Synthesis and Reactions of [1,2,4]Triazolo[4,3-*a*]pyridinium-3-aminides and [1,2,4]Triazolo[4,3-*a*]pyrimidinium-3-aminides: Evaluation of the Scope and Mechanism of a New Type of Heterocyclic Rearrangement

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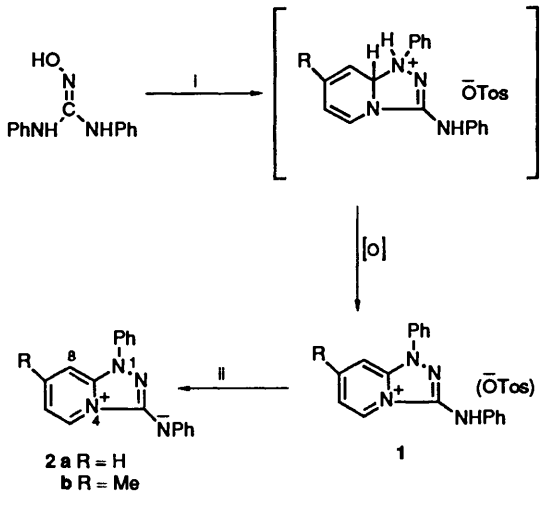
1,2,4-Triazolo[4,3-*a*]pyridinium betaines **6a, b** have been prepared by treating 2-pyridyl-4-phenylthiosemicarbazides **4a, b** with dicyclohexylcarbodiimide, and related compounds **6c–f** have been prepared through the intermediate *S*-methyl thiosemicarbazides **5c–f**. Reaction of the pyrimidin-2-yl thiosemicarbazide derivatives **8a–c** with dicyclohexylcarbodiimide (DCC) gave the 1,2,4-triazolo[4,3-*a*]pyrimidinium betaines **7a–c**, but attempted thermal cyclization of the free bases derived from methiodides **8j–o** gave a series of enamines **11**. The structure of one such enamine **11a** was elucidated by degradation with 2 mol dm^{-3} HCl which afforded a mixture of the amine **9** and the ketone **10**. Treatment of the thiosemicarbazide **8d** with dicyclohexylcarbodiimide gave the pyridinium betaine **14a**, and a related compound **14b** was prepared by reaction of the salt **12b** with diazabicyclo[5.4.0]undec-7-ene (DBU). The crystal and molecular structure of the maleate salt of **14b** was determined by X-ray crystallography. It was established that the betaine **14a** could be converted into an enamine derivative **11a** by heating it in toluene.

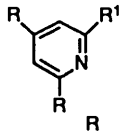
We have described the chemistry of 1,2,4-triazolo[4,3-*a*]pyrimidinium-3-olates and -3-thiolates[1] and of analogous compounds in the 1,2,4-triazolo[1,5-*a*]pyrimidine system.[2,3] Most recently, in a preliminary note we have reported the synthesis of 1,2,4-triazolo[4,3-*a*]pyridinium-3-aminides and the unusual mode of dimerisation of certain analogous aminides in the [1,2,4]triazolo[4,3-*a*]pyrimidine ring system.[4] In this paper we provide full details of our synthetic work in the aminide series, and describe the scope and mechanism of this new type of heterocyclic rearrangement.

1,2,4-*Triazolo*[4,3-a]*pyridinium*-3-*aminides*.—Two compounds in this series **2a, b** have been synthesised by the previously reported method outlined in Scheme 1.[5] Since product yields were not quoted,[5] it was decided to evaluate the scope of this type of reaction with a view to synthesising



Scheme 1 *Reagents:* i, TosCl,  PhMe; ii, NH_4OH

analogous triazolopyrimidinium betaines. Unfortunately, compound **2a** could never be synthesised through the salt **1** in greater than 20% yield by the optimised procedure described in the Experimental section, and alternative syntheses from



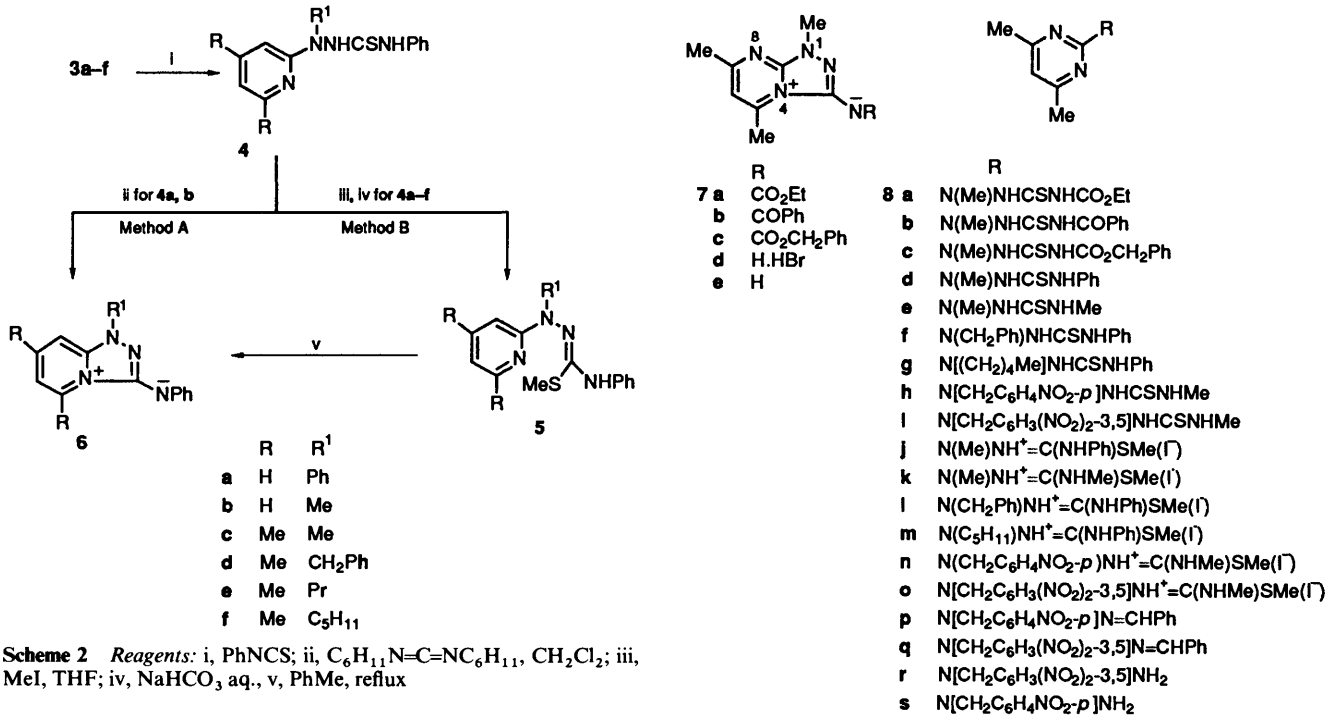
	R	R^1
3a	H	$N(Ph)NH_2$
b	H	$N(Me)NH_2$
c	Me	$N(Me)NH_2$
d	Me	$N(CH_2Ph)NH_2$
e	Me	$N(Pr)NH_2$
f	Me	$N(C_5H_{11})NH_2$
g	Me	NHN=CHPh
h	Me	$N(CH_2Ph)N$=CHPh
i	Me	N(Pr)N=CHPh
j	Me	$N(C_5H_{11})N$=CHPh

hydrazinopyridines were devised (see Scheme 2). Of the requisite 2-pyridylhydrazines **3a–f**, the monosubstituted derivatives **3a**[6] and **3b**[7a] had been previously reported, and **3c** was prepared in 85% yield from 2-bromo-4,6-dimethylpyridine and methylhydrazine. The remainder **3d–f** were synthesised through alkylation of 2-benzylidenehydrazino-4,6-dimethylpyridine **3g** and hydrolysis of the alkyl derivatives **3h–j** according to our recently described method for analogous pyrimidinyl hydrazines.[1] The hydrazine derivatives **3a–f** were treated with phenyl isothiocyanate in tetrahydrofuran to give a series of thiosemicarbazides **4a–f** in 76–95% yield. Treatment of two of the last mentioned compounds **4a** and **4b** with dicyclohexylcarbodiimide in dichloromethane gave the desired 1,2,4-triazolo[4,3-*a*]pyridinium-3-aminides **6a** and **6b**, (Method A) in 55 and 61% yield respectively, but higher yields and easier purification were achieved by preparing the betaines **6a–f** through intermediate *S*-methyl thiosemicarbazides **5a–f**. The

Table 1 ^{1}H NMR spectra (δ)[a] of 1,2,4-triazolo[4,3-*a*]pyridinium-3-phenylaminides **6**

Group compound	7-CH_3	5-CH_3	NCH_2	6-H	8-H	Others
6b			3.85s	6.87m		6.72m (ArH), 7.11–7.23m (8-H, ArH), 7.44–7.53m (7-H, ArH), 8.46m (5-H)
6c	2.21d (0.9)	3.11br s	3.59s	6.13br s	6.61br s	6.68–7.39m (ArH)
6d	2.25d (0.9)	3.23br s	5.21s	6.23br s	6.61br s	6.67–7.53m (ArH)
6e	2.29d (0.9)	3.20br s	3.99t (7.2)	6.21br s	6.68br s	0.99t (7.3) (CH_3), 1.96 sext (7.4) (CH_2), 6.6–7.4m (ArH)
6f	2.29d (0.9)	3.19br s	3.97t (7.1)	6.21br s	6.67br s	0.91t (6.9) (CH_3), 1.26–1.43m [$(CH_2)_2$], 1.90 quint (7.1) (CH_2), 6.61–7.46m (ArH)

[a] Recorded at 250 MHz in CD_2Cl_2 solution. Figures quoted (δ) are referred to $SiMe_4$. Coupling values *J* Hz are in parentheses.



Scheme 2 *Reagents:* i, PhNCS; ii, $C_6H_{11}N{=}C{=}NC_6H_{11}$, CH_2Cl_2; iii, MeI, THF; iv, $NaHCO_3$ aq., v, PhMe, reflux

latter were generated as red oils by treating the thiosemicarbazides **4a–f** with iodomethane and basifying the ensuing methiodides with aqueous sodium hydrogen carbonate. The oils were converted without rigorous purification into the orange–red betaines (58–82%) by heating them in toluene solution under reflux (Method B). Analytical data and spectral properties of the betaines were in accord with structure **6**. A notable feature (see Table 1) in the ^{1}H NMR spectra of the betaines **6c–f** is the coupling (*J* 0.9) between the 7-methyl substituent and 6-H; a coupling of comparable magnitude is also observed[1] from 6-H to a 5-methyl substituent in analogous 1,2,4-triazolo[4,3-*a*]pyrimidinium-3-olates and -3-thiolates and in 5,7-dimethyl-3-oxo-2,3-dihydro-1,2,4-triazolo[4,3-*a*]pyrimidine.

