Preparation of [1,2,4]triazoloquinazolinium betaines and molecular rearrangements of putative [1,2,4]triazolo[4,3-*a*][1,3,5]triazinium betaines

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3*H*-10λ^5-[1,2,4]Triazolo[4,3-*a*]quinazolin-10-ylium-1-aminides were prepared by treating 1-methyl-1-(4-methylquinazolin-2-yl)-4-(aryl)thiosemicarbazides with dicyclohexylcarbodiimide (DCC); the crystal and molecular structure of one such derivative has been investigated by X-ray crystallography. A quinazolinium-1-olate and a -thiolate analogue of the aminides have also been prepared. 2-(1-Methylhydrazino)-4,6-dimethyl-1,3,5-triazine was synthesised by condensing the free base derived from 1-methyl-1-aminoguanidine sulfate with ethyl *N*-acetylacetamidate. A series of thiosemicarbazides was prepared by treating the above hydrazine derivative with isothiocyanates. One such thiosemicarbazide was treated with DCC to afford a 1,2,4,6-tetraazahexadiene derivative. Thermal reaction of 1-(4,6-dimethyl-1,3,5-triazin-2-yl)-1,3-dimethyl-4-(phenyl)isothiosemicarbazide gave a product of dimerisation, the structure of which was elucidated by X-ray crystallography.

Introduction

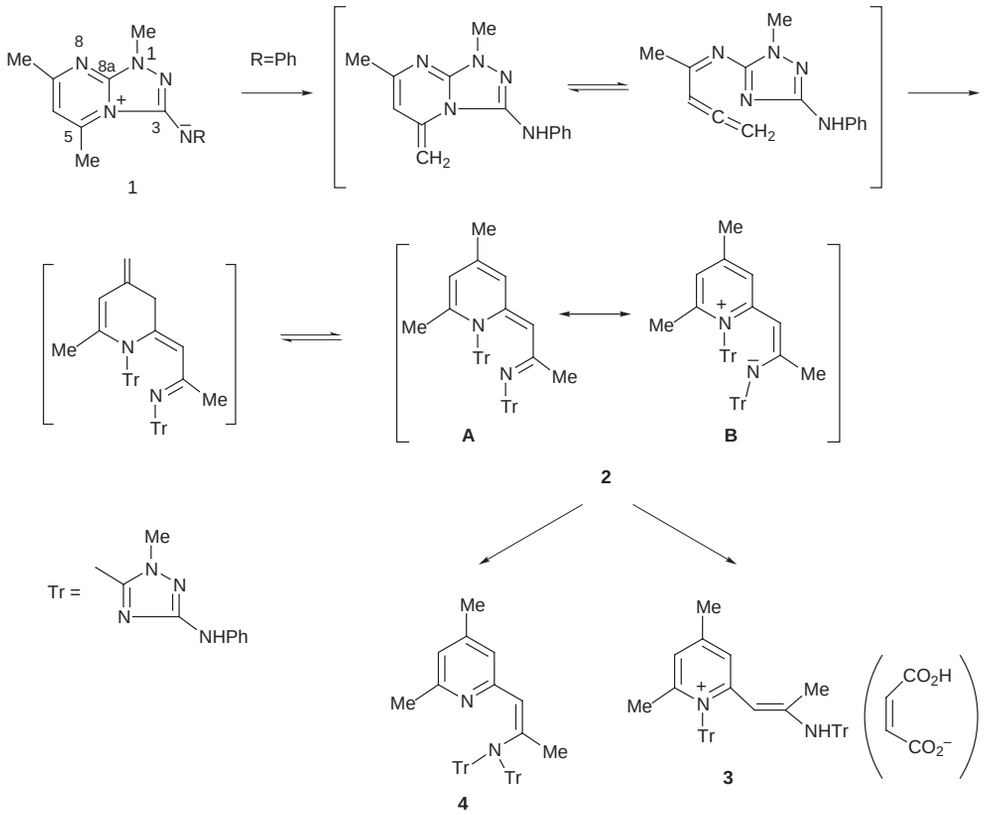
We have shown[1] that certain 1*H*-4λ^5-[1,2,4]triazolo[4,3-*a*]-pyrimidin-4-ylium-3-aminides (**1**, R = electron-withdrawing group) are stable and isolable whereas other (putative) compounds of this type in which R is not an electron-withdrawing group (*e.g.* **1**, R = Ph) are transformed into dimeric products, initially labile compounds [*e.g.* **2**, characterised through a crystalline maleate salt (**3**)] or products (*e.g.* **4**) arising from **2** by thermally induced isomerisation (see Scheme 1). We surmised[1] that a key feature of the dimerisation mechanism lay in the proximity of the aminide nitrogen atom and the 5-methyl substituent in the pyrimidinium ring. We subsequently discovered[2] that isosteric 1*H*-4λ^5-[1,2,4]triazolo[4,3-*c*]pyrimidin-4-ylium-3-aminides (**5**) and 1*H*-4λ^5-[1,2,4]triazolo[4,3-*a*]pyrazin-4-ylium-3-aminides (**6**) were stable and isolable, irrespective of whether the aminide substituent (R^2) was an electron-withdrawing group (*e.g.* CO_2Et) or otherwise (*e.g.* R^2 = Ph). We also examined the structure and electronic properties of condensed triazolium aminides of type (**1**) and related systems. It was concluded that bicyclic species (*cf.* **7**) that would ensue by proton transfer from the 5-methyl substituent to the aminide nitrogen are thermodynamically stable with respect to **1**, but that such a proton migration would be unlikely to proceed by a concerted intramolecular mechanism. In this work, we attempted the synthesis of aminides that are structurally analogous to 1*H*-4λ^5-[1,2,4]triazolo[4,3-*a*]pyrimidin-4-ylium-3-aminides (**1**), namely 3*H*-10λ^5-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-aminides (**8**), 1*H*-4λ^5-[1,2,4]triazolo[3,4-*b*]quinazolin-4-ylium-3-aminides (**9**) and 1*H*-4λ^5-[1,2,4]triazolo[4,3-*a*][1,3,5]triazin-4-ylium-3-aminides (**10**).

The present studies on the cyclodesulfurisation of (4-methylquinazolin-2-yl) thiosemicarbazides (**11c**–**i**) and a related compound (**11k**) are particularly relevant to the rearrangement described in Scheme 1 in two respects: first, they would give rise to annulated analogues of betaines (**1**); and secondly, they have the potential for two cyclization modes, one direction of which would be expected to provide an isolable aminide (*e.g.* **11c**→**8a**) whereas the other (*e.g.* **11c**→**9**) would possess the necessary features thought to promote dimerisation.

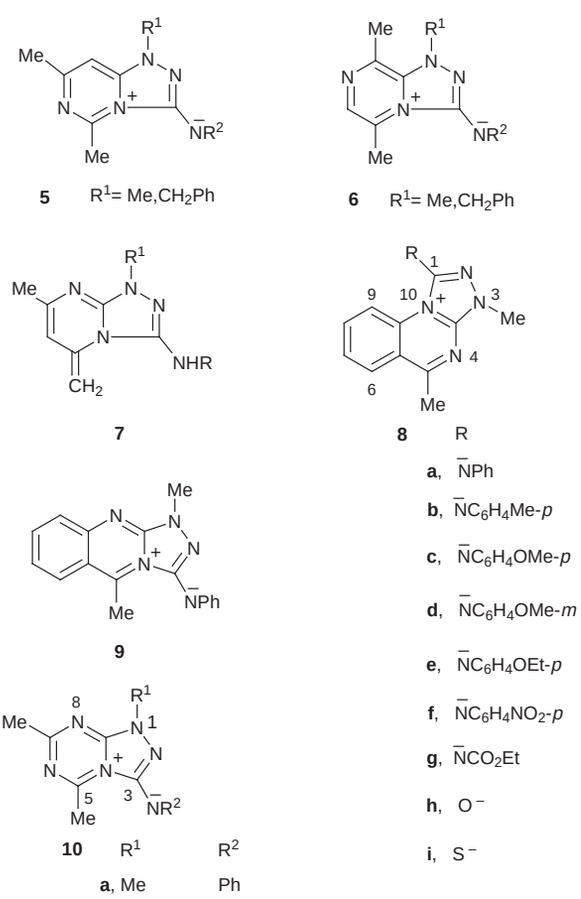
Results and discussion

3*H*-10λ^5-[1,2,4]Triazolo[4,3-*a*]quinazolin-10-ylium-1-aminides 8 and related compounds

2-(1-Methylhydrazino)-4-methylquinazoline (**11b**) was prepared in high yield from the chloro derivative (**11a**)[3] with methylhydrazine in ethanol. A series (**11c**–**i**) of thiosemicarbazides was then prepared routinely from the hydrazine derivative (**11b**) and the appropriate isothiocyanate derivative. An attempted synthesis of the desired quinazolinium-1-aminides (*cf.* **8**, **9**) by thermal cyclization of the isothiourea derivative (**11k**) [derived by base treatment of the methiodide (**11j**)][1] was unsuccessful; a complex product mixture was formed, and no pure products could be isolated. In contrast, treatment of the thiosemicarbazides (**11c**–**i**) with DCC in acetone at room temperature gave a series of purple (from **11c**–**g**), red (from **11h**) or yellow (from **11i**) solids (22–50% yield) for which analytical and routine spectral data (IR, ^{1}H NMR) suggested structure **8**. A characteristic feature in the ^{1}H NMR spectra of **8a**–**e** was a doublet at relatively low field (δ = 9.9–10.1 ppm) which was assigned to H(9) in structures **8a**–**e**. It is known, for example, that the 'bay area' protons in the ^{1}H NMR spectra of polynuclear aromatic hydrocarbons appear at low field (*e.g.* δ = 8.6 ppm in phenanthrene); of particular relevance to structure (**8**) is the condensed triazolium betaine (**12**) in which H_A is observed at δ 11 ppm.[4] Significantly, the ^{1}H NMR spectra of maleate salts of **8b** and **8f**



Scheme 1



show a shift to higher field of *ca.* 1 ppm in the resonance of H-9 in passing from the free base (δ *ca.* 10 ppm) to the salt (δ *ca.* 9 ppm). Formulation of the compounds as structure (**8**) was confirmed from X-ray crystallographic analysis of compound **8a**.

