Adenine isosteres with bridgehead nitrogen. Part 1. Two independent syntheses of the [1,2,4]triazolo[1,5-*a*][1,3,5]triazine ring system leading to a range of substituents in the 2, 5 and 7 positions

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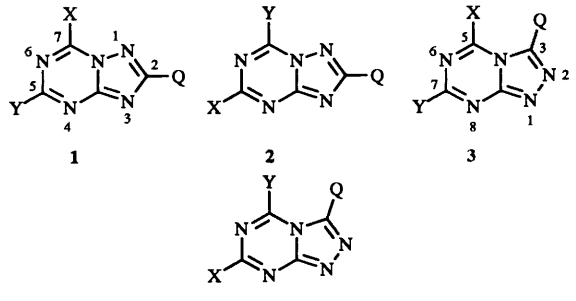
Condensation of a 3-substituted 5-amino-1,2,4-triazole with an *N*-cyanocarbonimidate $(RX)_2C{=}NCN$, yields the title compounds, in most cases as a mixture of isomers; separation and elaboration then gives [1,2,4]triazolo[1,5-*a*][1,3,5]triazines bearing a range of substituents in the 5 and 7 positions. Under milder reaction conditions, less stable isomeric products (*e.g.*, the [1,2,4]triazolo[4,3-*a*][1,3,5]triazine ring system or an uncyclised *N*-cyano intermediate) can be isolated and shown to rearrange to the [1,5-*a*] isomer. A second synthesis is described in which a suitably substituted 2-hydrazido-1,3,5-triazine is cyclodehydrated to give a single isomer with identical substituents in the 5 and 7 positions; the large difference in reactivity between these allows selective replacement at the 7-position with nucleophile. Additionally, the second synthesis is more readily adaptable to the introduction of substitutents at the 2 position of the bicyclic nucleus. 7 Amino-2-(2-furyl)-5-phenoxy[1,2,4]triazolo[1,5-*a*][1,3,5]triazine **12a** is prepared independently by both synthetic sequences and its structure verified by X-ray crystallographic analysis; ^{1}H NMR, ^{13}C NMR and MS data are also presented in support of the proposed structures.

The syntheses of [1,2,4]triazolo[1,5-*a*][1,3,5]triazines so far reported in the chemical literature have resulted in products (*e.g.*, **1** or **2**) in which the substituents in the 5 and 7 positions were either identical (X = Y) or not readily amenable to chemical elaboration (*e.g.*, XY = NR_2), or in some cases both.[1–8] As part of a programme of work around adenine isosteres, we required [1,2,4]triazolo[1,5-*a*][1,3,5]triazines in which either or both of the substituents in the 5 and 7 positions could be readily and, where appropriate, selectively replaced by nucleophiles. Particularly useful substituents would be the aryloxy or alkylsulfanyl groups, especially as the reactivity of the latter is profoundly influenced by the level of oxidation. Two ambident electrophiles, dimethyl *N*-cyanodithiocarbonimidate and diphenyl *N*-cyanocarbonimidate, have been used successfully to prepare a number of heterocyclic systems containing methylsulfanyl or phenoxy groups,[9–15] and therefore the reactions of these with 3-substituted 5-amino-1,2,4-triazoles **5–7** were investigated. In principle, reaction of such ambident electrophiles and nucleophiles could give rise to four isomeric products (**1–4**, X = NH_2, Y = MeS or PhO), representing two regioisomers of two possible ring systems, the [1,2,4]triazolo-[1,5-*a*]- and -[4,3-*a*]-[1,3,5]triazines; uncyclised adducts are also possible. The proportions of products **1–4** would be determined by a complex interplay of kinetic and thermodynamic factors, such as the relative reactivities of the N-1, N-4 and exocyclic NH_2 atoms of the aminotriazole, the relative stabilities of any intermediate (uncyclised) adducts, and the relative stabilities of the bicyclic products.