1,2,4-*Triazolo*[4,3-a]*pyrimidinium*-3-*aminides*.—The above procedures (Methods A and B) were then applied to hydrazinopyrimidines, but analogous 1,2,4-triazolo[4,3-*a*]pyrimidinium-3-aminides could be prepared only when an electron-withdrawing substituent was attached to the exocyclic nitrogen atom (*viz* **7a–c**). Analytical and spectra data were in accord with structures (**7a–c**) (see *e.g.* ^{1}H NMR data in Table 2). Thus, reaction of the thiosemicarbazides **8a–c** with dicyclohexylcarbodiimide in acetone at room temperature gave the betaines **7a–c** (> 60% yield), the spectroscopic and analytical data for which were in accord with the proposed structures. In contrast, conversion of the thiosemicarbazides **8d–i** with methyl iodide into methiodides **8j–o** followed by application of Method B (see Scheme 2) gave colourless (from **8j** and **k**) or orange (from **8n** and **o**) crystalline compounds or yellow oils (from **8l** and **m**) with molecular weights (mass spectroscopy) twice the value that were expected for structures akin to **7**. Although ^{1}H NMR spectroscopy (Table 3) provided insufficient information for unambiguous assignment of the dimer structures, a clue to the mechanism of dimerisation could be gleaned. Thus, the presence of only three resonances in the region expected for methyl groups (δ 1.99–2.38) indicated that one such substituent was involved in the rearrangement. In addition, the presence of two D_2O-exchangeable protons was attributed to the presence of two NHR groups which were also evident from IR spectra (ν_{max} 3310–3405 cm^{-1}).

The structure of the dimer from the methiodide **8j** was elucidated by chemical degradation, and its stereostructure (see **11**) determined X-ray crystallographically.[4] Thus, acidic hydrolysis of the dimer with 2 mol dm^{-3} HCl under reflux gave the amine **9** (70%) and the ketone **10** (90%) suggesting that the enamine **11a** was representative of the dimer structure. ^{1}H NMR spectra of this **11a** and related dimers **11b–f** were in accord with the proposed structures with chemical shifts of the pyridyl substituents in close agreement with those observed in model compounds. In order to establish the possible intermediacy of betaines (see **7**) in the dimerisation process, the preparation of two such compounds by cyclodesulfurisation of

Table 2 ^{1}H NMR spectra (δ)[a] of 1,2,4-triazolo[4,3-*a*]pyrimidinium-3-aminides **7**

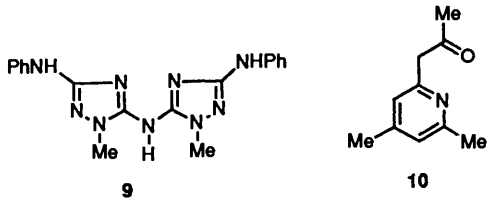
Group compound	5-CH_3	7-CH_3	NCH_3	6-H	Others
7a	3.03d (1.0)	2.63s	4.10s	6.98d (1.0)	1.28t (7.0) (CH_3), 4.12q (7.0) (CH_2O)
7b[b]	3.10d (1.0)	2.53s	3.96s	6.73d (1.0)	7.37, 8.01m (ArH)
7c[c]	3.0d (1.0)	2.49s	3.87s	6.50d (1.0)	5.01s (CH_2O), 7.26m (ArH)
7d[d]	3.01d (1.0)	2.69s	3.98s	7.17d (1.0)	

[a] Recorded at 250 MHz in CD_3OD solution. Figures quoted (δ) are referred to $SiMe_4$. Coupling values *J*/Hz are shown in parentheses. [b] In CD_2Cl_2–CD_3OD (1:1). [c] In CD_2Cl_2. [d] HBr salt.

Table 3 ^{1}H NMR spectra (δ)[a] of 1-(4,6-dimethylpyrid-2-yl)-2-(1,2,4-triazol-3-yl)aminopropenes **11**

Group compound	CH_3C=	CH=	py 3-H	py 5-H	py 4-CH_3	py 6-CH_3	Others
11a[b]	2.02s	6.36s	6.94s	6.78s	2.13s	2.25s	3.47s [$(NCH_3)_2$], 6.78–7.40m [ArH], 9.17br s [$(NH)_2$]
11b[c]	1.99d (1.0)	6.21br d (1.0)	6.89br s	6.74br s	2.16s	2.38 s	3.36s [$(NCH_3)_2$], 2.68d (5.2) [$(NHCH_3)_2$], 4.93br q (5.3) [$(NH)_2$]
11c[d]	1.81d (0.9)	6.30br d (0.9)	6.83s	6.69s	2.12s	2.39 s	4.89s [$(NCH_2)_2$], 6.86–7.40m [ArH]
11d[e]	2.10s	6.29s	7.02s	6.75s	2.15s	2.34s	3.77t (7.4) [$(NCH_2)_2$], 0.83t (6.6) [$(CH_3)_2$], 1.19–1.35m [$(CH_2)_4$], 1.73 quint (6.6), [$(CH_2)_2$], 6.76–7.42m [ArH]
11e[c]	1.77s	6.05s	6.76s	6.62s	2.19s	2.34 s	5.08s [$(NCH_2)_2$], 2.77d (5.0) [$(NHCH_3)_2$], 3.92q (5.5) [$(NH)_2$], 7.29–8.09m [ArH]
11f[d]	1.93d (0.8)	5.97d (0.8)	6.65s	6.42s	2.13s	2.15 s	5.27s [$(NCH_2)_2$], 2.79d (5.4) [$(NHCH_3)_2$], 4.17q (5.4) [$(NH)_2$], 8.91t (2.0), 8.56d (2.0) [ArH]

[a] Recorded at 250 MHz. Figures quoted (δ) are referred to $SiMe_4$. Coupling values *J*/Hz are shown in parentheses. [b] In $(CD_3)_2SO$. [c] In $(CD_3)_2CO$. [d] In $CDCl_3$. [e] In CD_3OD.



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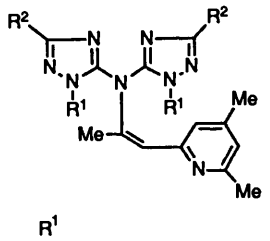


	R^1	R^2
11a	Me	NHPh
b	Me	NHMe
c	CH_2Ph	NHPh
d	C_5H_{11}	NHPh
e	$CH_2C_6H_4NO_2$-*p*	NHMe
f	$CH_2C_6H_3(NO_2)_2$-3,5	NHMe
g	Me	SMe

the thiosemicarbazides (**8d** and **8e**) was attempted under mild conditions (DCC, CH_2Cl_2, room temperature). A red amorphous solid (55% yield) was obtained from **8d** but no reaction occurred with **8e** under comparable conditions. The spectral parameters of the red compound were inconsistent with a betaine structure (see **7**): for example, the mass spectrum showed a molecular ion at *m*/*z* 506 consistent with a dimeric product, and the fragmentation pattern was similar to the colourless dimer formed from **8d** described earlier. The ^{1}H NMR spectrum indicated the presence of three CMe and two NMe substituents. However, the non-equivalence of the two *N*-methyl and two *N*-phenyl resonances was in contrast to the equivalence of these signals in the spectrum of the dimer described above. Additional features were the presence of two D_2O-exchangeable protons at δ 7.32 and 7.72, and an abnormally deshielded aromatic proton at δ 8.92; the presence of NH was confirmed from the IR spectrum (ν_{max} 3425 cm^{-1}).

It was then established qualitatively that the red dimeric compound was converted into the colourless dimer **11a** by heating it under reflux in toluene for a short period.

It was suspected that a key structural feature of the aminides (see **7**) that could be involved in the dimerisation was the acidic nature of the methyl group at C-5 and our earlier proposal[4] was that iminoallene intermediates (see **13**) might mediate dimer formation (see **11**). In this sense there is analogy in the base-promoted fragmentation and rearrangement of 1-methyl-1,2,3-triazolium salts *via* 1,2,5-triazahexa-1,3,5-trienes.[7b] To check this hypothesis, 3-methylthio-1,5,7-trimethyl-1,2,4-triazolo[4,3-*a*]pyrimidinium iodide **12b** was treated with diazabicyclo-[5.4.0]undec-7-ene (DBU) in tetrahydrofuran at room temperature. The resulting red compound isolated from the reaction by column chromatography, although not purified to analytical standard, was recognised from spectral data (^{1}H NMR) as being related to the red 'dimer' from **8d** described above. Reaction of red compound **14b** with maleic acid afforded an orange, crystalline salt whose structure was investigated by X-ray crystallography.

The fractional atomic coordinates obtained from the crystallographic analysis, and the subsequently derived interatomic distances and bond angles are compiled in Tables 4 and 5, respectively. The solid-state structure of the major ditriazolopyridinium cationic fragment is depicted in Fig. 1 together with the numbering system adopted in the structural study. Cursory inspection of the structure of the cation shows that it is consistent with structural formula **15** and, in turn, suggests that it is most likely to have been formed by specific protonation on the exocyclic nitrogen of the putative dimeric intermediate **14b**