The crystal structure of the betaine **8a** consists of well separated 3*H*-10λ^5-triazolo[4,3-*a*]quinazolin-10-ylium aminide units (no significant intermolecular contacts within 3.4 Å). The molecular structure of **8a** is depicted in Fig. 1 together with the crystallographic numbering system adopted in this study.† The condensed heterocyclic ring system is not strictly planar with a pronounced fold at the junction between the quinazoline and triazole rings. Mean deviations from least-squares planes through the atoms of these rings were ±0.006 and ±0.002 Å, respectively, with an interplanar angle of 2.62(7)°. Since the *N*-phenyl ring only deviates from co-planarity with the triazole ring by 7.21(8)°, a high degree of π-conjugation is maintained throughout the molecule.

The low field chemical shift observed for 'bay area' proton H(4) can be rationalised by its geometrically enforced proximity to N(5) [H(4) · · · N(5) 2.34 Å] which places it in the deshielding zone associated with the phenylaminido moiety.

The C–N bond lengths around the triazole ring are generally intermediate between the expected values for single (1.45–1.47 Å) and double bonds (1.32–1.36 Å) except for that observed for the C(9)–N(2) which is more consistent with a single bond [1.432(2) Å]. The N(3)–N(4) bond also exhibits a high degree of single bond character [1.384(2) Å, *cf.* 1.41–1.44 Å for N–N single bond]. The N(4)–C(9)–N(5) bond angle [133.7(2)°] deviates substantially from trigonal geometry.

An additional interesting feature in the molecular structure of **8a** in respect of bond length alternation is the significance of canonical form **13** in describing the overall structure (see Fig. 1). The implication from relatively short bond lengths observed for N(3)–C(2) and C(9)–N(5) [1.325(2) Å and 1.314(2) Å, respectively] is that N(3) and N(4) are sites of relatively deficient and excessive electron density, respectively. It is notable that localisation of positive charge within the triazole, and not the pyrimidine ring has analogy in the molecular structure of the [1,2,4]triazolo[4,3-*a*]pyrimidin-1-ium-3-olate (**14**) which is best

† In the ensuing discussion of the structure, the crystallographic numbering system (see appropriate Figure) will be used.

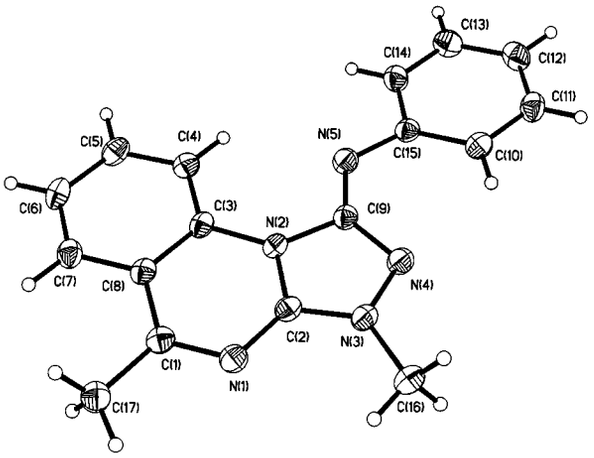
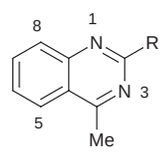
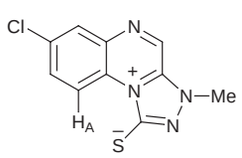


Fig. 1 The structure of betaine **8a** as determined by X-ray crystallographic analysis. The non-hydrogen atoms are represented by 50% probability ellipsoids and the hydrogen atoms by spheres of arbitrary radius.[12]



11 R
a, Cl
b, N(Me)NH_2
c, N(Me)NHCSNHPh
d, N(Me)NHCSNHC_6H_4Me-*p*
e, N(Me)NHCSNHC_6H_4OMe-*p*
f, N(Me)NHCSNHC_6H_4OMe-*m*
g, N(Me)NHCSNHC_6H_4OEt-*p*
h, N(Me)NHCSNH$C_6H_4NO_2$-*p*
i, N(Me)NHCSNHCO_2Et
j, N(Me)NH=C(SMe)NHPh (I)$^-$
k, N(Me)N=C(SMe)NHPh



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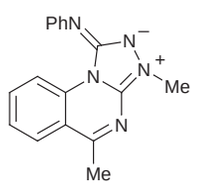

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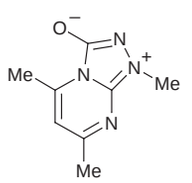

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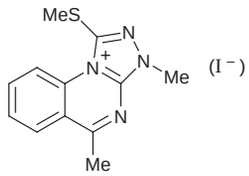
represented, in the solid state at least, by canonical structure **14**;[5] the results of molecular orbital calculations[2] also suggest that aminides analogous to **14**, and closely related compounds, are also best considered as condensed triazolium betaines with both positive and negative charges associated with the triazole ring.

The synthesis of triazolo[4,3-*a*]quinazolin-10-ylium-1-aminides (**8a**–**f**) was accompanied by the formation in each case of colourless compounds in variable yield (5–43%). The latter had poor solubility in common organic solvents (*e.g.* $CHCl_3$, EtOH) but were soluble in DMSO. Analytical data and FAB mass spectra suggested that they were dimeric in respect of the triazoloquinazolinium betaine structures (*cf.* **8**, **9**) [*e.g. m*/*z* 607 for the molecular ion of the compound derived from **11d**], but it has been impossible to ascertain their molecular structure from spectral data (IR, ^{1}H and ^{13}C NMR; see Experimental section for data on the compound described above); it also proved impossible to obtain a crystal suitable for X-ray analysis either of the parent 'dimers' or simple derivatives (*e.g.* picrate, sulfate, hydrobromide or maleate salts). The detailed chemistry of 'dimer' formation remains unclear, but it remains possible that triazolo[3,4-*b*]quinazolinium aminides (*cf.* **9**) are intermediates.

In contrast to certain [1,2,4]triazolo[4,3-*a*]pyrimidinium-3-



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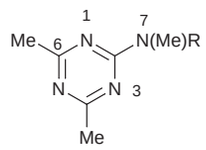
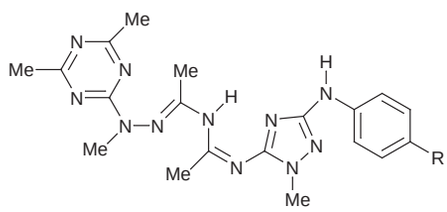


16 R
a, NH_2
b, NHCSNHPh
c, $NHCSNHC_6H_4NO_2$-*p*
d, $NHCSNHCO_2Et$
e, NHCSNHCOPh
f, N=C(SMe)NHPh



17 R
a, H
b, NO_2

aminides, analogous 3-olates and 3-thiolates (*cf.* **1**, O^- or S^- for N^-R) do not dimerise. It was, therefore, of interest to attempt the synthesis of such compounds in the condensed quinazolinium series (*cf.* **8**, **9**). Treatment of the hydrazine derivative (**11b**) in conventional fashion[5] with either triphosgene or (separately) carbon disulfide gave the desired compounds (**8h**, **i**) in 51 and 68% yields, respectively. Their structural assignment was based on the presence in ^{1}H NMR spectra of a low field doublet that can be assigned to the bay area H(9) proton (δ 9.3 and 11.2 ppm, in **8h** and **8i**, respectively); significantly, the low field doublet (δ 11.2 ppm) is absent in the ^{1}H NMR spectrum of the closely related triazoloquinazolinium salt (**15**), obtained in the present work by treating the thiolate (**8i**) with methyl iodide.

