* 7 Hz,

CO₂CH₂Me), 1.9 (6 H, s, Me), 3.7 (6 H, s, CO₂Me), 3.9–4.3 (4 H, m, CO₂CH₂Me and NH₂, D₂O-exch.), 6.3 (2 H, s, NH₂, D₂O-exch.), 6.7–7.5 (5 H, m, Ph), 8.4 (1 H, s, NH, D₂O-exch.), 9.2 (1 H, s, NH, D₂O-exch.), and 9.8 (1 H, s, NH, D₂O-exch.) (Found: C, 51.7; H, 5.9; N, 18.1. C₂₃H₂₉N₇O₈ requires C, 52.0; H, 5.5; N, 18.4%).

3a-Ethyl 3,4-dimethyl 6a-amino-1-ethoxycarbonylamino-2,5-dimethyl-6-ureido-1,3a,6,6a-tetrahydropyrrolo[2,3-b]pyrrole-3,3a,4-tricarboxylate (5t). M.p. 125–131 °C; ν_{\max} 3,500, 3,380, 3 210, 1 745, 1 720, 1 680, and 1 570 cm⁻¹; δ_{H} 0.9–1.3 (6 H, m, CO₂CH₂Me), 1.8 (6 H, s, Me), 3.5 (6 H, s, CO₂Me), 3.7–4.3 (6 H, m, 2 × CO₂CH₂Me and NH₂, D₂O-exch.), 6.1 (2 H, s, NH₂, D₂O-exch.), 9.2 (1 H, s, NH, D₂O-exch.), and 9.8 (1 H, s, NH, D₂O-exch.) (Found: C, 48.3; H, 6.2; N, 17.4. C₁₉H₂₈N₆O₉ requires C, 48.7; H, 6.0; N, 17.9%).

X-Ray Analysis of Compound (5e).—Intensity data were collected by a CAD4 diffractometer using $\omega/2\theta$ scan; θ range 2.5° ≤ θ ≤ 25°, Mo-K α radiation λ = 0.7107 Å. Diffraction intensities were measured with a 1.0° scan width and a scan speed variable between 0.7–8.0° min⁻¹. The unit-cell parameters were determined by a least-squares refinement on 25 independent 2θ values.

Crystal data of compound (5e). C₂₅H₃₈N₆O₈, *M* = 550.3, triclinic, space group *PI*, *a* = 8.199(2), *b* = 13.016(2), *c* = 15.681(2) Å, α = 110.88(1)°, β = 102.65(2)°, γ = 95.34(1)°, *V* = 1498.5 Å³, *Z* = 2, *D_c* = 1.22 g cm⁻³. Of 4 701 independent reflections, 1 156 having *I* < 2.5 σ (*I*) were considered unobserved.*

Structure Determination and Refinement. The structure was solved by direct methods and Fourier techniques, using the SHELX 76⁹ and SHELX 86¹⁰ program packages. Refinement proceeded by full-matrix least-squares methods using anisotropic thermal parameters for all non-hydrogen atoms. The H-atoms were found in the Fourier difference syntheses, but were not refined. The final agreement index was *R* = 0.053, *S* = 1.02.†

* Tests on the anticancer activity of these compounds were performed under the auspices of the Developmental Therapeutics Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, Maryland, USA.

† **Supplementary data** (see Instructions for Authors, section 5.6.3, in the January issue). H-Atom co-ordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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