Table 4 Refined fractional atomic coordinates of maleate salt of pyridinium betaine **14b** with estimated standard deviations (esds) in parentheses

	x	*y*	*z*
N(1)	0.851 12(21)	0.505 67(21)	1.112 74(21)
C(1)	0.913 9(3)	0.424 0(3)	1.079 7(3)
C(2)	1.022 3(3)	0.445 5(3)	1.190 5(3)
C(3)	1.061 7(3)	0.537 1(3)	1.327 3(3)
C(4)	0.994 4(3)	0.615 5(3)	1.353 7(3)
C(5)	0.892 6(3)	0.603 1(3)	1.248 2(3)
C(6)	0.824 1(4)	0.691 0(3)	1.272 7(3)
C(7)	1.173 9(4)	0.550 1(4)	1.443 0(3)
C(8)	0.863 3(3)	0.328 4(3)	0.935 4(3)
C(9)	0.880 6(3)	0.217 1(3)	0.881 3(3)
C(10)	0.945 9(3)	0.165 4(3)	0.961 6(3)
N(2)	0.834 1(3)	0.135 0(3)	0.741 09(25)
H(2N)	0.868(5)	0.077(5))	0.715(5)
C(11)	0.744 1(3)	0.132 9(3)	0.633 3(3)
N(3)	0.719 2(3)	0.055 9(3)	0.502 5(3)
N(4)	0.621 7(3)	0.066 9(3)	0.415 4(3)
C(12)	0.596 1(3)	0.150 9(3)	0.502 7(3)
N(5)	0.669 53(25)	0.197 00(24)	0.639 22(24)
C(13)	0.771 0(5)	−0.038 7(5)	0.446 3(4)
S(1)	0.473 32(9)	0.201 97(10))	0.450 76(10)
C(14)	0.418 5(4)	0.115 5(5)	0.267 8(4)
C(15)	0.746 68(25)	0.495 9(3)	1.003 4(3)
N(6)	0.615 70(22)	0.405 28(23)	0.935 62(24)
N(7)	0.541 96(24)	0.426 0(3)	0.840 1(3)
C(16)	0.638 9(3)	0.531 0(3)	0.862 0(3)
N(8)	0.767 64(24)	0.578 58(25)	0.962 4(3)
C(17)	0.548 7(3)	0.290 2(4)	0.939 9(4)
S(2)	0.615 08(11)	0.610 61(12)	0.774 03(12)
C(18)	0.433 0(4)	0.517 0(5)	0.660 0(5)
C(19)	0.054 9(5)	−0.055 9(5)	0.737 1(4)
C(20)	0.198 9(4)	0.011 5(4)	0.849 2(4)
C(21)	0.282 6(4)	−0.037 7(5)	0.880 9(4)
C(22)	0.257 4(7)	−0.179 1(7)	0.815 7(6)
O(1)	0.010 6(4)	0.018 8(5)	0.720 7(4)
O(2)	−0.011 5(3)	−0.182 1(4)	0.664 5(4)
O(3)	0.136 3(6)	−0.273 2(4)	0.719 9(5)
O(4)	0.354 3(6)	−0.200 8(7)	0.857 6(7)

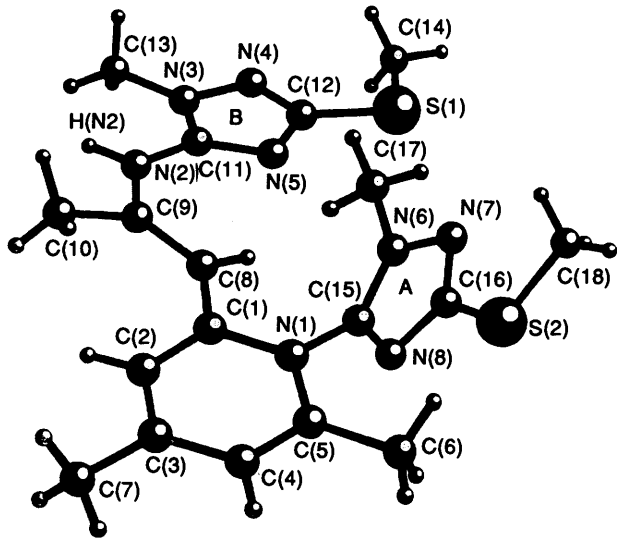


Fig. 1 Computer generated plot[16] of the cation derived from the pyridinium betaine **14**. For clarity, hydrogen atom labels have been generally omitted.

(see Scheme 3). As illustrated in the packing diagram (Fig. 2), the crystal structure of the orange salt derived from **14b** consists of well separated, discrete ditriazolopyridinium cations and maleate mono-anions in a 1:1 ratio as required by the stoichiometry of the salt. Although there are no significantly short non-bonding contacts between the two ionic fragments

Table 5 Derived geometrical parameters for maleate salt from pyridinium betaine **14b** with esds in parentheses

(a) Bond distances (Å)

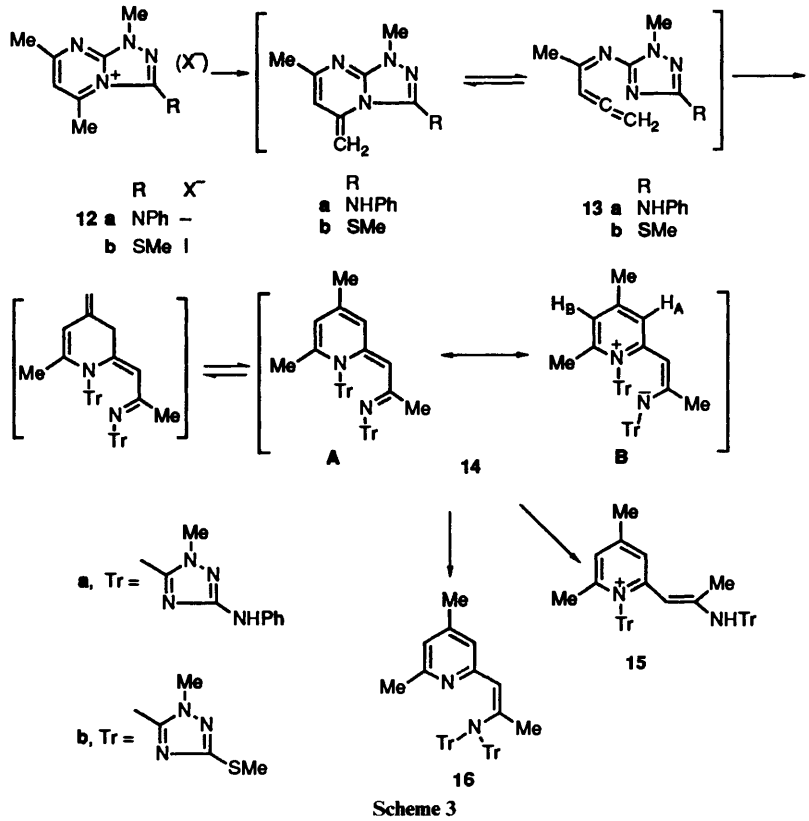
N(1)–C(1)	1.389(4)	N(4)–C(12)	1.305(5)
N(1)–C(5)	1.379(4)	C(12)–N(5)	1.360(5)
N(1)–C(15)	1.419(4)	C(12)–S(1)	1.748(4)
C(1)–C(2)	1.382(5)	S(1)–C(14)	1.790(5)
C(1)–C(8)	1.429(5)	C(15)–N(6)	1.321(4)
C(2)–C(3)	1.378(5)	C(15)–N(8)	1.309(4)
C(3)–C(4)	1.391(5)	N(6)–N(7)	1.372(4)
C(3)–C(7)	1.494(6)	N(6)–C(17)	1.454(5)
C(4)–C(5)	1.356(5)	N(7)–(16)	1.319(5)
C(5)–C(6)	1.490(5)	C(16)–N(8)	1.353(5)
C(8)–C(9)	1.354(5)	C(16)–S(2)	1.739(4)
C(9)–C(10)	1.500(5)	S(2)–C(18)	1.785(6)
C(9)–N(2)	1.372(5)	C(19)–C(20)	1.480(7)
N(2)–H(2N)	0.90(6)	C(19)–O(1)	1.226(8)
N(2)–C(11)	1.377(5)	C(19)–O(2)	1.257(7)
C(11)–N(3)	1.336(5)	C(20)–C(21)	1.315(7)
C(11)–N(5)	1.313(5)	C(21)–C(22)	1.481(10)
N(3)–N(4)	1.364(5)	C(22)–O(3)	1.276(10)
N(3)–C(13)	1.461(6)	C(22)–O(4)	1.223(11)

(b) Bond angles (°)

C(1)–N(1)–C(5)	122.6(3)	N(3)–N(4)–C(12)	101.5(3)
C(1)–N(1)–C(15)	119.1(3)	N(4)–C(12)–N(5)	116.4(3)
C(5)–N(1)–C(15)	118.1(3)	N(4)–C(12)–S(1)	123.2(3)
N(1)–C(1)–C(2)	116.4(3)	N(5)–C(12)–S(1)	120.5(3)
N(1)–C(1)–C(8)	117.4(3)	C(11)–N(5)–C(12)	101.6(3)
C(2)–C(1)–C(8)	126.1(3)	C(12)–S(1)–C(14)	99.78(21)
C(1)–C(2)–C(3)	122.4(3)	N(1)–C(15)–N(6)	123.4(3)
C(2)–C(3)–C(4)	118.3(3)	N(1)–C(15)–N(8)	124.1(3)
C(2)–C(3)–C(7)	120.1(3)	N(6)–C(15)–N(8)	112.5(3)
C(4)–C(3)–C(7)	121.5(3)	C(15)–N(6)–N(7)	108.5(3)
C(3)–C(4)–C(5)	121.2(3)	C(15)–N(6)–C(17)	131.0(3)
N(1)–C(5)–C(4)	118.8(3)	N(7)–N(6)–C(17)	120.2(3)
N(1)–C(5)–C(6)	118.6(3)	N(6)–N(7)–C(16)	101.8(3)
C(4)–C(5)–C(6)	122.6(3)	N(7)–C(16)–N(8)	115.5(3)
C(1)–C(8)–C(9)	126.5(3)	N(7)–C(16)–S(2)	126.0(3)
H(8)–C(8)–C(9)	116.8(4)	N(8)–C(16)–S(2)	118.5(3)
C(8)–C(9)–C(10)	125.9(3)	C(15)–N(8)–C(16)	101.6(3)
C(8)–C(9)–N(2)	122.0(3)	C(16)–S(2)–C(18)	101.61(23)
C(10)–C(9)–N(2)	112.0(3)	C(20)–C(19)–O(1)	115.6(5)
C(9)–N(2)–H(2N)	116.7(36)	C(20)–C(19)–O(2)	119.6(5)
C(9)–N(2)–C(11)	128.2(3)	O(1)–C(19)–O(2)	124.8(6)
H(2N)–N(2)–C(11)	115.0(36)	C(19)–C(20)–H(20)	114.5(5)
N(2)–C(11)–N(3)	121.2(3)	C(19)–C(20)–C(21)	130.9(5)
N(2)–C(11)–N(5)	127.7(3)	H(20)–C(20)–C(21)	114.5(6)
N(3)–C(11)–N(5)	111.1(3)	C(20)–C(21)–C(22)	129.5(5)
C(11)–N(3)–N(4)	109.5(3)	C(21)–C(22)–O(3)	119.3(7)
C(11)–N(3)–C(13)	129.9(4)	C(21)–C(22)–O(4)	118.1(7)
N(4)–N(3)–C(13)	120.4(3)	O(3)–C(22)–O(4)	122.6(8)

located in the same asymmetric unit of the cell, the carboxylate group oxygen O(1) appears to form a localised hydrogen bond with the amino hydrogen atom H(2N') [O(1)···H(2N') 1.94 (6) Å] of an adjacent cation in the next unit cell related by translation along the direction of the *a* axis [1 + *X*, *Y*, *Z*].