Attempted synthesis of 1*H*-4λ^5-[1,2,4]triazolo[4,3-*a*][1,3,5]-triazin-4-ylium-3-aminides (10)

The key synthetic precursor for the triazinium aminides (**10**), 2-(1-methylhydrazino)-4,6-dimethyl-1,3,5-triazine (**16a**), was prepared in 46% yield by generating the free base from 1-methyl-1-aminoguanidine sulfate,[6] and treating it with ethyl *N*-acetylacetimidate.[7] Reaction of the hydrazine derivative (**16a**) with the appropriate isothiocyanate derivative in *tert*-butyl methyl ether gave the triazinyl thiosemicarbazides (**16b**–**e**) in 71–79% yield. The ethoxycarbonyl derivative (**16d**) was unreactive under the normal[1,2] cyclodesulfurisation conditions (DCC, room temperature, 24 h) and attempts were then made to cyclise **16b** and **c**. The (phenyl)thiosemicarbazide (**16b**) was also consumed slowly (rt, 72 h) in the presence of *ca.* 1 molar excess of DCC, but the reaction was complete after 72 h at room temperature in the presence of an additional 2.6 mol equiv. of DCC. A product was isolated in 50% yield, spectral data for which (MS, ^{1}H and ^{13}C NMR) indicated that it was neither the desired condensed triazolium betaine (**10a**) nor a dimer (*cf.* **3** or **4**) that might have been anticipated by analogy with the process outlined in Scheme 1. Microanalytical and mass spectral data indicated a molecular formula of $C_{19}H_{25}N_{11}$ but it proved impossible to definitively ascertain the structure from NMR and IR spectroscopy. The structural problem was resolved by X-ray crystallographic analysis (see structure **17a** and Fig. 2) and the product arising from the reaction of **16c**

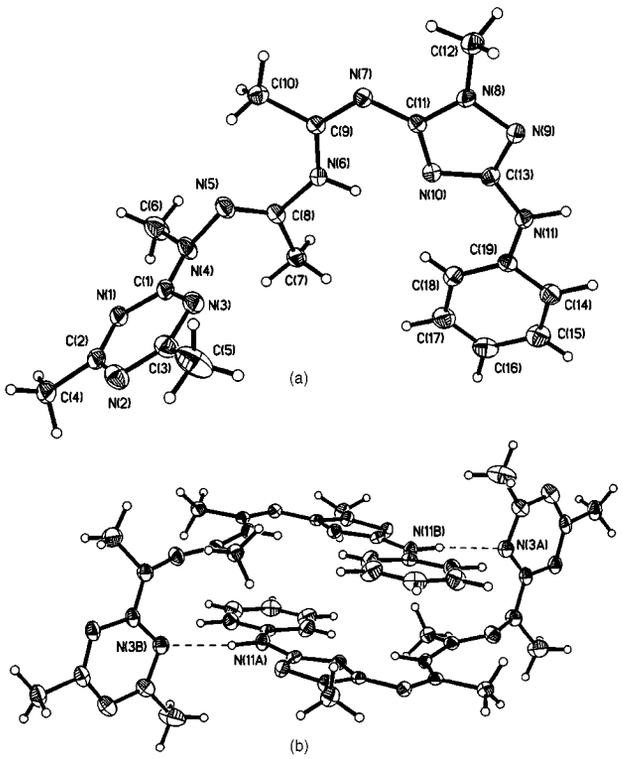


Fig. 2 The structure of 1,2,4,6-tetraazidine **17a** as determined by X-ray crystallographic analysis. The non-hydrogen atoms are represented by 50% probability ellipsoids and the hydrogen atoms by spheres of arbitrary radius.[12]

with DCC was assigned as **17b** from comparative NMR spectral data.

The molecular structure of the unusual 1,2,4,6-tetraazadiene derivative **17a**, as determined by X-ray crystallography, is depicted in Fig. 2 together with the crystallographic numbering system adopted in this study (Fig. 2a).† In the solid state, molecules of **17a** form dimers grouped about a crystallographic inversion centre and are held together by an intermolecular hydrogen bond between H(11) and N′(3) [H(11)···N′(3) 2.13 Å] (Fig. 2b).

The C–N bond lengths around the 1,3,5-triazine and 1,2,4-triazole rings lie between the expected values for single and double bonds consistent with delocalised heterocyclic ring systems. The N(8)–N(9) bond of the triazole ring is slightly longer than that in **8a** [1.397(3) *cf.* 1.384(2) Å]. In the acyclic portion of **17a**, the values of the C–N bond lengths suggest that N(5)–C(8) and N(7)–C(9) are consistent with localised double bonds [1.286(4) and 1.301(3) Å, respectively] whereas the N(6)–C(8) and N(6)–C(9) bonds [1.390(3) and 1.378(3) Å, respectively] have a high degree of single bond character. The value of the N(4)–N(5) bond distance [1.444(3) Å] would correspond to a pure N–N single bond.

Molecules of **17a** adopt a conformation in which the 1,3,5-triazine ring lies almost orthogonal with respect to the remainder of the molecule [interplanar angle of 86.87(5)° for planes through {C(1)–C(3), N(1)–N(4)} and {N(5)–N(11), C(8), C(9), C(11)–C(19)}]. As a result, the π-system in **17a**, which could potentially be fully conjugated, is disrupted at the N(4)–N(5) bond though this conformation would seem to provide an optimal arrangement for the intermolecular hydrogen bonding interactions described above.

There is an intramolecular hydrogen bond between H(6) and N(10) [H(6)···N(10) 1.89 Å] which presumably stabilises the observed stereochemical relationship between the acyclic side-chain and the triazole ring.

In a formal sense, products **17a** and **b** can be considered to arise from nucleophilic attack of N(8) of the thiosemicarbazide

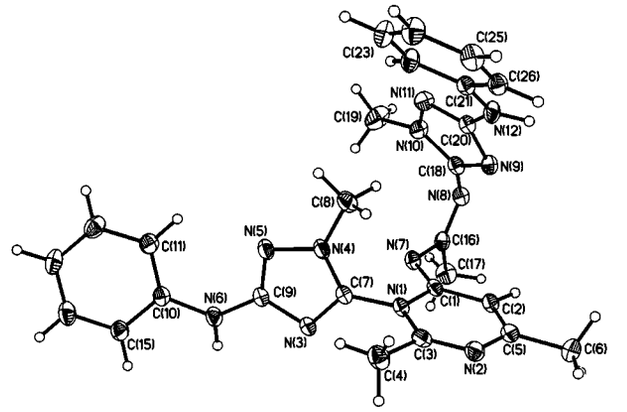
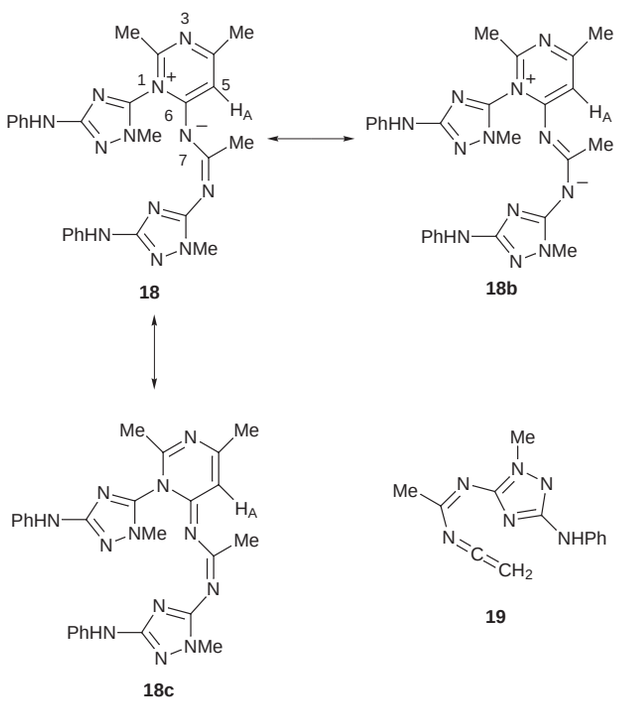


Fig. 3 The structure of pyrimidine derivative **18** as determined by X-ray crystallographic analysis. The non-hydrogen atoms are represented by 50% probability ellipsoids and the hydrogen atoms by spheres of arbitrary radius.[12].



(**16b**) at C(5) of the putative triazinium betaine (**10a**) with ensuing loss of phenyl isothiocyanate, and whilst such nucleophilic ring-opening reactions of analogous triazolium betaines (*e.g.* **5**) are documented, we have no evidence in this work for the reaction intermediates. No further studies of this extraordinary triazole synthesis were carried out, and the alternative method[1] of triazole formation was investigated. Thus the thiosemicarbazide (**16b**) was converted routinely[1] into **16f** and the latter was heated under reflux in toluene. A complex mixture was formed from which a pure product was isolated in 18% yield. The $M^{\cdot+}$ + 1 ion (*m*/*z* 509) in the FAB mass spectrum of this compound indicated a molecular weight (508) twice that anticipated for the 'monomeric' triazolium betaine structure **10a**, and the ^{1}H NMR spectrum was complex with evidence for the existence of rotamers. This structure was determined by X-ray crystallographic analysis (see structure **18** and Fig. 3).