Isomeric [1,2,4]triazolo[1,5-*a*][1,3,5]triazines **1,2** and [1,2,4]triazolo-[4,3-*a*][1,3,5]triazines **3,4**

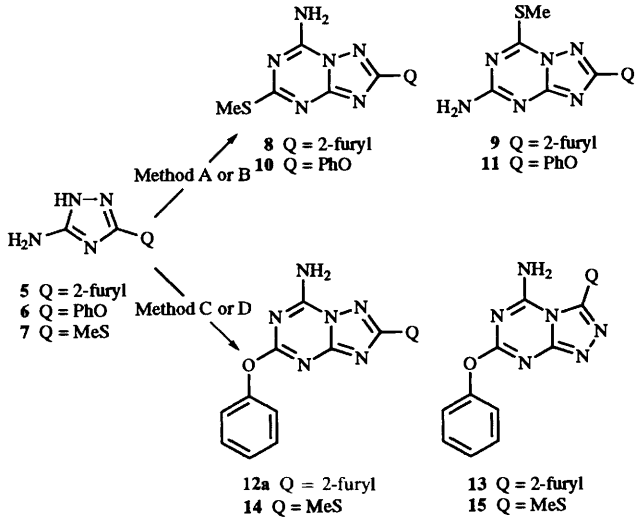
Reactions of 3-substituted 5-amino-1,2,4-triazoles with *N*-cyanocarbonimidates

The thermal reaction of 5-amino-3-(2-furyl)-1,2,4-triazole **5** with a 10% excess of dimethyl *N*-cyanodithiocarbonimidate (Scheme 1, Method A) produced a separable mixture of isomers in an approximate ratio of 5:1, which were shown by spectroscopic means to be regioisomers of the [1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine ring system, structures **8** and **9**, respectively. While the ratio of isomers varied, no significant difference was detected between performing the reaction as a melt or in refluxing xylenes, neither did the nature of substituent Q appear to affect the isomer ratio in any consistent way. Additionally, no thermal interconversion of regioisomers **8** and **9** was observed on heating of either isomer to its mp, decomposition being the only result. With Q = PhO, compounds **10** and **11** were obtained in approximately equal amounts, but not in synthetically useful yields, probably as a consequence of the thermal instability of both starting material and products.

By contrast, reaction of the preformed anion of substrate **5** with dimethyl *N*-cyanodithiocarbonimidate in a solvent at or below 0 °C (Method B) produced compound **9** as the sole product, albeit in modest yield.

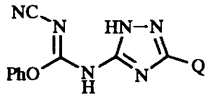
In an attempt to circumvent the somewhat forcing conditions required to effect cyclisation of the aminotriazoles with the bis(methylsulfanyl) reagent, the latter was replaced with the more reactive diphenyl *N*-cyanocarbonimidate. Thus, reaction of compound **5** with diphenyl *N*-cyanocarbonimidate in an aprotic solvent at, or slightly above, room temperature (Method

C) gave rise to a mixture of two isomers from which could be isolated the relatively unstable 5-amino-3-(2-furyl)-7-phenoxy-[1,2,4]triazolo[4,3-*a*][1,3,5]triazine **13**, the other component being the expected compound **12a**. The ratio of isomers was approximately 1 : 1, though this is presumably merely a function of the reaction time and temperature, and it is probable that the less stable [4,3-*a*] isomer would be converted completely into the [1,5-*a*] isomer with a longer reaction time. For Q = MeS, Method C gave rise exclusively to the less stable [4,3-*a*] isomer, plus a considerable amount of polymeric material. Alternatively, extended refluxing of the reaction mixture (Method D, Q = 2-furyl or MeS) gave compound **12a** or **14** as the sole product. The [4,3-*a*] isomers **13** and **15** were subsequently shown by TLC to rearrange smoothly to the more stable isomers **12a** and **14** either by refluxing in neat ethanol for a few minutes, or by refluxing in a less polar solvent [*e.g.*, acetonitrile or 1,2-dimethoxyethane (DME)] with a catalytic amount of base, the rearrangement again being essentially complete in a few minutes. Also, compound **13** was found to melt momentarily, resolidify, and then remelt at the mp of the corresponding, more stable isomer **12a**.



Scheme 1 *Reagents and conditions:* Method A: $(MeS)_2C{=}NCN$, 160 °C, no solvent, or $(MeS)_2C{=}NCN$, xylene, reflux. Method B: DMF, NaH, 0 °C, then $(MeS)_2C{=}NCN$; Method C: $(PhO)_2C{=}NCN$, MeCN or DME, room temp.; Method D: as C, reflux.