The bond distances around each of the pyridinium and 1,2,4-triazole rings are indicative of extensively delocalised π-systems. There is generally good agreement between corresponding geometrical parameters in both triazole rings A and B in **15**, and also in other similarly substituted triazole derivatives.[8] The three heterocyclic rings are planar (mean deviations from least-squares planes: pyridinium ring 0.016 Å; triazole ring A 0.003 Å; triazole ring B 0.004 Å) and the atoms in the acyclic link between the pyridinium ring and triazole ring B are also essentially coplanar [mean deviation from plane through atoms C(8)–C(10)–N(2) 0.005 Å]. Although triazole ring A is almost orthogonal to the central pyridinium ring (interplanar angle 81.04°), there should be a substantial degree of extended π-conjugation between the pyridinium and triazole B rings since the ring atoms together with atoms C(8), C(9) and N(2) all lie



Scheme 3

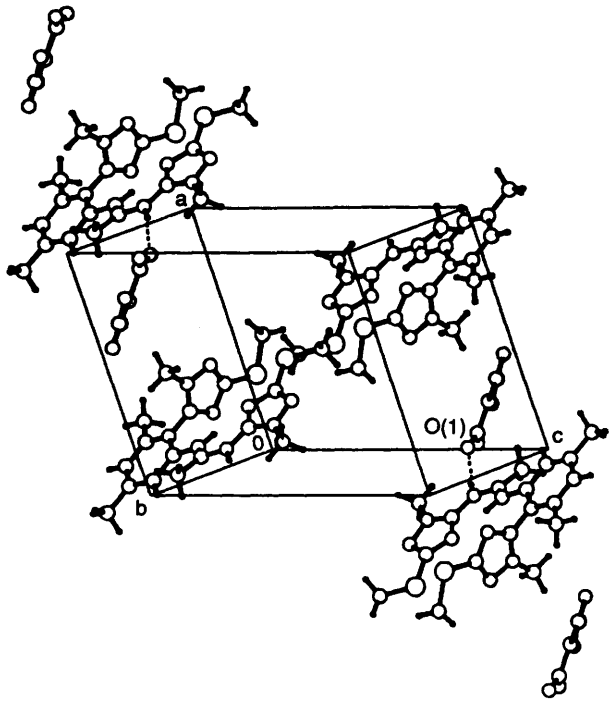
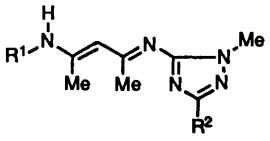


Fig. 2 Crystal packing diagram[17] for the maleate salt derived from pyridinium betaine **14**

within a 0.25 Å range of the least-squares plane through that portion of the structure. The eclipsed conformations adopted by the *C*-methylthio substituents of the triazole rings [N(4)–C(12)–S(1)–C(14) −2.7°; N(7)–C(16)–S(2)–C(18) 2.0°] has been observed previously.[8]

The general structural features of the cation **15**, which results from protonation of **14b**, also provide direct evidence to support the notion that a pyridinium betaine resonance structure (see **14B**) may also be important in describing the ground states of (**14a**, **b**) in which H_B is strongly deshielded (δ 8.92 and 8.72 respectively) whereas H_A experiences an anisotropic effect from the electron-rich substituent at the adjacent 2-position (δ 6.00 for H_A in **14b**).

With the structures of both the initial red (see **14**) and rearranged (see **16**) dimers to hand, a pathway from the putative 1,2,4-triazolo[4,3-*a*]pyrimidinium intermediates (see **12a**) or compound **12b** can be envisaged (Scheme 3). Thus, intramolecular proton transfer in the betaine **12a** or intermolecular proton abstraction from the pyridinium salt **12b** would give rise to a common type of dihydro-1,2,4-triazolo[4,3-*a*]pyrimidine intermediate which could form iminoallenic intermediates **13** *via* a cycloreversion process. Although little is known about the reactivity of such heterocumulenes, the iminoallenic functionality has been incorporated into azines,[9] and the ensuing intramolecular reactions can be rationalised in terms of dipolar intermediates of significance in criss-cross cycloadditions.[10] Of relevance to this discussion is the observation of electrocyclisation of *N*-phenyliminoallenes (see **13**; *N*-Ph for *N*-triazolyl moiety) leading to quinolines.[11] In the present work, it seems feasible that the iminoallenic intermediate could dimerise in a Diels–Alder fashion (**13**→**14**) with a subsequent [1,5] sigmatropic migration of a triazole group, thus providing a stereospecific interconversion of the initially formed red (see **14**) to rearranged dimers (see **16**). To our knowledge, this type of ring fragmentation (see **12**→**13**) has not been previously observed in reactions of methyl-substituted, condensed pyrimidinium compounds or in related heteroarenes. It is interesting to note from our earlier work[1] that the salt **12b** undergoes ring opening with methylamine as the nucleophile to give the triazole derivative **17b** (see also ref. 12). In contrast, the present work indicates that reaction of the salt **12a** with the hindered base DBU may follow a route through proton abstraction from the C-5 methyl substituent (**12b**→**13b**). Assuming that aminides (see **7**) are intermediates in dimer formation, the substituent



	R^1	R^2
17a	H	NH_2
b	Me	SMe

effects can be rationalised: an electron-withdrawing substituent on the exocyclic nitrogen reduces the nucleophilicity of the nitrogen atom, and aminides (see **7**) can be isolated; in contrast, exocyclic *N*-alkyl or *N*-aryl substituents bear higher charge density on the nitrogen atom and facilitate intramolecular proton transfer leading to dimer formation (*e.g.* **8j**→[**12a**]→ **14a**→**16a**).

It was of interest to attempt the synthesis of a 5,7-dimethyl-1,2,4-triazolo[4,3-*a*]pyrimidinium-3-aminide derivative with an exocyclic NH substituent **7e** with a view to evaluating its behaviour towards dimerisation. The hydrobromide salt **7d** of the desired free base **7e** was prepared analytically pure in good yield by treating the benzyloxycarbonylaminide **7c** with hydrogen bromide in acetic acid at room temperature. Unfortunately, when the hydrobromide **7d** was basified at room temperature, either a complex mixture was obtained (using aqueous Na_2CO_3), or a product **17a** was isolated (using NH_3 in CH_2Cl_2) which resulted from cleavage of the pyrimidinium ring (see the interconversion of **12b**→ **17b** by methylamine).[1]

Summary.—5,7-Dimethyl-1,2,4-triazolo[4,3-*a*]pyridinium betaines bearing an exocyclic 3-phenylaminide group **6a–f** are stable heteroaromatic compounds but this is not the case for condensed pyrimidinium analogues [*e.g.* **7** (R = Ph)]. A complicated skeletal rearrangement occurs in the latter series unless electron-withdrawing groups are present on the exocyclic aminide nitrogen atom. The present work suggests that a variety of novel heterocyclic compounds should be accessible from transient, condensed heteroaromatic betaines in which there is appropriate juxtaposition of a methyl- or benzylic hydrogen and a suitably substituted aminide function.

Experimental

M.p.s were determined on a Buchi 510 m.p. apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. ^1H NMR spectra were obtained on Bruker WP-60 (60 MHz) or Bruker AM-250 (250 MHz) spectrometers with tetramethylsilane as internal standard. ^{13}C NMR spectra were run on a Bruker AM-250 (250 MHz) spectrometer. Mass spectra were obtained using a VG-Micromass-16F spectrometer using a direct insertion probe. Merck Kieselgel 60 was used for column chromatography unless otherwise stated; for analytical TLC, pre-coated Merck Kieselgel 60 F 254 plates were used.

Reaction of Pyridine with N-*Hydroxy*-N′,N″-*diphenylguanidine and Toluene*-p-*sulfonyl Chloride*.—Toluene-*p*-sulfonyl chloride (4.2 g, 22 mmol) was added in portions over 1.5 h to a stirred mixture of *N*-hydroxy-*N*′,*N*″-diphenylguanidine (5.0 g, 22 mmol), dry pyridine (6.75 g, 85 mmol) and toluene (22 cm^3) maintained at 5 °C. During the addition, the mixture developed a deep red colour which changed to black at the end of the addition period. The mixture was stirred at 5 °C for 24 h and then decanted to afford a black tarry deposit. The tar was dissolved in hot ethanol (100 cm^3) to give the toluene-*p*-sulfonate salt **1a** as an off-white solid, m.p. 228–229 °C (lit.,[5] 228–229 °C). The salt was suspended in concentrated aqueous ammonium hydroxide (25 cm^3) and the mixture first stirred vigorously and then extracted with chloroform (2 × 50 cm^3). The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was then recrystallised from ethanol to give 1-phenyl-1,2,4-triazolo[4,3-*a*]pyridinium-3-phenylaminide **2a** as orange–red plates (1.25 g, 20%), m.p. 203–205 °C (lit.,[5] 204–205 °C). Detailed spectroscopic data for this compound **2a** are presented below (see under **6a**).

Preparation of Hydrazine Derivatives **3**.—*4,6-Dimethyl-2-(1-Methylhydrazino)pyridine* **3c**. A solution of 2-bromo-4,6-dimethylpyridine (1.86 g, 10 mmol) and methylhydrazine (1.84 g, 40 mmol) in toluene (30 cm^3) was heated at reflux for 48 h. The mixture was cooled, washed with water (20 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give a brown oil. The oil was distilled in a Kugelrohr apparatus (oven temperature 55 °C, pressure 0.01 Torr) to give the *title compound* **3c** as a colourless liquid (1.28 g, 85%); ν_{max}(thin film)/cm^{-1} 3300 (NH), 3180 (NH), 1600 and 1560; $\delta_H(CDCl_3)$ 2.22 (s, 3 H, 4-CH_3), 2.36 (s, 3 H, 6-CH_3), 3.21 (s, 3 H, NCH_3), 4.23 (br s, 2 H, NH_2), 6.33 (s, 1 H, 5-H) and 6.49 (s, 1 H, 3-H); *m*/*z* 151 (50%) ($M^{+\cdot}$), 136 (32), 135 (100), 108 (15), 107 (69), 106 (43), 79 (17), 77 (16) and 28 (14).

2-Benzylidenehydrazino-4,6-dimethylpyridine **3g**. A stirred solution of 2-hydrazino-4,6-dimethylpyridine (7.0 g, 51 mmol) in ethanol (100 cm^3) was treated with benzaldehyde (5.2 cm^3, 51 mmol) at room temperature. An exothermic reaction ensued and the internal temperature rose to 30 °C. The mixture was allowed to cool to room temperature and then stirred for 30 min. The solvent was evaporated under reduced pressure and the residue crystallised from hexane to give the *title compound* **3g** (10.5 g, 91%), m.p. 107–109 °C; ν_{max}(Nujol)/cm^{-1} 3280 (NH), 1610, 1300, 1221, 1167, 1148, 751 and 690; $\delta_H(CD_2Cl_2)$ 2.29 (s, 3 H, 4-CH_3), 2.34 (s, 3 H, 6-CH_3), 6.50 (s, 1 H, 5-H), 7.03 (s, 1 H, 3-H), 7.25–7.74 (m, 5 H, ArH) and 9.06 (s, 1 H, NH).