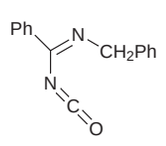
The molecular structure of 'dimeric' compound **18**, as shown in Fig. 3 along with the crystallographic numbering system, consists of a bis(triazole) linked by a pyrimidine and an amidine group.† One of the pendant phenyl groups [C(21)–C(26)] lies over the pyrimidine ring giving a U-shaped conformation, whilst the phenyl group at the opposite end of the molecule lies in the same plane (mean deviation from the plane, 0.138 Å) as its neighbouring triazole group [*cf.* **17a** above]. This plane is orthogonal [84.56(5)°] to the pyrimidine ring. There are several

intermolecular contacts between nitrogen and hydrogen atoms [N(6)···H(19C) 2.611(6), N(8)···H(26A) 2.571(3), N(9)···H(12A) 2.167(3) Å]. There are no significant intermolecular contacts involving the solvent molecule.

Structure **18** can be represented by a variety of canonical forms (see *e.g.* **18a**–**c**) but it is clear that the dihydropyrimidine formulation (**18c**) is the most significant, at least in the solid state. Thus N(2)–C(3), N(7)–C(1) and N(8)–C(16) possess considerable double bond character [1.282(3) and 1.288(3) and 1.290(3) Å, respectively] in contrast to N(1)–C(1) and N(7)–C(16) [1.406(3) and 1.390(3) Å] which are essentially single bonds.

With the detailed structure **18** to hand, the ^{1}H NMR data were clarified through COSY and NOESY spectra. Thus C-Me and N-Me resonances were assigned in three and two rotameric pairs, respectively, and the pyrimidine proton (H_A, see structure **18**) was assigned to the two resonances at δ 5.92 and 7.06 ppm. These data can be explained in terms of anisotropic effects within conformations of **18** that would arise through restriction of C6–N7 bond rotation (*cf.* **18a**↔**18c**).

It is interesting to speculate upon the mechanism of formation of this dimer in terms of the route to **2** in Scheme 1. An early intermediate would be a 1,3-diazabutadiene (**19**),[8] and whilst the formation of **18** would imply a regioselective dimerisative cyclisation, the yield is low, and the alternative isomer may be present but not isolated. Assuming that species **19** does exist as a reaction intermediate, its structure and reactivity have analogy in the chemistry of imidoyl isocyanates, certain derivatives of which undergo dimerisation through [4 + 2] cycloaddition (see *e.g.* **20**→**21**).[9] It is notable that **18**, the analogue of



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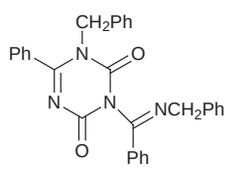

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2, is unreactive toward the subsequent thermal rearrangement experienced by **2** (see **2**→**4**).

Conclusions

The remarkable dimerisation of certain putative 1*H*-4λ^5-[1,2,4]triazolo[4,3-*a*]pyrimidin-4-ylium aminides (Scheme 1) is mimicked by an analogous triazinium betaine (**10a**) but not by the closely related pyrimidines **5**[2] and **6**[6]. It is interesting to note that the N4–C8a–N8 connectivity feature in aminides of type **1** is also present in **10a** but not in **5** and **6**. The unanticipated formation of triazoles (**17a**,**b**) from attempted synthesis of triazinium betaines (*cf.* **10**) suggests that the latter may be prone to ring-opening reactions promoted by nucleophilic attack at C(5). Further investigations are now underway on the synthesis and properties of aminides related to **1** in which the 1,2,4-triazole ring is replaced by heteroaromatic isosteres; chemical evidence, for example from trapping experiments, for the tentatively suggested azadiene (Scheme 1) and diazadiene intermediates (*e.g.* **19** from **10a**) is also desirable.

Experimental

Mps were determined on a Buchi 510 mp apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on Bruker AM-250 and -400 spectrometers with tetramethylsilane as internal standard. 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.

2-(1-Methylhydrazino)-4-methylquinazoline (11b)

Methylhydrazine (1.60 g, 36 mmol) was added to a solution of 2-chloro-4-methylquinazoline (**11a**) (3.20 g, 18 mmol) in ethanol (70 cm^3) and the mixture was stirred at room temperature for 6 h. The product was evaporated under reduced pressure and the residue recrystallized from hexane to give 2-(1-methylhydrazino)-4-methylquinazoline (**11b**) as yellow plates (3.1 g, 92%), mp 88–89 °C (Found: C, 63.8; H, 6.4; N, 29.6. $C_{10}H_{12}N_4$ requires C, 63.8; H, 6.4; N, 29.8%); ν_{max} (Nujol)/cm^{-1} 3250 (NH), 3130 (NH); δ_H (CD_2Cl_2) 2.75 (s, 3H, 4-CH_3), 3.45 (3H, s, NMe), 7.18 (ddd, 1H, J = 8.5, 1.3 and 0.6 Hz, H-6), 7.52 (ddd, 1H, J = 8.5, 1.3 and 0.6 Hz, H-8), 7.62 (ddd, 1H, J = 8.5, 6.5 and 1.3 Hz, H-7), 7.82 (ddd, 1H, J = 8.5, 1.3 and 0.6 Hz, H-5); *m*/*z* (EI) 188 (91%) ($M^{\bullet+}$), 173 (14), 172 (100), 145 (38), 144 (38), 143 (33), 130 (11), 129 (23), 128 (17), 117 (17).

General procedure for the preparation of 1-methyl-1-(4-methylquinazolin-2-yl)-4-substituted thiosemicarbazides (11c–i)

2-(1-Methylhydrazino)-4-methylquinazoline (**11b**) (4 mmol) and the appropriate isothiocyanate derivative (4 mmol) were stirred in diethyl ether (20 cm^3) at room temperature for 18 h. The resulting precipitate was separated by filtration and recrystallised to give the pure title compound. The following compounds were synthesised.

1-Methyl-1-(4-methylquinazolin-2-yl)-4-(phenyl)thiosemicarbazide (11c). Colourless solid (81%), mp 170–172 °C (decomp.) [from chloroform–hexane (1:1)] (Found: C, 63.55; H, 5.3; N, 21.35. $C_{17}H_{17}N_5S$ requires C, 63.15; H, 5.3; N, 21.65%) ν_{max} (Nujol) (cm^{-1}) 3340 (NH), 1616, 1575, 1563, 1520, 350; δ_H (CD_2Cl_2) 2.99 (s, 3H, 4-CH_3), 3.57 (s, 3H, NCH_3), 7.15–7.79 (m, 8H, Ar-H), 7.97–8.20 (m, 1H, H-5); *m*/*z* (EI) 290 (29%) $(M - SH)^+$, 189 (14), 188 (66), 173 (17), 172 (84), 145 (32), 144 (38), 143 (31), 136 (11), 135 (100), 130 (10).

1-Methyl-1-(4-methylquinazolin-2-yl)-4-(*p*-tolyl)thiosemicarbazide (11d). Colourless amorphous solid (93%), mp 269–270 °C (Found: C, 64.0; H, 6.0; N, 21.1; S, 9.9%. $C_{18}H_{19}N_5S$ requires C, 64.1; H, 5.7; N, 20.8; S, 9.5%); ν_{max} (KBr)/cm^{-1} 3315 (NH), 3180 (NH), 1616, 1538, 1468, 1170; δ_H ($CDCl_3$) 2.3 (3H, s, Ar-Me), 2.85 (3H, s, 4-Me), 3.55 (3H, s, NMe), 7.1 (2H, m, Ar-H), 7.35 (3H, m, Ar-H), 7.7 (1H, m, Ar-H), 7.9 (1H, m, Ar-H), 8.15 (1H, br s, NH), 8.55 (1H, br s, NH); *m*/*z* (FAB) 338 (73%) ($M^+ + 1$) 304 (100), 231 (19), 190 (37), 174 (32), 173 (43), 172 (32), 145 (24), 144 (28).

1-Methyl-1-(4-methylquinazolin-2-yl)-4-(*p*-methoxyphenyl)-thiosemicarbazide (11e). Colourless amorphous solid (99%), mp 179–181 °C (Found: C, 60.9; H, 5.7; N, 19.7; S, 9.5%. $C_{18}H_{19}N_5OS$ requires C, 61.2; H, 5.4; N, 19.8; S, 9.1%); ν_{max} (KBr)/cm^{-1} 3288 (NH), 3165 (NH), 2970, 1661, 1616, 1541, 1512, 1351, 1120, 1029; δ_H ($CDCl_3$) 2.85 (3H, s, 4-Me), 3.55 (3H, s, NMe or Ar-OMe), 3.8 (3H, s, NMe or Ar-OMe), 6.9 (2H, m, Ar-H), 7.4 (3H, m, Ar-H), 7.75 (2H, m, Ar-H), 7.9 (1H, m, Ar-H), 8.05 (1H, br s, NH), 8.4 (1H, br s, NH); *m*/*z* (FAB) 354 (29%) ($M^{\bullet+} + 1$) 320 (60), 189 (21), 174 (21), 173 (30), 172 (22), 169 (23), 144 (23).