In the thermal reaction starting from dimethyl *N*-cyanodithiocarbonimidate no evidence was found for the existence of the [4,3-*a*] isomers **3** or **4**; presumably such compounds would rearrange spontaneously under the reaction conditions. At no stage in the synthetic sequences starting from diphenyl *N*-cyanocarbonimidate was evidence found for the existence of compounds corresponding to structures **2** or **4** (X = NH_2, Y = PhO), or to the uncyclised *N*-cyano structure **16**, which might be expected to cyclise under similar conditions to give [1,5-*a*] isomers, **12** or **14**.



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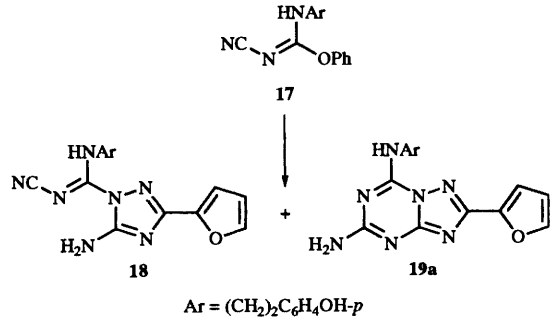
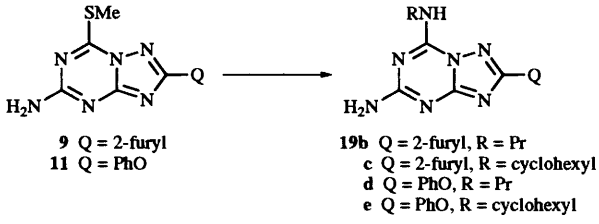
In order to explore the cyclisation in greater depth, we replaced one of the methylsulfanyl groups of the dimethyl *N*-cyanodithiocarbonimidate, or one of the phenoxy groups of the diphenyl *N*-cyanocarbonimidate, with an amine prior to reaction with the aminotriazole. However, the reaction of an *N*-cyanoisothiourea, MeS(NHR)C=NCN, with compound **5** did not proceed at a temperature below 200 °C; above this temperature decomposition took place and no products could be isolated. When an amino derivative **17** of diphenyl *N*-cyanocarbonimidate was used, not only was the expected isomer ***19a*** obtained, but also a previously undetected isomer, the uncyclised *N*-cyano compound **18** (*cf.* structure **16**) (Scheme 2), the structure of which was assigned by ^{13}C NMR and IR spectroscopy, and which cyclised to compound **19a** on being warmed in dil. ethanolic ammonia. The uncyclised compound again represents a relatively unstable intermediate (*cf.* Scheme 1) and its formation can be explained as a function of the reaction time and temperature.



Scheme 2 *Reagents and conditions:* **5**, MeCN, reflux

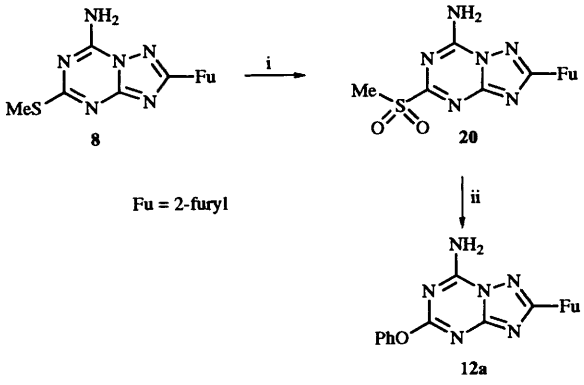
Reactions of the 5/7 methylsulfanyl groups of [1,2,4]triazolo-[1,5-*a*][1,3,5]triazines with nucleophiles

A profound difference in reactivity was found between the methylsulfanyl groups in positions 5 and 7 of the [1,2,4]-triazolo[1,5-*a*][1,3,5]triazine nucleus (*e.g.*, in compounds **8** and **9**); the 5-methylsulfanyl group was totally inert to amine nucleophiles, whereas the 7-methylsulfanyl could be replaced easily by refluxing in ethanol with the appropriate amine (Scheme 3) to give the 7-alkylamino compounds **19b–e**, analogous to that formed in Scheme 2.