General Method for the Preparation of N-*Alkyl*-N-(*4,6-dimethyl-2-pyridyl*)*benzaldehyde Hydrazones* **3h–i**.—A solution of 2-benzylidenehydrazino-4,6-dimethylpyridine **3g** (4.5 g, 20 mmol) in tetrahydrofuran (40 cm^3) was added dropwise over 15 min to a stirred suspension of sodium hydride (55% dispersion in oil; 0.77 g, 20 mmol) in tetrahydrofuran (20 cm^3) at room temperature. The resulting mixture was stirred for 10 min whereupon a solution of the alkyl halide (20 mmol) in tetrahydrofuran (10 cm^3) was added. The mixture was heated at reflux for 1.5 h and then cooled to room temperature and diluted with water (50 cm^3). The mixture was extracted with diethyl ether (2 × 50 cm^3) and the combined organic extracts were dried (Na_2SO_4) and filtered through a plug of silica gel. The filtrate was evaporated under reduced pressure and the crude product purified by crystallization. The following compounds were prepared.

Benzaldehyde benzyl (*4,6-dimethyl-2-pyridyl*)*hydrazone* **3h**. Colourless needles (5.25 g, 84%), m.p. 120–121 °C (EtOAc) (Found: C, 80.05; H, 6.75; N, 13.4. $C_{21}H_{21}N_3$ requires C, 80.0; H, 6.7; N, 13.3%); $\nu_{max}(CHCl_3)$/cm^{-1} 1602, 1555, 1168, 1145 and 692; $\delta_H(CDCl_3)$ 2.32 (s, 3 H, 4-CH_3), 2.38 (s, 3 H, 6-CH_3), 5.66 (s, 2 H, CH_2Ph), 6.52 (s, 1 H, 5-H) and 7.10–7.71 (m, 12 H, 3-H, N=C*H*Ph and ArH); *m*/*z* 315 (19%) ($M^{+\cdot}$), 266 (16), 264 (13), 238 (38), 224 (43), 211 (100), 203 (29), 107 (28), 106 (34) and 91 (39).

Benzaldehyde (*4,6-dimethyl-2-pyridyl*)*propylhydrazone* **3i**. Colourless needles (3.8 g, 72%), m.p. 64–65 °C [EtOAc–hexane]; analytical and spectroscopic data are given in Suppl. Pub. 56922 (11 pp.), Table 1.*

* For full details of the British Library Supplementary Publication Deposition Scheme see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1993, Issue 1.

Benzaldehyde (4,6-Dimethyl-2-pyridyl)(pentyl)hydrazone **3j**. Colourless needles (4.4 g, 74%), m.p. 48–49 °C (EtOAc–hexane); analytical and spectral data are given in Suppl. Pub. 56922 (11 pp.), Table 1.*

General Method for the Preparation of 2-(1-Alkylhydrazino)-4,6-dimethylpyridines **3d–f**.—A solution of the benzaldehyde alkyl (4,6-dimethyl-2-pyridyl)hydrazone **3h–j** (12 mmol) in 2 mol dm^{-3} aqueous hydrochloric acid (40 cm^3) was heated at reflux for 6 h. Benzaldehyde was removed from the reaction mixture by co-distillation with water. The solution was cooled to room temperature and basified with 2 mol dm^{-3} aqueous sodium hydroxide. The resulting mixture was extracted with diethyl ether (2 × 50 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to leave an oil. The oil was distilled in a Kugelrohr apparatus to give the pyridine derivatives **3d–f** as colourless oils. The following compounds were prepared.

2-(1-*Benzylhydrazino*)-4,6-*dimethylpyridine* **3d** (2.34 g, 86%), b.p. (Kugelrohr) 150 °C at 1 Torr (Found: C, 74.0; H, 7.55; N, 18.5. $C_{14}H_{17}N_3$ requires C, 74.0; H, 7.55; N, 18.5%); ν_{max}(thin film)/cm^{-1} 3305 (NH), 3200 (NH), 1610 and 1570; $\delta_H(CDCl_3)$ 2.22 (s, 3 H, 4-CH_3), 2.36 (s, 3 H, 6-CH_3), 4.93 (s, 2 H, CH_2Ph), 6.35 (s, 1 H, 5-H), 6.67 (s, 1 H) and 7.28 (br d s, 5 H, ArH).

4,6-*Dimethyl*-2-(1-*propylhydrazino*)*pyridine* **3e** (1.83 g, 85%), b.p. (Kugelrohr), 100 °C/0.5 Torr; analytical and spectral data are given in Suppl. Pub. 56922 (11 pp.),* Table 2.

4,6-*Dimethyl*-2-(1-*pentylhydrazino*)*pyridine* **3f** (2.09 g, 84%), b.p. (Kugelrohr), 110 °C/0.3 Torr; analytical and spectral data are given in Suppl. Pub. 56922 (11 pp.),* Table 2.

General Method for the Preparation of Pyridylthiosemicarbazides **4a–j**.—A mixture of the 2-(1-alkylhydrazino)pyridine **3a–f** (10 mmol) and phenyl isothiocyanate (10 mmol) in tetrahydrofuran (50 cm^3) was stirred at room temperature for 24 h. The resulting mixture was evaporated under reduced pressure and the crude product purified by crystallisation. The following compounds were prepared; analytical and spectra data for compounds **4b–f** are given in Suppl. Pub. 56922 (11 pp.),* Tables 3 and 4.

1,4-*Diphenyl*-1-(2-*pyridyl*)*thiosemicarbazide* **4a**. Colourless needles (2.78 g, 85%), m.p. 178–180 °C (EtOH) (Found: C, 67.3; H, 5.1; N, 17.2. $C_{18}H_{16}N_4S$ requires C, 67.5; H, 5.0; N, 17.5%); ν_{max}(Nujol)/cm^{-1} 3130 (NH), 1588, 1315, 1265, 1200, 740 and 692; $\delta_H[(CD_3)_2SO]$ 6.85–8.20 (m, 14 H, ArH), 10.08 (br s, 1 H, NH) and 10.12 (br s, 1 H, N*H*); *m/z* (CI) 321 (M + 1)$^+$, 287 (6), 172 (5), 171 (43), 170 (3), 154 (5), 153 (56), 35 (65), 30 (2) and 28 (2).

1-*Methyl*-4-*phenyl*-1-(2-*pyridyl*)*thiosemicarbazide* **4b**. Colourless needles (2.25 g, 87%), m.p. 169–171 °C (EtOH).

1-(4,6-*Dimethyl*-2-*pyridyl*)-1-*methyl*-4-*phenylthiosemicarbazide* **4c**. Colourless needles (2.49 g, 87%), m.p. 147–148 °C (EtOH–hexane).

1-*Benzyl*-1-(4,6-*dimethyl*-2-*pyridyl*)-4-*phenylthiosemicarbazide* **4d**. Yellow needles (3.44 g, 95%), m.p. 128.5–129 °C (EtOAc–hexane).

1-(4,6-*Dimethyl*-2-*pyridyl*)-4-*phenyl*-1-*propylthiosemicarbazide* **4e**. Colourless plates (2.98 g, 81%), m.p. 139–140 °C (MeOH).

1-(4,6-*Dimethyl*-2-*pyridyl*)-1-*pentyl*-4-*phenylthiosemicarbazide* **4f**. Colourless needles (2.61 g, 76%), m.p. 80–82 °C (MeOH).

Synthesis of 1,2,4-Triazolo[4,3-a]pyridinium-3-phenylaminides **6**.—*Method A* (*for* **6a** *and* **6b**). Dicyclohexylcarbodiimide (5 mmol) was added to a stirred mixture of the 1-substituted 4-phenyl-1-(2-pyridyl)thiosemicarbazide (**4a** or **4b**) (3.33 mmol) in dichloromethane (20 cm^3) at room temperature, and the resultant red solution was stirred for 72 h. The mixture was evaporated under reduced pressure and the crude product (**6a**, **b**) was purified by crystallisation from toluene.

Method B (*for* **6a–f**). A solution of the 1-substituted 4-phenyl-1-(2-pyridyl)thiosemicarbazide **4a–f** (5 mmol) and iodomethane (7.5 mmol) in tetrahydrofuran was stirred at room temperature for 48 h. The resulting yellow solution was partitioned between saturated aqueous sodium hydrogen carbonate (30 cm^3) and diethyl ether (40 cm^3) and the mixture was vigorously stirred for 10 min. The organic layer was separated, washed with water (30 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the intermediate thioether (**5a–f**) as a red oil. The oil was dissolved in toluene (60 cm^3) and the resultant wine-coloured solution heated at reflux for 5 h. The solution was concentrated by distillation and the concentrate was allowed to cool to room temperature and then stirred for 3 h. The precipitate was washed with toluene and then hexane and the crude product was purified by crystallisation. The following compounds were prepared [analytical and spectral data for compounds (**6d–f**) are given in Suppl. Pub. 56922 (11 pp.),* Tables 5 and 6].

1-*Phenyl*-1,2,4-*triazolo*[4,3-a]*pyridinium*-3-*phenylaminide* **6a**. Orange–red plates (Method A, 55%; method B, 62%), m.p. 203–205 °C (from PhMe) [lit.,[5] 204–205 °C]; $\nu_{max}(CHCl_3)$/cm^{-1} 1610, 1579, 1550 and 1510; *m/z* 286 (92) (M$^{\cdot+}$), 285 (44), 169 (78), 168 (49), 143 (5), 78 (9), 77 (17), 51 (12), 32 (45) and 28 (100); $\delta_H(CD_2Cl_2)$ 6.75 (m, 1 H, ArH), 7.06 (m, 1 H, 6-H), 7.22 (m, 2 H, ArH), 7.47 (m, 1 H, ArH) 7.52–7.79 (m, 8 H, 7-H, 8-H and ArH) and 8.68 (m, 1 H, 5-H).