1-Methyl-1-(4-methylquinazolin-2-yl)-4-(*m*-methoxyphenyl)-thiosemicarbazide (11f). Yellow amorphous solid (51%), mp 94–96 °C (Found: C, 61.0; H, 5.7; N, 19.5; S, 9.4%. $C_{18}H_{19}N_5OS$ requires C, 61.2; H, 5.4; N, 19.8; S, 9.1%); ν_{max}(KBr)/cm^{-1} 3280 (NH), 2957, 1564, 1037; δ_H ($CDCl_3$) 2.85 (3H, s, 4-Me), 3.55 (3H, s, NMe or OMe), 3.75 (3H, s, NMe or OMe), 6.7 (1H, m, Ar-H), 7.05 (1H, m, Ar-H), 7.15 (1H, m, Ar-H), 7.35 (2H, m, Ar-H), 7.7 (2H, m, Ar-H), 7.9 (1H, m, Ar-H), 8.55 (1H, br s, NH); *m*/*z* (FAB) 354 (50%) ($M^{\bullet+} + 1$), 320 (100), 189 (45), 174 (57), 173 (63), 172 (49), 145 (40), 144 (4), 77 (31).

1-Methyl-1-(4-methylquinazolin-2-yl)-4-(*p*-ethoxyphenyl)-thiosemicarbazide (11g). Colourless amorphous solid (89%), mp 148–149 °C (Found: C, 61.9; H, 6.1; N, 18.8; S, 8.8%. $C_{18}H_{21}N_5OS$ requires C, 62.1; H, 5.8; N, 19.1; S, 8.7%); ν_{max}(KBr)/cm^{-1} 3322 (NH), 3164 (NH), 2977, 1616, 1538, 1240, 1120, 1036; δ_H ($CDCl_3$) 1.4 (3H, t, J = 7 Hz, OCH_2CH_3), 2.85 (3H, s, 4-Me), 3.55 (3H, s, NMe), 4.0 (2H, q, J = 7 Hz, OCH_2CH_3) 6.85 (2H, m, Ar-H), 7.35 (3H, m, Ar-H), 7.75 (2H, m, Ar-H), 7.9 (1H, m, Ar-H), 8.05 (1H, br s, NH), 8.45 (1H, br s, NH); *m*/*z* (FAB) 368 (43%) (M^+ + 1), 335 (24), 334 (100), 231 (24), 189 (44), 174 (39), 173 (69), 172 (40), 145 (29), 144 (43).

1-Methyl-1-(4-methylquinazolin-2-yl)-4-(*p*-nitrophenyl)thiosemicarbazide (11h). Colourless amorphous solid (98%), mp 220 °C (from DMSO) (Found: C, 55.6; H, 4.5; N, 22.5; S, 8.7%. $C_{17}H_{16}N_6O_2S$ requires C, 55.4; H, 4.4; N, 22.8; S, 8.7%); ν_{max} (KBr)/cm^{-1} 3305 (NH), 3155 (NH), 2976, 1614, 1566, 1547, 1508, 1337, 1280; δ_H (d_6-DMSO), 2.85 (3H, s, 4-Me), 3.4 (3H, s, NMe), 7.3–8.3 (8H, m, Ar-H), 10.25 (1H, br s, NH), 10.35 (1H, br s, NH); *m*/*z* (FAB) 369 (86%) (M^+ + 1), 335 (100), 231 (27), 189 (30), 174 (37), 173 (71), 172 (49), 145 (39), 144 (48).

1-Methyl-1-(4-methylquinazolin-2-yl)-4-(ethoxycarbonyl)thiosemicarbazide (11i). Colourless amorphous solid (94%), mp 198–199 °C (decomp.) (from $CHCl_3$) (Found: C, 52.8; H, 5.4; N, 21.7; S, 10.4%. $C_{14}H_{17}N_5O_2S$ requires C, 52.7; H, 5.3; N, 21.9; S, 10.0%); ν_{max} (KBr)/cm^{-1} 3215 (NH), 2982, 1718 (C=O), 1616, 1592, 1570, 1522, 1483; δ_H ($CDCl_3$) 1.35 (3H, t, J = 7 Hz, OCH_2CH_3), 2.85 (3H, s, Me), 3.65 (3H, s, NMe), 4.3 (2H, q, J = 7 Hz, OCH_2CH_3), 7.3 (1H, m, Ar-H), 7.7 (2H, m, Ar-H), 7.9 (1H, m, Ar-H), 8.25 (1H, br s, NH); *m*/*z* (EI) 287 (14%), 286 (100), 240 (91), 172 (64), 145 (36), 144 (34), 143 (34).

Preparation of 1,3-dimethyl-1-(4-methylquinazolin-2-yl)-4-(phenyl)isothiosemicarbazide hydroiodide (11j)

Iodomethane (0.66 g, 4.65 mmol) was added to 1-methyl-1-(4-methylquinazolin-2-yl)-4-(phenyl)thiosemicarbazide (**11c**) (1.0 g, 3.1 mmol) in methanol (10 cm^3) and the mixture was stirred at room temperature for 24 h. The product was diluted with diethyl ether (5 cm^3), stirred for 30 min, and then filtered to give *1,3-dimethyl-1-(4-methylquinazolin-2-yl)-4-(phenyl)thiosemicarbazide hydroiodide* (**11j**) as bright yellow crystals (1.3 g, 90%), mp 180–182 °C (decomp.) (Found: C, 46.45; H, 4.40; N, 14.95. $C_{18}H_{20}N_5IS$ requires C, 46.3; H, 4.5; N, 15.0%); ν_{max}-($CHCl_3$) 3450–3000 (NH, br), 1660, 1630, 1530, 1510; δ_H [$(CD_3)_2CO$] 2.57 (s, 3H, SCH_3), 2.93 (s, 3H, 4-CH_3), 3.55 (s, 3H, NCH_3), 7.10–8.05 (m, 8H, Ar-H), 8.21–8.29 (m, 1H, H-5); *m*/*z* 337 (1%) (M − HI)$^{\bullet+}$, 291 (23), 290 (100), 289 (21), 288 (18), 215 (14), 173 (20), 172 (21).

General procedure for the reaction of 1-methyl-1-(4-methylquinazolin-2-yl)-4-substituted thiosemicarbazides (11c–h) with dicyclohexylcarbodiimide: formation of 3*H*-[1,2,4]triazolo[4,3-*a*]quinazolinium betaines (8a–f)

A mixture of the appropriate thiosemicarbazide derivative (**11c–i**) (1 mol equiv.) and dicyclohexylcarbodiimide (1.5 mol equiv.) in acetone (20 cm^3 g^{-1} of **11c–i**) was stirred at room temperature for seven days during which time a coloured precipitate formed. The mixture was filtered and the solid was reprecipitated from dichloromethane solution by addition of petroleum ether (bp 40–60 °C). The following compounds were isolated.

***N*-Phenyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-aminide (8a).** Purple amorphous solid (28%), mp 205–208 °C (Found: C, 70.6; H, 5.3; N, 24.1%. $C_{17}H_{15}N_5$ requires C, 70.6; H, 5.2; N, 24.2%); ν_{max} (KBr)/cm^{-1} 1614, 1588, 1561, 1530, 1497; δ_H ($CDCl_3$) 2.87 (s, 3H, 5-CH_3), 3.99 (s, 3H, NCH_3), 6.81–6.89 (m, 1H, Ar-H), 7.26–7.38 (m, 2H, Ar-H), 7.52 (ddd, J = 7, 1 Hz, 1H, H-7), 7.60–7.68 (m, 2H, Ar-H), 7.87–7.97 (m, 2H, H-6 and H-8), 10.21 (d, J = 9 Hz, 1H, H-9); *m*/*z* 289 (100) ($M^{\bullet+}$), 288 (84), 287 (27), 273 (11), 145 (123), 144 (12), 143 (25), 102 (11), 77 (13), 51 (10), 32 (35), 28 (144).

Evaporation of the filtrate gave a compound of unidentified structure believed to be derived from **8a**.

***N*-*p*-Tolyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-aminide (8b).** Purple solid (24%), mp 203–204 °C (Found: C, 71.1; H, 5.4; N, 23.2%. $C_{18}H_{17}N_5$ requires C, 71.3; H, 5.6; N, 23.1%); ν_{max}(KBr)/cm^{-1} 1632, 1563, 1532, 1502; δ_H ($CDCl_3$) 2.3 (3H, s, Ar-Me), 2.85 (3H, s, 5-Me), 3.95 (3H, s, NMe), 7.1 (2H, m, Ar-H) 7.5 (3H, m, Ar-H), 7.9 (2H, m, Ar-H), 10.1 (1H, d, J = 9 Hz H-9); *m*/*z* (FAB) 304 (100%) (M^+ + 1), 303 (40), 302 (8), 172 (5), 143 (6).

***N*-*p*-Methoxyphenyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo-[4,3-*a*]quinazolin-10-ylium-1-aminide (8c).** Purple solid (29%), mp 202–203 °C (Found: C, 67.7; H, 5.7; N, 22.2%. $C_{18}H_{17}N_5O$ requires C, 67.7; H, 5.4; N, 21.9%); ν_{max} (KBr)/cm^{-1} 1611, 1567, 1534, 1365, 1019; δ_H ($CDCl_3$) 2.85 (3H, s, 5-Me), 3.75 (3H, s, OMe), 3.95 (3H, s, NMe), 6.8–6.9 (2H, m, Ar-H), 7.4–7.6 (3H, m, Ar-H), 7.85–7.95 (2H, m, Ar-H), 10.1–10.2 (1H, d, J = 9 Hz, H-9); *m*/*z* (FAB) 320 (100%) (M^+ + 1), 319 (63), 304 (33), 100 (18).