Scheme 3 *Reagents and conditions:* RNH_2, EtOH, reflux

In order to enhance the reactivity of the 5-methylsulfanyl group of compound **8**, it was oxidised to the sulfone **20** by using 3-chloroperbenzoic (MCPBA) (Scheme 4). In practice, since attempts to oxidise compound **8** completely to the sulfone led to



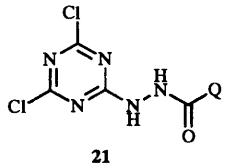
Scheme 4 *Reagents:* i, MCPBA, CH_2Cl_2; ii, phenol (excess), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), solvent

reduced yields, substitution reactions were routinely performed on a mixture of sulfoxide and sulfone. The sulfonyl group could be replaced by phenoxy by reaction with an excess of phenol in the presence of base to give a compound identical in all respects to compound **12a** formed as shown in Scheme 1.

Synthesis from 1,3,5-triazines

In view of the somewhat unpredictable outcome of the cyclisations of the necessarily unsymmetrical 1,2,4-triazoles, a synthetic route was sought in which cyclisation would take place onto a symmetrical intermediate, thus avoiding the problem of regioisomers. The intramolecular dehydrative and oxidative cyclisations of 2-hydrazino-1,3,5-triazines to give the [1,2,4]triazolo-[4,3-*a*]- or -[1,5-*a*]-[1,3,5]triazine ring systems are well documented in the literature,[2,4–6,8] although the substituents at the 4 and 6 positions of the triazine ring, ultimately positions 5 and 7 in the bicyclic products **1**–**4**, have invariably been groups of little synthetic utility. We therefore attempted to effect a synthetic sequence in which the C-4 and C-6 substituents were (a) identical, (b) amenable to nucleophilic attack in the cyclised product, and (c) stable to the cyclisation conditions.

The obvious choice of starting material would be 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride), but all attempts at cyclisation of compound **21** were unsuccessful, resulting only in decomposition of the starting material with no isolable products.

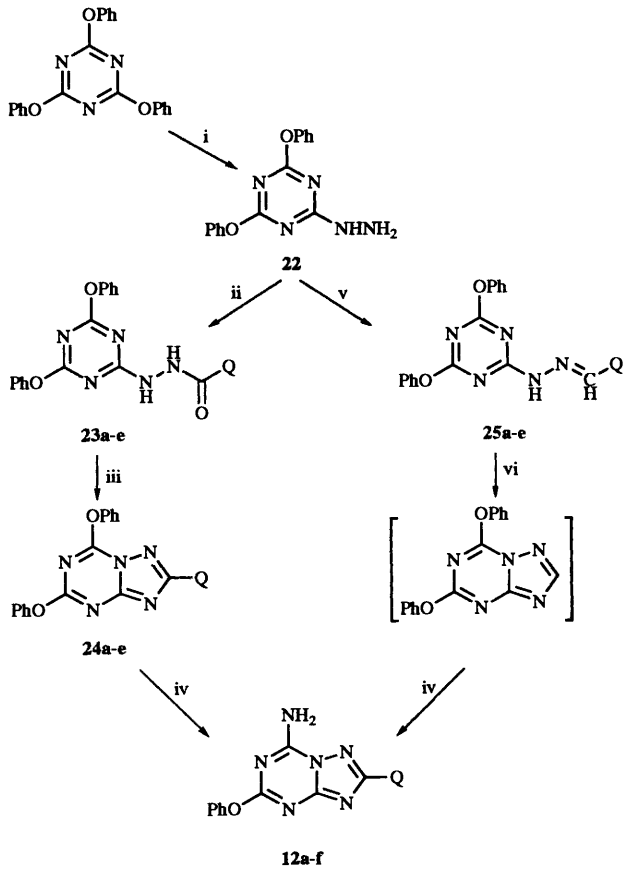


21

We next turned our attention to the readily available 2,4,6-triphenoxy-1,3,5-triazine, the substituents being considerably less labile than in the corresponding chloro compound, and yet still capable of undergoing nucleophilic displacement.[16] Thus, reaction with hydrazine hydrate gave, in good yield, the 2-hydrazino-4,6-diphenoxy-1,3,5-triazine **22** (Scheme 5), which was then treated with an acid chloride or anhydride to give the acyl hydrazides **23a**–**e**. Cyclisation of hydrazides **23a**–**e** under dehydrative conditions led to the key intermediate 2-substituted 5,7-diphenoxy[1,2,4]triazolo[1,5-*a*][1,3,5]triazines **24a**–**e**, which could be converted in refluxing ethanolic ammonia into the 7-amino derivatives **12a**–**e**, one of which (the 2-furyl compound **12a**) was shown to be identical with the compound prepared previously by the aminotriazole route and whose structure has been verified by X-ray crystallographic analysis.