1-*Methyl*-1,2,4-*triazolo*[4,3-a]*pyridinium*-3-*phenylaminide* **6b**. Orange–red prisms (Method A, 61%; Method B, 58%), m.p. 190–192 °C (PhMe) (Found: C, 69.6; H, 5.45; N, 25.0. $C_{13}H_{12}N_4$ requires C, 69.5; H, 5.4; N, 24.8%); $\nu_{max}(CHCl_3)$/cm^{-1} 1601, 1580 and 1515; *m/z* 224 (100) (M$^{\cdot+}$), 223 (48), 107 (8), 79 (6), 78 (25) and 28 (13); $\delta_H(CD_2Cl_2)$ 3.85 (s, 3 H, NCH_3), 6.72 (m, 1 H, ArH), 6.87 (m, 1 H, 6-H), 7.11–7.23 (m, 3 H, 8-H and ArH), 7.44–7.53 (m, 3 H, 7-H and ArH) and 8.46 (m, 1 H, 5-H).

1,5,7-*Trimethyl*-1,2,4-*triazolo*[4,3-a]*pyridinium*-3-*phenylaminide* **6c**. Orange–red needles (80%), m.p. 180–182 °C (PhMe) (Found: C, 71.4; H, 6.4; N, 22.2. $C_{15}H_{16}N_4$ requires C, 71.4; H, 6.4; N, 22.15%); $\nu_{max}(CHCl_3)$/cm^{-1} 1608, 1582 and 1510; *m/z* 252 (100) (M$^{\cdot+}$), 251 (31), 236 (21), 136 (16), 118 (21), 108 (6), 107 (14), 106 (8) and 91 (9); $\delta_H(CD_2Cl_2)$ 2.21 (d, 3 H, *J* 0.9, 7-Me), 3.11 (br s, 3 H, 5-Me), 3.59 (s, 3 H, NMe), 6.13 (br s, 1 H, 6-H), 6.61 (br s, 1 H, 8-H) and 6.68–7.39 (m, 5 H, ArH).

1-*Benzyl*-5,7-*dimethyl*-1,2,4-*triazolo*[4,3-a]*pyridinium*-3-*phenylaminide* **6d**. Orange–red needles (82%), m.p. 230–231 °C (PhMe).

5,7-*Dimethyl*-1-*propyl*-1,2,4-*triazolo*[4,3-a]*pyridinium*-3-*phenylaminide* **6e**. Orange–red needles (83%), m.p. 158–159 °C (Pr^{i}OH).

5,7-*Dimethyl*-1-*pentyl*-1,2,4-*triazolo*[4,3-a]*pyridinium*-3-*phenylaminide* **6f**. Yellow needles (87%), m.p. 78–79.5 °C (cyclohexane).

Preparation of Benzaldehyde N-Substituted 4,6-Dimethylpyrimidin-2-ylhydrazones **8p** *and* **8q**.—A solution of 2-benzylidenehydrazino-4,6-dimethylpyrimidine[1] (1.5 g, 6.6 mmol) in tetrahydrofuran (20 cm^3) was added dropwise over 10 min to a stirred mixture of sodium hydride (50% dispersion in oil; 0.2 g, 6.6 mmol) in tetrahydrofuran (10 cm^3) at room temperature. The resulting mixture was stirred for 10 min and then cooled to 5 °C. A solution of 3,5-dinitrobenzylchloride (1.43 g, 6.6 mmol)

* For full details of the British Library Supplementary Publication Deposition Scheme see 'Instructions for Author's, *J. Chem. Soc., Perkin Trans. 1*, 1993, Issue 1.

in tetrahydrofuran (10 cm^3) was added over 15 min maintaining a temperature < 10 °C. The resulting black solution was allowed to warm to room temperature and then diluted with water (50 cm^3). The precipitate was filtered off and washed with ether to give the crude product as an orange solid (2.4 g, 90%). Recrystallization of the crude product from ethyl acetate–hexane gave *benzaldehyde* (4,6-*dimethylpyrimidin*-2-*yl*)(3,5-*dinitrobenzyl*)*hydrazone* **8q** as orange needles (2.19 g, 82%), m.p. 117–119 °C (Found: C, 59.1; H, 4.6; N, 20.7. $C_{20}H_{18}N_6O_4$ requires C, 59.1; H, 4.45; N, 20.7%); ν_{max}(Nujol)/cm^{-1} 1582, 1540 and 1345; δ_H[$(CD_3)_2CO$] 2.41 (s, 6 H, 4-CH_3 and 6-CH_3), 5.96 (s, 2 H, CH_2Ar), 6.81 (s, 1 H, 5-H), 7.26–7.77 (m, 5 H, ArH), 8.21 (s, 1 H, N=CH), 8.63 (m, 2 H, ArH) and 8.83 (t, 1 H, *J* 3.0, ArH); *m*/*z* 406 (23%) ($M^{\bullet+}$), 329 (37), 303 (56), 225 (36), 192 (27), 136 (29), 108 (100), 89 (27), 77 (21) and 67 (35).

The above procedure was used to prepare *benzaldehyde* (4,6-*dimethylpyrimidin*-2-*yl*)(4-*nitrobenzyl*)*hydrazone* **8p** (2.1 g, 85%), m.p. 163–164.5 °C [see Suppl. Pub. 56922 (11 pp.),* Tables 7 and 8].

Preparation of Hydrazinopyrimidines.—Hydrazinopyrimidines **8** [R = N(R')NH_2; R' = Me, CH_2Ph and C_5H_{11}] were prepared as previously described.[1]

4,6-*Dimethyl*-2-[1-(3,5-*dinitrobenzyl*)*hydrazino*]*pyrimidine* **8r**. A stirred solution of benzaldehyde 4,6-dimethylpyrimidin-2-yl)(3,5-dinitrobenzyl)hydrazone **8q** (2.03 g, 5 mmol) in 2 mol dm^{-3} aqueous hydrochloric acid (60 cm^3) was steam distilled for 1 h and then cooled to room temperature and basified with 2 mol dm^{-3} aqueous sodium hydroxide. The resulting mixture was extracted with dichloromethane (3 × 50 cm^3) and the combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was recrystallised from isopropyl alcohol to give the *title compound* **8r** as orange needles (1.43 g, 90%), m.p. 119–121 °C (Found: C, 49.2; H, 4.55; N, 26.3. $C_{13}H_{14}N_6O_4$ requires C, 49.05; H, 4.45; N, 26.4%); ν_{max}($CHCl_3$)/cm^{-1} 3320 (NH), 3100 (NH) and 1340 (NO_2); δ_H($CDCl_3$) 2.34 (d, 6 H, *J* 0.3, 4-CH_3 and 6-CH_3), 4.37–4.51 (br s, 2 H, NH_2), 5.17 (s, CH_2Ar), 6.42 (s, 1 H, 5-H), 8.61 (d, 2 H, *J* 2.1, ArH) and 8.92 (t, 1 H, *J* 2.1, ArH); *m*/*z* 318 (38%) ($M^{\bullet+}$), 302 (28), 138 (10), 137 (78), 109 (100), 108 (28), 107 (10), 93 (14), 82 (13) and 67 (18).

The above procedure was used to prepare 4,6-dimethyl-2-[1-(4-nitrobenzyl)hydrazino]pyrimidine **8s** (90%), m.p. 96–98 °C [see Suppl. Pub. 56922 (11 pp.),* Tables 7 and 8].

General Method for the Preparation of 1-*Substituted* 1-(4,6-*Dimethylpyrimidin*-2-*yl*)*thiosemicarbazides* **8a–i**.—A solution of the appropriate hydrazinopyrimidine derivative (10 mmol) and the isothiocyanate (10 mmol) in diethyl ether was stirred at room temperature for 18 h. The product was precipiated to give, for example 1-(4,6-*dimethylpyrimidin*-2-*yl*)-1-*methyl*-4-*phenylthiosemicarbazide* **8d** as colourless needles (2.35 g, 82%), m.p. 143–144 °C (EtOH) (Found: C, 58.5; H, 6.0; N, 24.4. $C_{14}H_{17}N_5S$ requires C, 58.5; H, 6.0; N, 24.5%); ν_{max}($CHCl_3$)/cm^{-1} 3340 (NH), 2990, 1588, 1520, 1360, 1340 and 690; δ_H(CD_3OD) 2.37 (s, 6 H, 4-CH_3 and 6-CH_3), 3.39 (s, 3 H, NCH_3), 6.66 (s, 1 H, 5-H), 6.85 (q, 1 H, *J* 5, N*H*CH_3), 7.12–7.52 (m, 5 H, ArH) and 8.17 (s, 1 H, NH); *m*/*z* (CI) 288 (24%) $(M + 1)^+$, 255 (17), 254 (99), 153 (72), 152 (93), 136 (100), 135 (88), 109 (35), 108 (41) and 107 (20).

The above procedure was used to give the following compounds (form, yield, m.p. and solvent for recrystallisation quoted): **8a**, colourless needles, 91, 150–151 °C, EtOH–Et_2O; **8b**, colourless needles, 93, 188–189 °C; **8c**, colourless needles, 40, 158–159 °C; **8e**, colourless needles, 86, 171 °C (decomp.), EtOAc; **8f**, colourless prisms, 70, 112–114 °C; **8g**, colourless prisms, 78, 78 °C, EtOAc–hexane; **8h**, orange–yellow needles, 83, 138–140 °C, EtOAc–hexane; **8i**, orange needles, 77, 181–182 °C, EtOAc–hexane; analytical and spectral data for compounds (**8a**, **b** and **8e–i**) are given in Suppl. Pub. 56922 (11 pp.),* Tables 7 and 8.

General Method for the Preparation of S-*Methyl Pyrimidinylthiosemicarbazide Hydroiodic Salts* **8i–o**.—A solution of the thiosemicarbazide (10 mmol) and iodomethane (15 mmol) in tetrahydrofuran (40 cm^3) was stirred at room temperature for 48 h. The mixture was evaporated under reduced pressure and the crude product recrystallised from the appropriate solvent to give, for example, *S*-methyl-1-(4,6-*dimethylpyrimidin*-2-*yl*)-1-*methyl*-4-*phenylthiosemicarbazide hydroiodide* **8j** (2.6 g, 85%), m.p. 168–169 °C [MeOH–Et_2O] (Found: C, 42.1; H, 4.7; N, 6.05. $C_{15}H_{20}IN_5S$, C, 41.95; H, 4.7; N, 16.3%; ν_{max}(Nujol)/cm^{-1} 1580, 1370, 1335, 1290, 738 and 691; δ_H(CD_3OD) 2.45 (s, 6 H, 4-CH_3 and 6-CH_3), 2.69 (s, 3 H, SCH_3), 3.50 (br s, 3 H, NCH_3), 6.81 (s, 1 H, 5-H) and 7.48–7.75 (m, 5 H, ArH); *m*/*z* (CI) 302 (77) $(M + 1\text{-}HI)^+$, 258 (24), 256 (65), 255 (20), 254 (100), 253 (15), 240 (10), 138 (32) and 136 (11).