***N*-*m*-Methoxyphenyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo-[4,3-*a*]quinazolin-10-ylium-1-aminide (8d).** Purple solid (37%), mp 214–215 °C (Found: C, 67.6; H, 5.4; N, 21.8%. $C_{18}H_{17}N_5O$ requires C, 67.7; H, 5.4; N, 21.9%); ν_{max}(KBr)/cm^{-1} 1627, 1559, 1532, 1496, 1241; δ_H ($CDCl_3$) 2.9 (3H, s, Ar-Me), 3.8 (3H, s, 5-Me), 4.05 (3H, s, NMe), 7.5–7.7 (1H, m, Ar-H), 8.0–8.1 (2H, m, Ar-H), 9.95 (1H, m, H-9); *m*/*z* (FAB) 320 (69%) (M^+ + 1), 150 (10), 100 (20).

***N*-*p*-Ethoxyphenyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo-[4,3-*a*]quinazolin-10-ylium-1-aminide (8e).** Purple solid (33%), mp 185–187 °C; δ_H ($CDCl_3$) 1.3–1.4 (3H, t, J = 7 Hz CH_2CH_3), 2.9 (3H, s, 5-Me), 4.0 (3H, s, NMe), 4.0 (2H, q, J = 7 Hz, CH_2CH_3), 6.8–6.9 (2H, m, Ar-H), 7.5–7.6 (3H, m, Ar-H), 7.9–8.0 (2H, m, Ar-H), 10.0 (1H, d, J = 9 Hz, H-9); *m*/*z* (FAB) 334 (100%) (M^+ + 1), 333 (19), 304 (16), 241 (25). This compound could not be purified to analytical standard because of slight contamination by dicyclohexylurea.

***N*-*p*-Nitrophenyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]-quinazolin-10-ylium-1-aminide (8f).** Red solid (50%), mp 203–204 °C (Found: C, 60.8; H, 4.5; N, 25.1%. $C_{17}H_{14}N_6O_2$ requires C, 61.0; H, 4.5; N, 25.1%) ν_{max} (KBr)/cm^{-1} 1612, 1554, 1515, 1272, 1105; *m*/*z* (FAB) 336 (16%) (M^+ + 1), 335 (66), 90 (33), 89 (45), 69 (43), 63 (62), 62 (41), 51 (58), 50 (73).

***N*-Ethoxycarbonyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-aminide (8g).** Yellow amorphous solid (22%), mp 140 °C (decomp.) (Found: C, 58.6; H, 5.0; N, 24.3%. $C_{14}H_{15}N_5O_2$ requires C, 58.9; H, 5.3; N, 24.5%); ν_{max} (KBr)/cm^{-1} 1646 (C=O), 1591, 1524, 1493; δ_H ($CDCl_3$) 1.35 (3H, t, J = 7 Hz, OCH_2CH_3), 2.95 (3H, s, 5-Me), 4.1 (3H, s, NMe), 4.25 (2H, q, J = 7 Hz, OCH_2CH_3), 7.63 (1H, m, H-7), 7.95 (1H, m, H-8), 8.6 (1H, m, H-6), 9.95 (1H, d, J = 9 Hz, H-9); *m*/*z* (FAB) 286 (75%) [$M^{\bullet+}$ + 1], 241 (16), 240 (100), 213 (16).

Preparation of the maleate salts of *N*-aryl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-aminides (8b and 8f)

The aminide derivatives (**8b** and **8f**) (0.3 mmol) were dissolved, separately, in dichloromethane (8 cm^3) and stirred with maleic acid (0.3 mmol) for 24 h.

For the reaction of **8b**, the purple solution turned gradually

yellow. The solution was evaporated under reduced pressure to leave the pure *maleate salt of* **8b** (65%), mp 168 °C (decomp.) (Found: C, 63.0; H, 5.3; N, 16.4%. $C_{22}H_{21}N_5O_4$ requires C, 63.0; H, 5.0; N, 16.7%); ν_{max} (KBr)/cm^{-1} 2500–3300 (OH), 1701 (C=O), 1620, 1540, 1356, 1192; δ_H ($CDCl_3$) 2.3 (3H, s, Ar-Me), 3.05 (3H, s, 5-Me), 4.1 (3H, s, NMe), 5.9 (2H, s, HC=CH), 7.35 and 7.1 (4H, 2 d, J = 8 Hz, A_2B_2 system of Ar-Me), 7.75 (1H, m, Ar-H), 8.05 (1H, m, Ar-H), 8.29 (1H, m, Ar-H), 9.0 (1H, d, J = 9 Hz, H-9), 11.05 (1H, br s, OH or NH); *m*/*z* (FAB) 304 (100%), 303 (17), 136 (17), 89 (10).

For the reaction of **8f**, the red solid gradually dissolved but eventually some orange material remained undissolved in an orange solution. The mixture was filtered and the filtrate was treated with petroleum ether (40–60 °C) causing the *maleate salt of* **8f** to precipitate as a peach solid (60%) mp 160 °C (decomp.) (Found: C, 55.7; H, 4.0; N, 18.7%. $C_{21}H_{18}N_6O_6$ requires C, 56.0; H, 4.0; N, 18.7%); ν_{max} (KBr)/cm^{-1} 2500–3300 (OH), 1714 (C=O), 1614, 1538, 1329, 1260, 1112; δ_H ($CDCl_3$) 3.1 (3H, s, 5-Me), 4.25 (3H, s, NMe), 6.05 (2H, s, HC=CH), 7.6 (2H, m, Ar-H), 7.8 (1H, m, Ar-H), 8.05 (1H, m, Ar-H), 8.2 (3H, m, Ar-H), 8.3 (1H, m, Ar-H), 8.95 (1H, d, J = 9 Hz, H-9); *m*/*z* (FAB) 335 (100) ($M^+ + 1$).

Preparation of 3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-olate (8h)

A solution of 2-(1-methylhydrazino)-4-methylquinazoline (**11b**) (1.00 g, 5.3 mmol) in dry dichloromethane (20 cm^3) was added dropwise over 15 min to a solution of triphosgene (0.523 g, 1.76 mmol) in dichloromethane (20 cm^3) at 5 °C. After complete addition, a bright yellow precipitate was formed. The mixture was stirred at room temperature for several days after which gaseous ammonia was bubbled through it for 15 min to basify it. The product was filtered and the filtrate was evaporated under reduced pressure to give a yellow solid. Chromatography of the residue on silica using MeOH–CH_2Cl_2 (2:98) as eluent afforded the title compound as a polar bright yellow solid (0.57 g, 51%), mp ~150 °C (decomp.); ν_{max} (KBr)/cm^{-1} 1683 (C=O), 1667, 1597, 1538, 1385, 1238, 793; δ_H ($CDCl_3$) 2.9 (3H, s, 5-Me), 3.95 (3H, s, NMe), 7.55 (1H, m, Ar-H), 7.9 (1H, m, Ar-H), 8.0 (1H, m, Ar-H), 9.3 (1H, d, J = 9 Hz, H-9); *m*/*z* (EI) 214.0824 (80%). $C_{11}H_{10}N_4O$ requires 214.0855 ($M^{\cdot+}$); 172 (45), 143 (100), 74 (42).

Preparation of 3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-thiolate (8i)

A solution of 2-(1-methylhydrazino)-4-methylquinazoline (**11b**) (1.0 g, 5.3 mmol) and carbon disulfide (4.05 g, 0.053 mmol) in acetonitrile (25 cm^3) was stirred at room temperature for 3 days. The product was filtered and the solid material was washed with petroleum ether (bp 60–80 °C) to afford the orange *title compound* (**8i**) (0.83 g, 68%), mp 312–314 °C; ν_{max} (KBr)/cm^{-1} 1682, 1618, 1560, 1543, 1377, 1347, 1200, 1129; δ_H ($CDCl_3$) 3.0 (3H, s, 5-Me), 4.1 (3H, s, NMe), 7.6–8.2 (3H, m, Ar-H), 11.2 (1H, d, J = 9 Hz, H-9); *m*/*z* (EI) 230.062 (5%). $C_{11}H_{10}N_4S$ requires 230.063 ($M^{\cdot+}$); 188 (81), 172 (90), 144 (50).

Preparation of 3,5-dimethyl-1-methylthio-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium iodide (15)

A suspension containing 3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo-[4,3-*a*]quinazolin-10-ylium-1-thiolate (**8i**) (0.10 g, 0.43 mmol) and methyl iodide (0.09 g, and 0.43 mmol) in tetrahydrofuran (10 cm^3) was stirred at room temperature for 24 h. The product was filtered and the solid was washed with dichloromethane to afford the orange *title compound* (**15**) (0.13 g, 80%), mp 200 °C (decomp.); ν_{max} (KBr)/cm^{-1} 1650, 1602, 1550, 1508, 1232; δ_H (d_6-DMSO) 3.0 (3H, s, 5-Me or S-Me); 3.2 (3H, s, 5-Me or S-Me), 4.2 (3H, s, NMe), 8.05 (1H, m, Ar-H), 8.4, (1H, m, Ar-H) 8.7 (2H, m, Ar-H); *m*/*z* (EI) 244.078 (55%). $C_{12}H_{12}N_4S^+$ requires 244.076; 244 (55), 229 (4), 142 (100), 127 (35).