Whilst the less stable [4,3-*a*] isomer must be an intermediate in the cyclodehydration of intermediate **23**, it presumably rearranges spontaneously under the conditions of the reaction, as no other product is evident in the reaction mixture. By contrast, oxidative cyclisation of the hydrazones **25a**, **f** gives a mixture (by TLC) from which no pure product can be isolated; instead, treatment of the crude reaction mixture with ethanolic ammonia leads directly to compounds **12a**, **f**, albeit in poor yield. The 2-(3-pyridyl) compound **12f** was prepared by the oxidative route as all attempts to prepare it by cyclodehydration were unsuccessful.

As well as giving a single bicyclic product, an additional feature of this synthetic route is that the group Q is introduced at a relatively late stage in the sequence, thus leading more easily to a range of analogues substituted at the 2-position. The yields obtained in the cyclisation of the acyl hydrazides **23** were dependent on the nature of the group Q; thus with Q = 2- or 3-pyridyl or 2-pyrrolyl none of the cyclised product was obtained. The oxidative cyclisation also failed with Q = 2-pyrrolyl, presumably because of the susceptibility of pyrrole to oxidation.



12a-f

Scheme 5 *Key:* **a**, Q = 2-furyl; **b**, Q = isoxazo-5-yl; **c**, Q = 3-methyl-isoxazol-5-yl; **d**, Q = 2-methyloxazol-4-yl; **e**, Q = CF_3; **f**, Q = 3-pyridyl. *Reagents and conditions:* i, Hydrazine hydrate, CH_2Cl_2; ii, QCOCl, CH_2Cl_2, Et_3N; iii, phosphorus pentaoxide, xylene, reflux **or** toluene-*p*-sulfonyl chloride, pyridine, 100 °C iv, ethanolic ammonia; v, QCHO, propan-2-ol; vi, lead tetraacetate (LTA), benzene or CH_2Cl_2.

Spectroscopic and X-ray crystallographic data

The foregoing syntheses of bicyclic products from monocyclic starting materials (*e.g.*, Schemes 1, 2 and 5) yield an array of ring- and regio-isomers, the structures of which are by no means apparent from the starting materials and the reaction conditions. Although mass spectroscopic and ^1H NMR data are suggestive of the precise structures (*vide infra*) they are by no means conclusive and only an analysis of the ^{13}C spectra of selected compounds, followed by an X-ray crystallographic analysis of the unifying compound **12a** allowed unambiguous structural assignments to be made.

The main feature of the ^1H NMR spectra of the regioisomers of the [1,2,4]triazolo[1,5-*a*][1,3,5]triazines is that the protons of an amino group in the 5 position group typically resonate at δ 6.5–7.0 as a broad singlet, while those of a 7-amino group resonate at δ 8.0–10.0 as a broad doublet which coalesces on heating of the sample. The doublet results from the coplanarity of the 7-amino group with the ring system and the consequent deshielding of one of the protons. This coplanarity is confirmed by the X-ray diffraction data (*vide infra*).

The first step in analysing the ^{13}C NMR data was to assign unambiguously the four ring-carbon atoms, aided by the multiplicity of these signals in their ^1H-coupled ^{13}C spectra. The signal for the triazole carbon atom always appears as a broad singlet when Q = 2-furyl, due to coupling from the furyl ring protons. All other carbon signals appear as sharp singlets except

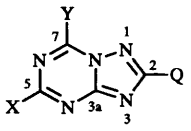
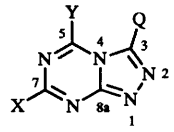



Table 1 ^{13}C Chemical shifts for regioisomers of [1,2,4]triazolo-[1,5-*a*]- and -[4,3-*a*]-[1,3,5]triazines