Also prepared were the following compounds (yield, m.p. and solvent for recrystallisation quoted): **8k**, 90, 181–182 °C, MeOH–Et_2O; **8o**, 91, 181–182 °C, EtOH–Et_2O [see Suppl. Pub. 56922 (11 pp.),* Tables 7 and 8].

The methiodides **8l–n** were not obtained analytically pure and were transformed directly into the enamines **11**.

General Procedure for 1,5,7-*Trimethyl*-[1,2,4]*triazolo*[4,3-a]-*pyrimidinium*-3-*aminides* **7a–c**.—A solution of the appropriate thiosemicarbazide **8a–c** (5 mmol) and dicyclohexylcarbodiimide (7.5 mmol) in acetone was stirred at room temperature for 24 h and the precipitated product filtered off. The following pure compounds were isolated.

1,5,7-*Trimethyl*-1,2,4-*triazolo*[4,3-a]*pyrimidinium*-3-*ethoxycarbonylaminide* **7a**. Yellow solid (0.82 g, 66%), m.p. 182–183 °C (decomp.) (Found: C, 53.05; H, 6.1; N, 28.1. $C_{11}H_{15}N_5O_2$ requires C, 53.0; H, 6.07; N, 28.10%); ν_{max}(Nujol)/cm^{-1} 3040, 1635, 1555 and 1510; δ_H(CD_3OD) 1.28 (t, 3 H, *J* 7.0, CH_2CH_3), 2.63 (s, 3 H, 7-CH_3), 3.03 (d, 3 H, *J* 1.0, 5-CH_3), 4.10 (s, 3 H, NCH_3), 4.12 (q, 2 H, *J* 7.0, CH_2CH_3) and 6.98 (d, 1 H, *J* 1.0, 6-H).

1,5,7-*Trimethyl*-1,2,4-*triazolo*[4,3-a]*pyrimidinium*-3-*benzoylaminide* **7b**. Yellow solid (0.89 g, 63%), m.p. 208–209 °C (decomp.) (Found: C, 63.9; H, 5.4; N, 25.0. $C_{15}H_{15}N_5O$ requires C, 64.04; H, 5.37; N, 24.90%); ν_{max}(Nujol)/cm^{-1} 3040, 1640, 1600 and 1560; δ_H(1:1, CD_2Cl_2–CD_3OD) 2.53 (s, 3 H, 7-CH_3), 3.10 (d, 3 H, *J* 1.0, 5-CH_3), 3.96 (s, 3 H, NCH_3), 6.73 (d, 1 H, *J* 1.0, 6-H) and 7.37 and 8.01 (m, 5 H, Ph).

1,5,7-*Trimethyl*-1,2,4-*triazolo*[4,3-a]*pyrimidinium*-3-*benzyloxycarbonylaminide* **7c**. Yellow solid (1.05 g, 68%), m.p. 177–178 °C (decomp.) (Found: C, 61.7; H, 5.6; N, 22.4. $C_{16}H_{17}N_5O_2$ requires C, 61.72; H, 5.50; N, 22.50%); ν_{max}(Nujol)/cm^{-1} 3040, 1635 and 1510; δ_H(CD_2Cl_2) 2.49 (s, 3 H, 7-CH_3), 3.0 (d, 3 H, *J* 1.0, 5-CH_3), 3.87 (s, 3 H, NCH_3), 5.01 (s, 2 H, CH_2), 6.50 (d, 1 H, *J* 1.0, 6-H) and 7.26 (m, 5 H, Ph).

General Method for the Preparation of 1-(4,6-*Dimethyl*-2-*pyridyl*)-2-[N,N-*bis*(2,5-*disubstituted*-1,2,4-*triazol*-3-*yl*)]*aminopropenes* **11a–f**.—A solution of the 1-(pyrimidin-2-yl)-1,4-disubstituted *S*-methyl-thiosemicarbazide hydroiodide **8j–o** (0.5 mmol) in chloroform (40 cm^3) was washed with saturated aqueous sodium hydrogen carbonate (2 × 10 cm^3) and water (10 cm^3). The resulting red solution was dried (Na_2SO_4)

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and evaporated under reduced pressure to give the intermediate thioether as an orange oil. The oil was dissolved in toluene (50 cm^3) and the solution heated at reflux for 6–48 h and then cooled to room temperature. The crude product was either filtered off or obtained by evaporation of the reaction mixture under reduced pressure. The crude product was purified by either recrystallisation or by chromatography on silica gel. Two such compounds were as follows.

1-(4,6-*Dimethyl*-2-*pyridyl*)-2-[N,N-*bis*-(2-*methyl*-5-*phenyl*-*amino*-1,2,4-*triazol*-3-*yl*)]*aminopropene* **11a**. Colourless needles from toluene (1.03 g, 82%), m.p. 227–228 °C (Found: C, 66.4; H, 6.0; N, 27.65. $C_{28}H_{30}N_{10}$ requires C, 66.4; H, 6.0; N, 27.65%); ν_{max}(Nujol)/cm^{-1} 3405 (NH), 1673 (enamine C=C), 1610, 1560 and 1540; δ_H[$(CD_3)_2SO$] 2.02 (s, 3 H, allylic CH_3), 2.13 (s, 3 H, pyridyl 4-CH_3), 2.25 (s, 3 H, pyridyl 6-CH_3), 3.47 (s, 6 H, 2 × NCH_3), 6.36 (s, 1 H, olefinic H), 6.78 (s, 1 H, pyridyl 5-H), 6.78–7.40 (m, 10 H, ArH), 6.94 (s, 1 H, pyridyl 3-H) and 9.17 (br s, 2 H, NH); *m/z* 506 (24%) ($M^{\bullet+}$), 360 (16), 146 (18), 145 (33), 144 (21), 83 (100), 82 (20), 49 (28), 48 (35), 47 (67) and 28 (95).

1-(4,6-*Dimethylpyrid*-2-*yl*)-2-{N,N-*bis*[2-(3,5-*dinitrobenzyl*)-5-*methylamino*-1,2,4-*triazol*-3-*yl*]}aminopropene **11f**. Orange plates from CH_2Cl_2–hexane (98:2) (1.09 g, 61%), m.p. 128–130 °C (Found: C, 50.7; H, 4.3; N, 26.9. $C_{30}H_{30}N_{14}O_8$ requires C, 50.4; H, 4.3; N, 27.4); ν_{max}(Nujol)/cm^{-1} 3290 (NH), 1598, 1535, 1340 and 725; $\delta_H(CDCl_3)$ 1.93 (d, 3 H, *J* 0.8, allylic CH_3), 2.13 (s, 3 H, pyridyl 4-CH_3), 2.15 (s, 3 H, pyridyl 6-CH_3), 2.79 (d, 6 H, *J* 5.4, 2 × $NHCH_3$), 4.17 (q, 2 H, *J* 5.4, 2 × NH), 5.27 (s, 4 H, 2 × NCH_2), 5.97 (d, 1 H, *J* 0.9, olefinic H), 6.42 (s, 1 H, pyridyl 5-H), 6.65 (s, 1 H, pyridyl 3-H), 8.91 (t, 2 H, *J* 2, ArH) and 8.56 (d, 4 H, *J* 2, ArH); *m/z* 714 (70%) ($M^{\bullet+}$) 698 (16), 697 (40), 569 (10), 422 (27), 304 (15), 188 (16), 147 (36), 146 (100), 145 (19) and 131 (32).

The following compounds were also prepared (form, yield, m.p. and solvent for recrystallisation quoted): **11b**, colourless needles, 63%, 190–192 °C, EtOAc; **11c**, yellow oil, 61%, —, —; **11d**, yellow oil, 55%, —, —; **11e**, orange needles, 60%, 203–205 °C, CH_2Cl_2–hexane [see Suppl. Pub. 56922 (11 pp.),* Tables 9 and 10].

Acidic Hydrolysis of 1-(4,6-*Dimethyl*-2-*pyridyl*)-2-[N,N-*bis*-(2-*methyl*-5-*phenylamino*-1,2,4-*triazol*-3-*yl*)]*aminopropene* **11a**.—1-(4,6-Dimethyl-2-pyridyl)-2-[*N*,*N*-bis(2-methyl-5-phenylamino-1,2,4-triazol-3-yl)]aminopropene **11a** (1.3 g, 2.6 mmol) was suspended in aqueous hydrochloric acid (2 mol dm^{-3}; 40 cm^3) and the stirred mixtured heated to 80 °C. Complete dissolution was briefly obtained before precipitation of a solid occurred. This mixture was maintained at 80 °C for 30 min and then allowed to cool to room temperature. The precipitate was washed with water and then suspended in chloroform (75 cm^3). To this suspension was added saturated aqueous sodium hydrogen carbonate (50 cm^3) and the resulting mixture stirred vigorously for 10 min; the layers were then separated. The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure and the product recrystallised from ethanol to give N,N-*bis*(1-*methyl*-3-*phenylamino*-1,2,4-*triazol*-5-*yl*)*amine* **9** as off-white needles (0.65 g, 70%), m.p. 191–192 °C (Found: C, 59.7; H, 5.35; N, 34.8. $C_{18}H_{19}N_9$ requires C, 59.8; H, 5.3; N, 34.9%); ν_{max}(Nujol)/cm^{-1} 3300 (NH), 3150, 1640, 1620 and 735; δ_H[$(CD_3)_2SO$] 3.60 (s, 6 H, $NHCH_3$), 6.82 (t, 2 H, ArH), 7.21 (t, 4 H, ArH), 7.48 (d, 4 H, ArH) and 9.66 (br s, 1 H, NH); *m/z* (FAB) 361 ($M^{\bullet+}$). The aqueous acidic filtrate was evaporated under reduced pressure. The residue was partitioned between dichloromethane (50 cm^3) and saturated aqueous sodium hydrogen carbonate (5 cm^3) and the mixture stirred for 10 min. The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure to leave a red oil. The oil was chromatographed on silica gel using dichloromethane–methanol (98:2) as eluent to give 1-(4,6-*dimethyl*-2-*pyridyl*)*propan*-2-*one* **10** as a yellow liquid (0.4 g, 96%); ν_{max}(liq. film)/cm^{-1} 1710 (C=O), 1610 and 1550; δ_H[$(CD_3)_2CO$] 2.12 (s, 3 H, 4-CH_3), 2.27 (s, 3 H, 2-CH_3), 2.40 (s, 3 H, CH_3), 3.79 (s, 2 H, CH_2), 6.89 (s, 1 H, 5-H) and 6.92 (s, 1 H, 3-H); *m/z* 163.0985 (14%, $M^{\bullet+}$ requires 163.0997), 121 (100), 106 (10), 91 (6) and 79 (11).