2-(1-Methylhydrazino)-4,6-dimethyl-1,3,5-triazine (16a)

1-Methyl-1-aminoguanidine sulfate[6] (5.0 g, 18.2 mmol) was suspended in anhydrous propan-2-ol (100 cm^3) and the stirred suspension treated with sodium methoxide (2.0 g, 37.0 mmol) in portions at room temperature. The mixture was stirred for 15 min. and then diluted with *tert*-butyl methyl ether (300 cm^3). The mixture was cooled to 0 °C and treated with a solution of ethyl *N*-acetylacetimidate[7] (4.80 g, 37.0 mmol) in *tert*-butyl methyl ether (50 cm^3) over 10 min. The mixture was allowed to warm to room temperature and stirred overnight. The product was filtered and the filtrate was evaporated under reduced pressure to leave a semi-solid residue. The residue was digested with hot hexane (40 cm^3) and the solids removed by filtering the hot mixture. The hexane solution was evaporated under reduced pressure to leave the title compound as a colourless crystalline solid (2.58 g, 46%), mp 75–77 °C (Found: C, 47.2; H, 7.3; N, 45.6%. $C_6H_{11}N_5$ requires C, 47.0; H, 7.2; N, 45.7%); δ_H (CD_2Cl_2) 2.34 (6H, s, 4-CH_3 and 6-CH_3), 3.31 (3H, s, NCH_3), 4.57 (2H, br s, NH_2).

General method for the preparation of triazinyl thiosemicarbazides (16b–e)

To a solution of 2-(1-methylhydrazino)-4,6-dimethyl-1,3,5-triazine (**16a**) (1 mol equiv.) in *tert*-butyl ether at room temperature was added the appropriate isothiocyanate (1 mol equiv.). The mixture was stirred at room temperature overnight and the precipitated products collected by filtration. The crude products were recrystallised from ethanol to give the following compounds.

1-(4,6-Dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(phenyl)thiosemicarbazide (16b). Colourless needles (79%), mp 191–193 °C (Found: C, 54.2; H, 5.6; N, 29.1; S, 11.3%. $C_{13}H_{16}N_6S$ requires: C, 54.1; H, 5.6; N, 29.15; S, 11.1%); δ_H ($(CD_3)_2CO$) 2.38 (6H, s, 4-CH_3, and 6-CH_3), 3.45 (3H, s, N-CH_3), 7.13–7.63 (5H, m, Ph), 9.04 (1H, br s, NH), 9.42 (1H, br s, NH).

1-(4,6-Dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(*p*-nitrophenyl)thiosemicarbazide (16c). Pale buff crystals (72%), mp 212–214 °C (Found: C, 46.7; H, 4.55; N, 29.3; S, 9.7%. $C_{13}H_{15}N_7O_2S$ requires: C, 46.8; H, 4.5; N, 29.4; S, 9.6%); δ_H (d_6-DMSO) 2.40 (6H, s, 4-CH_3 and 6-CH_3), 3.38 (3H, s, N-CH_3), 7.92–8.23 (m, 4H, Ar-H), 10.17 (1H, br s, NH), 10.35 (1H, br s, NH).

1-(4,6-Dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(ethoxycarbonyl)thiosemicarbazide (16d). Colourless needles (77%), mp 194–195 °C (Found: C, 42.2; H, 5.7; N, 29.4; S, 11.3%. $C_{10}H_{16}N_6O_2S$ requires: C, 42.2; H, 5.7; N, 29.6; S, 11.3%); δ_H (CD_2Cl_2) 1.31 (3H, t, 7 J Hz, CH_2CH_3), 2.42 (6H, s, 4-CH_3 and 6-CH_3 3.47 (3H, s, N-CH_3), 4.26 (2H, q, 7 J Hz, CH_2CH_3), 8.73 (1H, br s, NH), 11.23 (1H, br s, NH).

1-(4,6-Dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(benzoyl)thiosemicarbazide (16e). Colourless plates (1.55 g, 41%), mp 155–157 °C (Found: C, 53.1; H, 5.15; N, 25.6; S, 10.4%. $C_{14}H_{16}N_6OS$ requires C, 53.15; H, 5.1; N, 26.6; S, 10.1%), δ_H (CD_2Cl_2) 2.42 (s, 6H, 4-CH_3 and 6-CH_3), 3.52 (s, 3H, NCH_3), 7.49–7.90 (m, 5H, Ph), 9.41 (br s, 1H, NH), 12.39 (br s, 1H, NH).

Reaction of 1-(4,6-dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(phenyl)thiosemicarbazide (16b) with dicyclohexylcarbodiimide. Formation of 1,2,4,6-tetraazahexadiene derivative 17a

1-(4,6-Dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(phenyl)thiosemicarbazide (**16b**) (0.50 g, 1.73 mmol) in acetone (60 cm^3) was treated with a solution of dicyclohexylcarbodiimide (0.36 g,

2.60 mmol) in acetone (10 cm^3). The mixture was stirred at room temperature for 72 h after which TLC analysis (SiO_2 9 : 1 CH_2Cl_2–MeOH) showed incomplete reaction. Additional dicyclohexylcarbodiimide (0.36 g, 2.60 mmol) was added and stirring at room temperature was continued for a further 72 h until the starting material (**16b**) was consumed (TLC analysis). The precipitated solid was collected by filtration, washed with acetone (10 cm^3) and dried *in vacuo* at 40 °C to afford the 1,2,4,6-tetraazadiene derivative **17a** as a white solid (0.21 g, 50%), mp 206–208 °C (Found: C, 55.85; H, 6.2; N, 37.8%. $C_{19}H_{25}N_{11}$ requires C, 56.0; H, 6.2; N, 37.8%). ν_{max} (Nujol)/cm^{-1} 3277 (NH), 1662, 1614, 1564; δ_H (CD_2Cl_2) 1.74 and 1.98 (2 × s (rotamers), 3H, C-CH_3), 2.35 (s, 6H, 2 × triazine CH_3), 2.46 and 2.64 (2 × s (rotamers), 3H, C-CH_3), 3.36 and 3.41 (2 × s (rotamers), 3H, N-CH_3), 3.69 and 3.75 (2 × s (rotamers), 3H, N-CH_3), 6.77 and 7.05 (2 × br s (rotamers), 1H, NH), 6.87–7.54 (m, 5H, Ph), 11.63 and 12.07 (2 × br s (rotamers), 1H, NH); *m*/*z* (EI) 408 (100%) (M^+), 154 (26%).

Reaction of 1-(4,6-dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(*p*-nitrophenyl)thiosemicarbazide (16c) with dicyclohexylcarbodiimide. Formation of 1,2,4,6-tetraazahexadiene derivative 17b

A solution of 1-(4,6-dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(*p*-nitrophenyl)thiosemicarbazide (**16c**) (0.50 g, 1.5 mmol) in acetone (100 cm^3) was treated with a solution of dicyclohexylcarbodiimide (0.47 g, 2.25 mmol) in acetone (10 cm^3) and the mixture stirred at room temperature for 25 h. The resulting yellow solution was evaporated under reduced pressure to a semi-solid residue. This residue was triturated with acetone and the resulting solid was separated, washed with acetone and dried *in vacuo* at 40 °C to afford the 1,2,4,6-tetraazadiene derivative **17b** as a yellow solid (0.18 g, 40%), mp 212–213 °C (Found: C, 50.4; H, 5.4; N, 37.0. $C_{19}H_{24}N_{12}O_2$ requires: C, 50.4; H, 5.35; N, 37.15%). δ_H (CD_2Cl_2) 1.59 and 1.99 [2 × s (rotamers), 3H, C-CH_3], 2.36 (s, 6H, 2 × triazine CH_3), 2.47 and 2.64 [2 × s (rotamers), 3H, C-CH_3] 3.37 and 3.41 [2 × s (rotamers) 3H, N-CH_3], 3.73 and 3.78 [2 × s (rotamers), 3H, N-CH_3], 7.54–8.22 (m, 5H, 4 × Ar-H + NH), 11.41 and 12.28 [2 × br s (rotamers)], 1H, NH).

1-(4,6-Dimethyl-1,3,5-triazin-2-yl)-1,3-dimethyl-4-(phenyl)isothiosemicarbazide (16f)

A solution of 1-(4,6-dimethyl-1,3,5-triazin-2-yl)-1-methyl-4-(phenyl)thiosemicarbazide (**16b**) (2.00 g, 6.94 mmol) in tetrahydrofuran (100 cm^3) was treated with iodomethane (1.48 g, 10.0 mmol) and the mixture was stirred at room temperature for 72 h. The mixture was evaporated under reduced pressure and the residue was partitioned between methylene chloride (50 cm^3) and saturated aqueous $NaHCO_3$ (25 cm^3). The organic phase was washed with saturated aqueous $NaHCO_3$ (25 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to afford the crude product as a viscous oil that crystallised on standing (2.37 g). This product was purified by column chromatography (SiO_2 using 95% EtOAc–5% MeOH eluant) to afford the *title compound* (**16f**) as a white solid (1.54 g, 73%), mp 108–110 °C (from *t*-BuOMe) (Found: C, 55.6; H, 6.0; N, 27.8; S, 10.7%. $C_{14}H_{18}N_6S$ requires C, 55.6; H, 6.0; N, 27.8; S, 10.6%); δ_H (CD_2Cl_2) 2.38 (s, 6H, 2 × triazine CH_3), 2.41 and 2.43 (2 × s, 3H, S-CH_3), 3.34 and 3.37 (2 × s, 3H, N-CH_3), 6.84–7.36 (m, 6H, Ph, NH).