Compound	X	Y	Q	C-2	C-3a	C-5	C-7
8	SMe	NH_2	2'-furyl	156.19 (br s)	157.16 (s)	173.34 (q)	149.56 (s)
9	NH_2	SMe	2'-furyl	156.84 (br s)	151.54 (s)	160.53 (s)	160.98 (q)
12a	PhO	NH_2	2'-furyl	156.79 (br s)	158.86 (s)	164.97 (s)	151.98 (s)
24a	PhO	PhO	2'-furyl	158.04 (br s)	160.08 (s)	164.35 (s)	154.93 (q)
14	PhO	NH_2	SMe	166.70 (q)	158.92 (s)	164.80 (s)	151.05 (s)
15	PhO	NH_2	SMe	138.21 (q) (C-3)	157.43 (s) (C-8a)	164.42 (s) (C-7)	152.25 (s) (C-5)

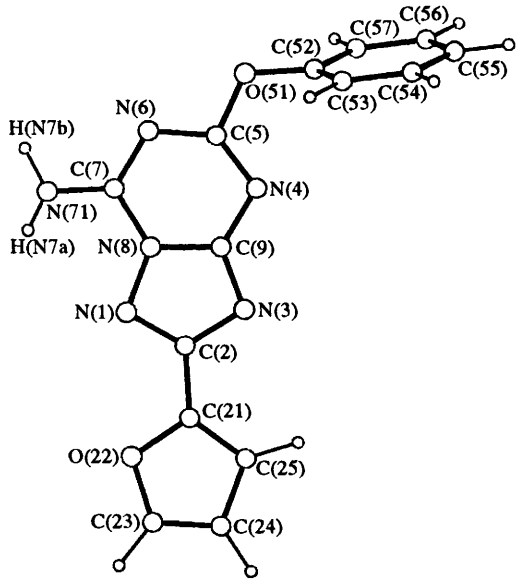


Fig. 1 The X-ray molecular structure of compound **12a**, with crystallographic numbering scheme

when substituted with a methylsulfanyl group (quartet). Thus we can assign unambiguously C-2 (or C-3 in **15**) from its multiplicity.

Comparison of a series of compounds reveals that one carbon always resonates in a very small range between δ_C 157.1 and 160.1 and is assigned to C-3a; an unambiguous assignment of C-5 and C-7 will allow us to characterise the regioisomers at these positions (*i.e.*, compounds **8** and **9**). It is well established in nitrogen heterocycles[17] that a carbon atom between two sp^2 nitrogen atoms resonates at lower field than one between an sp^2 and an sp^3 nitrogen atom. Hence, taking into account substituent chemical-shift effects, signals for C-5 should in general appear at lower field than those for C-7, the shift difference being of the order of 10 ppm. Thus, C-5 and C-7 in compound **24a**, both bearing PhO substituents, appear at δ_C 164.35 and 154.93, respectively ($\Delta\delta$ = 9.42 ppm). The ^{13}C NMR data for compound **12a** are consistent with the proposed structure (confirmed by X-ray analysis), with chemical shifts very similar to those of compound **24a**, the largest shift difference being that for C-7 with PhO replaced by NH_2.

In general, when X or Y = NH_2 or PhO, C-5 resonates in the range δ_C 160–165, with C-7 in the range δ_C 149–155. This observation allows us to distinguish between the regioisomers **8** and **9** since the signals for carbon atoms bearing the amino substituent appear in these chemical-shift ranges (C-5 in **9** at δ_C 160.53, C-7 in **8** at δ_C 149.56). Also, the carbon atoms bearing the SMe group, C-5 in **8** and C-7 in **9**, show the predicted shift difference, their lower-field shift values being the consequence of the greater deshielding of the methyl sulfanyl group (see Table 1).

The pair of ring isomers **14** and **15** are readily distinguished by the chemical shifts of their triazole ring carbon atoms C-2 or C-3. Both isomers show similar shifts for the triazine ring, whilst the triazole ring carbon atom (C-3) in isomer **15** appears at much higher field ($\Delta\delta$ = 28.5 ppm). This shift difference is much greater than those normally seen in azole systems[17] but compares reasonably well with that reported[18] for 1,2,4-triazolo[1,5-*a*]pyrimidones (C-2 = 163 ppm) and their [4,3-*a*] analogues (C-C = 143 ppm, $\Delta\delta$ = 20 ppm).