Reaction of 1-(4,6-*Dimethylpyrimidin*-2-*yl*)-1-*methyl*-4-*phenylthiosemicarbazide* **8d** *with dicyclohexylcarbodiimide: Preparation of the Pyridinium Betaine* **14a**.—Dicyclohexylcarbodiimide (1.55 g, 7.5 mmol) was added to a stirred solution of 1-(4,6-dimethylpyrimidin-2-yl)-1-methyl-4-phenylthiosemicarbazide **8d** (1.44 g, 5 mmol) in dichloromethane (30 cm^3) at room temperature. The colourless solution immediately changed to deep red and this solution was stirred at room temperature for 3 days. TLC [SiO_2; chloroform–methanol (9:1)] showed the formation of a major orange–red product (R_f 0.25→0.4). The mixture was evaporated under reduced pressure and the residue chromatographed on silica gel using chloroform–methanol (98:2) as eluent. The fractions containing the orange–red product were combined and evaporated under reduced pressure to give a red amorphous powder later recognised as the pyridinium betaine **14a** (0.70 g, 55%), m.p. 126 °C (decomp.); $\nu_{max}(CHCl_3)$/cm^{-1} 3425 (NH), 1650, 1595, 1568, 1465, 1432, 1280 and 1240; $\delta_H(CD_2Cl_2)$ 1.98 (s, 3 H, CH_3), 2.11 (br s, 3 H, CH_3), 2.21 (br s, 3 H, CH_3), 3.60 (s, 3 H, NCH_3), 3.69 (s, 3 H, NCH_3), 4.20 (br s, 1 H), 6.79 (m, 1 H, ArH), 6.91 (m, 1 H, ArH), 7.13–7.52 [m, 9 H, 8 × ArH and 1 exchangeable (D_2O) proton], 7.72 (s, 1 H, D_2O exchangeable) and 8.92 (s, 1 H); *m/z* 506 (89%) ($M^{\bullet+}$), 364 (64), 318 (35), 293 (100), 253 (28), 215 (36), 214 (37), 146 (57), 131 (31), 70 (31) and 28 (44). This compound was not purified to analytical standard.

Reaction of 3-*Methylthio*-1,5,7-*trimethyl*-1,2,4-*triazolo*-[4,3-a]*pyrimidinium Iodide* **12b** *with Diazabicyclo*[5.4.0]*undec*-7-*ene* (*DBU*): *Preparation of the Pyridinium Betaine* **14b** *and Conversion into the Maleate Salt*.—DBU (1.52 g, 10 mmol) was added to a stirred mixture of 3-methylthio-1,5,7-trimethyl-1,2,4-triazolo[4,3-*a*]pyrimidinium iodide (3.36 g, 10 mmol) in tetrahydrofuran (400 cm^3) at room temperature. The resultant red mixture was stirred for 18 h and then evaporated under reduced pressure. The residue was chromatographed on silica gel using EtOAc as eluent to give the *pyridinium betaine* **14b** as a red solid (0.9 g, 43%); ν_{max}(Nujol)/cm^{-1} 1648 and 1262; $\delta_H(CD_2Cl_2)$ 1.92 (s, 3 H, CH_3), 2.17 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 2.50 (s, 3 H, SCH_3), 2.61 (s, 3 H, SCH_3), 3.64 (s, 3 H, NCH_3), 3.69 (s, 3 H, NCH_3), 4.07 (s, 1 H), 6.00 (s, 1 H) and 8.72 (s, 1 H); *m/z* 416 (81%) ($M^{\bullet+}$), 273 (26), 271 (74), 195 (16), 170 (17), 169 (16), 146 (100), 131 (34) and 43 (19). This compound was not further purified to analytical standard, but was converted into a maleate salt as follows. A sample of the betaine **14b** (100 mg) was dissolved in dichloromethane (3 cm^3) and to this solution was added maleic acid (1 mol equiv.). The resultant solution was allowed to evaporate slowly over a period of a few days to give the *crystalline maleate salt of the pyridinium betaine* **14b**, m.p. 125–128 °C; ν_{max}(KBr)/cm^{-1} 3600–2700 (br), 1700, 1635, 1580, 1550, 1515, 1480, 1440, 1360, 1290, 1250, 1200, 1160m, 1000br and 870.

Thermolysis of the Pyridinium Betaine **14b**.—A sample of the pyridinium betaine **14b** (240 mg, 0.57 mmol) was heated in toluene (20 cm^3) under reflux for 1.5 h. TLC analysis [SiO_2, EtOAc–MeOH (4:1)] showed a major product (R_f 0.6), no

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starting material (R_f 0.4) being observed. The solution was cooled to room temperature and evaporated under reduced pressure. The residue was chromatographed on silica gel using EtOAc–MeOH (95:5) as eluent to give 1-(4,6-dimethyl-2-pyridyl)-2-[*N*,*N*-bis(2-methyl-5-methylthio-1,2,4-triazol-3-yl)-aminopropene **11g** as a solid (170 mg, 71%). An analytical sample was obtained by recrystallisation from EtOAc–toluene, m.p. 139–141 °C (Found: C, 51.8; H, 5.8; N, 26.95%. $C_{12}H_{24}N_8S_2$ requires C, 51.9; H, 5.8; N, 26.95%); ν_{max}(Nujol)/cm^{-1} 1605, 1552, 1495, 1290, 765 and 720; δ_H(CD_2Cl_2) 2.03 (d, *J* 1, CH_3), 2.21 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 2.44 (s, 6 H, 2 × NCH_3), 3.50 (s, 6 H, 2 × NCH_3), 6.29 (d, 1 H, *J* 1 olefinic H), 6.74 (s, 1 H, pyridyl H) and 6.80 (s, 1 H, pyridyl H); *m*/*z* 416 (66%) ($M^{\cdot+}$) 273 (25), 248 (48), 170 (16), 146 (100), 145 (18), 131 (32) and 43 (22).

3-Amino-1,5,7-trimethyl-1,2,4-triazolo[4,3-a]*pyrimidinium Hydrobromide* **7d**.—1,5,7-Trimethyl-1,2,4-triazolo[4,3-*a*]pyrimidinium-3-benzyloxycarbonylaminide **7c** (0.62 g, 2 mmol) was dissolved in glacial acetic acid (2 cm^3) and the solution was treated with a solution of hydrogen bromide in acetic acid (35%; 2 cm^3). The mixture was stirred at room temperature for 24 h. TLC (SiO_2; 9:1 CH_2Cl_2–MeOH) showed complete reaction. The mixture was diluted with diethyl ether and the precipitate filtered off to afford the title compound as pale yellow plates (0.45 g, 87%), m.p. 283 °C (decomp.) (Found: C, 36.95; H, 4.7; N, 27.0; Br, 31.0. $C_8H_{12}BrN_5$ requires C, 37.22; H, 4.69; N, 27.13; Br, 30.96%); ν_{max}(Nujol)/cm^{-1} 3280, 3220, 3180, 1675, 1645 and 1605; δ_H(CD_3OD) 2.69 (s, 3 H, 7-CH_3), 3.01 (d, 3 H, *J* 1.0, 5-CH_3), 3.98 (s, 3 H, NCH_3), 7.17 (d, 1 H, *J* 1.0, 6-H).

Attempted Preparation of 1,5,7-*Trimethyl*-1,2,4-*triazolo*[4,3-a]*pyrimidinium*-3-*aminide* **7e**.—3-Amino,1,5,7-trimethyl-1,2,4-triazolo[4,3-*a*]pyrimidinium hydrobromide **7d** (0.5 g, 1.9 mmol) was suspended in dichloromethane (50 cm^3) and gaseous ammonia was passed into the mixture at room temperature for 2 h. The mixture was stirred overnight and the ammonium bromide filtered off. The filtrate was evaporated to give the triazole derivative **17a** as yellow needles (0.3 g, 80%), m.p. 184–186 °C (from toluene) (Found: C, 49.5; H, 7.35; N, 43.15. $C_8H_{14}N_6$ requires C, 49.45; H, 7.25; N, 43.25%); δ_H(CD_3OD) 1.97 (s, 3 H, CMe), 2.06 (s, 3 H, CMe), 3.46 (s, 3 H, NMe) and 4.77 (br s, 1 H, CH=).

X-Ray Crystal Structure Determination of the Maleate Salt of the Pyridinium Betaine **14b**.—*Crystal data.* $C_{22}H_{28}N_4O_3$, *M* = 532.6, orange prisms, triclinic, space group $P\bar{1}$ (No. 2), *a* = 11.4565 (25), *b* = 12.384 (4), *c* = 12.052 (4) Å, α = 114.96 (3), β = 107.642 (19), γ = 105.78 (3)°, *U* = 1309.6 Å^3, *Z* = 2, D_c = 1.351 g cm^{-3}, *F*(000) 560, μ(Mo-Kα) 2.36 cm^{-1}.

Data collection. The intensity data were collected on an Enraf–Nonius CAD4 diffractometer over the hemisphere (θ range: 1.50–25.0°; *h*: −13–+13, *k*: 0–+14, *l*: −14–+14) using graphite monochromated Mo-Kα X-radiation (λ 0.710 693 Å) and ω–2θ scanning. Of the 4609 unique data measured, 3128 had $I > 2\sigma(I)$ and were used in subsequent structural solution and refinement. The data were corrected for Lorentz and polarisation effects, but not for absorption.

Structure solution. The approximate locations of the non-hydrogen atoms were determined by direct methods (SHELXS-86).[13] The structure was refined by full-matrix least squares methods (SHELX76)[14] using anisotropic temperature factors for all the non-hydrogen atoms. The positions of all the hydrogen atoms, except the carboxylate hydrogen, were located from a series of difference Fourier maps. The located hydrogen atoms were included in the refinement process at idealised positions (d_{C-H} 0.95 Å) with fixed isotropic temperature factors (U_{iso} 0.10 Å^2), except for the amino hydrogen atom H(2N) whose positional parameters were allowed to refine as normal. At convergence, the discrepancy factors *R* and R_w were 0.049 and 0.083 respectively. The weighting scheme, $w^{-1} = [\sigma^2(F) + 0.0104(F)^2]$ was found to give satisfactory analyses of variance. The final difference Fourier map was essentially featureless (general noise level less that ±0.14 e Å^{-3}), apart from two peaks (*ca.* 0.34, 0.25 e Å^{-3}) in the region around the disordered maleate ion.

Incidental crystallographic calculations and compilation of tables were carried using the computer program CALC.[15] Lists of refined thermal parameters and hydrogen atom coordinates, are available from the Cambridge Crystallographic Data Centre.*

* For full details of the CCDC deposition scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1993, Issue 1.

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