Thermolysis of 1,3,5-triazine derivative 16f. Formation of pyrimidine derivative 18

A solution of 1-(4,6-dimethyl-1,3,5-triazin-2-yl)-1,3-dimethyl-4-(phenyl)isothiosemicarbazide (**16f**) (0.92 g, 3.04 mmol) in anhydrous toluene (25 cm^3) was heated under reflux for 72 h, after which TLC analysis showed no residual starting material. The mixture was concentrated *in vacuo* to a dark gum. The crude product was purified by column chromatography on SiO_2 (20.0 g) using 9 : 1 ethyl acetate–methanol as eluant to afford the pyrimidine derivative **18** as a pale yellow solid (0.14 g, 18%), mp 209–210 °C (from EtOAc) (Found: C, 61.0; H, 5.6; N, 32.9%. $C_{26}H_{28}N_{12}$ requires: C, 61.4; H, 5.55; N, 33.05%); δ_H (CD_2Cl_2) 2.11 and 2.27 (2 × s, 3H, C-Me rotamers), 2.18 and 2.27 (2 × s, 3H, C-Me rotamers), 2.19 and 2.26 (2 × d, 3H, C-Me rotamers), 3.26 and 3.57 [2 × s, 3H, N-Me (rotamers)], 3.48 and 3.62 [2 × s, 3H, N-Me (rotamers)], 5.92 and 7.06 [2 × s, 1H, H-5 (rotamers)], 6.96, 7.00 and 7.15 [3 × s, 2H, 2 × NH (rotamers)], 6.78–7.46 (m, 10H, 2 × Ph); δ_C (CD_2Cl_2) 22.9, 23.3, 23.5, 24.4, 24.7, 25.4, 34.20, 34.29, 35.23, 35.27, 106.3 and 107.4 (C-5), 116.7, 117.2, 120.6, 121.6, 129.6, 129.8, 141.3, 142.4, 144.6, 149.3, 154.5, 157.3, 157.8, 158.4, 158.5, 159.7, 160.2, 162.3, 169.5, 171.6; *m*/*z* (FAB) 509 (100%) [M^+ + 1], 361 (60), 307 (58), 214 (59).

Crystal structure determination of *N*-phenyl-3,5-dimethyl-3*H*-10λ^4-[1,2,4]triazolo[4,3-*a*]quinazolin-10-ylium-1-aminide (8a)¶

An optically clear crystal of **8a**, having dimensions *ca.* 0.40 × 0.20 × 0.15 mm, was mounted in a Lindemann capillary tube and used subsequently for data collection.

Crystal data. $C_{17}H_{15}N_5$, M = 289.34, dark-red blocks, monoclinic, space group $P2_1/n$ (non-standard setting of No. 14), a 9.7511(7), b 7.3223(12), c 20.122(5) Å, β 101.377(12)° U 1408.5(4) $Å^3$, Z = 4, D_c 1.364 g cm^{-3}, F(000) 608, μ(Mo-Kα) 0.086 mm^{-1}.

X-Ray data collection and reduction. Following preliminary Weissenberg photography, the intensity data were collected on an Enraf-Nonius FAST area detector diffractometer (θ range: 2.06 to 24.85°; $-10 \le h \le 10$, $-8 \le k \le 5$, $-21 \le l \le 21$; temperature 140(2) K) using graphite monochromated Mo-Kα X-radiation (λ 0.71073 Å) and ω-scanning. Full details of the instrumental settings and the procedures used for data collection and cell refinement are published elsewhere.[10] Of the 2100 unique data (R_{int} = 0.068) measured, 1661 had $F > 4\sigma(F)$. The intensity data were corrected for Lorentz and polarisation effects, but not for absorption.

Structure solution and refinement. The approximate positions of the non-hydrogen atoms were determined by direct methods (SHELXS-86[11]). The structure was refined by full-matrix least-squares methods on F^2 (SHELXTL/PC[12]) using all F_o^2 data and anisotropic temperature factors for all the non-hydrogen atoms. All the hydrogen atoms groups were located on difference Fourier maps and included in the refinement process; the methyl groups were treated as idealised tetrahedra, which were allowed rotation about the C–C bond, with isotropic temperature factors for the hydrogen atoms (1.2 times U_{iso} of the bonded heavy atom). At convergence, the discrepancy factors R [$F_o > 4\sigma(F_o)$] and wR^2 were 0.044 and 0.103 respectively. The weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.0598P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$, was found to give satisfactory analyses of variance. The final difference Fourier map was essentially featureless (general noise level less than ±0.10 e $Å^{-3}$) with largest difference peak and hole of 0.25 and −0.21 e $Å^{-3}$ respectively.

Crystal structure determination of the 1,2,4,6-tetraazahexadiene derivative 17a

An optically clear crystal of **17a**, having dimensions *ca.* 0.20 × 0.15 × 0.10 mm, was mounted in a Lindemann capillary tube and used subsequently for data collection.

Crystal data. $C_{19}H_{25}N_{11}$, M = 407.50, colourless blocks, triclinic, space group $P\bar{1}$ (No. 2), a 8.023(2), b 11.419(2), c

¶ CCDC reference number 207/321. See http://www.rsc.org/suppdata/p1/1999/1517 for crystallographic files in .cif format.

11.582(2) Å, α 91.53(3), β 97.30(3), γ 105.76(3)°, U 1010.8(3) Å^3, $Z = 2$, D_c 1.339 cm^{-3}, $F(000)$ 432, μ(Mo-Kα) 0.089 mm^{-1}.

Much of the detail concerning the data collection, and structure solution and refinement is similar to that for (**8a**). The intensity data were collected on an Enraf-Nonius FAST area detector diffractometer (θ range: 1.78 to 24.94°; $-8 \le h \le 6$, $-13 \le k \le 12$, $-13 \le l \le 13$; temperature 120(2) K; Mo-Kα X-radiation; ω-scanning). Of the 2628 unique data ($R_{int} = 0.069$) measured, 1941 had $F > 4\sigma(F)$. At convergence of the refinement process, the discrepancy factors R [$F_o > 4\sigma(F_o)$] and wR^2 were 0.050 and 0.123 respectively.[12] The weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.0681P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$, was found to give satisfactory analyses of variance. The final difference Fourier map was essentially featureless (general noise level less than ±0.10 e Å^{-3}) with largest difference peak and hole of 0.37 and −0.27 e Å^{-3} respectively.

Crystal structure determination of the pyrimidine derivative 18

A small single crystal of **18** of approximate dimensions 0.050 × 0.030 × 0.02 mm was mounted on a glass wool fibre in perfluoropolyether oil.

Crystal data. $C_{26}H_{28}N_{12}\cdot CHCl_3$, $M = 627.97$, yellow plates, triclinic, space group $P\bar{1}$ (No. 2), a 9.576(7), b 12.716(9), c 13.076(9) Å, α 78.89(2), β 76.29(2), γ 78.57(2)°, U 1498.3(18) Å^3 (by least squares refinement of 70 reflections), $Z = 2$, D_c 1.384 g cm^{-3}, $F(000)$ 652, $\mu(\lambda = 0.6849$ Å) 0.345 mm^{-1}.

X-Ray data collection and reduction. The intensity data were collected at 160 K on a specially adapted Siemens SMART CCD area detector diffractometer located at Station 9.8 on the Daresbury Laboratory Synchrotron Radiation Source[13] with narrow frames (0.15° in ω) which covered a hemisphere of reciprocal space to a θ_{max} of 27.13°. Corrections were applied for incident beam decay. Of the 8345 reflections measured, 6089 were unique ($R_{int} = 0.027$) and 5189 had $F > 4\sigma(F)$.

Structure solution and refinement. The structure was solved by direct methods and refined by full matrix least squares against F^2 to R and wR^2 [$F_o > 4\sigma(F_o)$] = 0.0735 and 0.214, w^2 (all data) = 0.226.[11,12] The weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.1547P^2 + 1.194P]$ where $P = (F_o^2 + 2F_c^2)/3$, was found to give satisfactory analyses of variance. All non-hydrogen atoms were anisotropic and hydrogens were constrained to be riding on the heavy atom with U_{iso}(H) 1.2 × U_{eq}(C or N) for phenyl, pyrimidine and amine H atoms, and U_{iso}(H) 1.5 × U_{eq}(C) for methyl H atoms. A disordered chloroform molecule was present with two sites for the carbon atoms, each of which was assigned occupancies of 0.5. No H atoms were included in the solvent model.

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