The structure of the uncyclised *N*-cyano compound **18** was assigned from the presence of a cyano carbon signal at δ_C 113.80, which would not be present in any cyclised structures.

The X-ray single-crystal structure analysis of compound **12a** confirms that the molecular structure is as postulated (Fig. 1). The atoms of the fused ring system are coplanar to within 0.03 Å; the two pendant rings, however, adopt very different conformations: the furyl ring is nearly coplanar with the fused rings (with a dihedral angle of 5.8°) while the phenyl ring is almost orthogonal to the fused rings (dihedral angle 74.8°). The atoms of the amino group are coplanar, indicating delocalisation between the lone pair of electrons of the amino nitrogen atom and the ring system, and the short N(71)–C(7) bond length of 1.315 Å is consistent with this. The molecules of compound **12a** exist as centrosymmetric hydrogen-bonded dimers in the solid state [H(N7b) · · · N(6′) 2.08 Å] (see Fig. 2).

Experimental

^1H NMR spectra were recorded on a Bruker AM200 spectrometer at 200 MHz, and ^{13}C spectra on a Bruker AC250 spectrometer at 250 MHz; spectra were run in $(CD_3)_2SO$ ($[^2H_6]$DMSO) with addition of $[^2H_4]$acetic acid where necessary for reasons of clarity or elucidation. Mass spectra were recorded under alternating EI-CI conditions on a VG 70-250 SE spectrometer. Microanalyses were performed on a Perkin-Elmer PE 2400 automatic analyser.† Mps were obtained on a Buchi oil-bath-type Melting Point apparatus, and are uncorrected. Flash chromatography was performed

† The unusually high nitrogen content of the compounds sometimes led to an overestimate of the carbon content, which was often 0.3–0.6% *higher* than the theoretical value; this problem was later corrected by using a high-N standard for calibration. Additionally, the final products often contained variable and non-stoichiometric amounts of solvent and/or water which was difficult to remove even on prolonged drying.

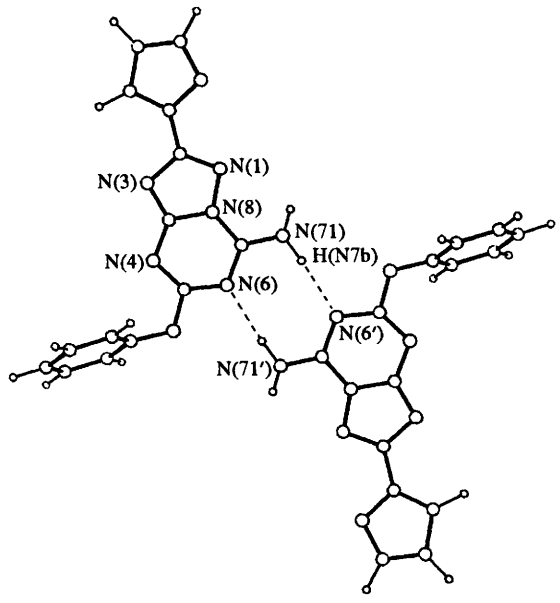


Fig. 2 The centrosymmetric dimer in the solid-state structure of compound **12a** formed by hydrogen bonding between an amino H-atom and an N(6)-atom of the triazine ring (crystallographic numbering scheme is shown)

using Merck 9385 silica as the stationary phase, typically at a pressure of 3–5 psi (2067–3445 Pa).

5-Amino-3-(2-furyl)-1,2,4-triazole 5

Hydrogen chloride gas (20 g) was bubbled into an ice-cooled solution of 2-furonitrile (46.5 g) in absolute ethanol (30 cm^3). The solid which crystallised out was filtered off, and heated in pyridine (300 cm^3) with aminoguanidine nitrate (56.0 g) under reflux for 4 h. The mixture was cooled, any solid material was removed by filtration, and the filtrate was evaporated to give crude product, to which was added nitric acid (400 cm^3 of 50% v/v). The crystalline nitrate salt was filtered off, and washed sequentially with water (100 cm^3) and ethanol (50 cm^3). The free base was regenerated by addition of sodium carbonate to a hot aqueous suspension of the salt; the basic solution was allowed to cool, to give the title compound **5** as prisms, mp 204–206 °C; δ 6.05 (2 H, br s), 6.6 (1 H, s), 6.7 (1 H, s), 7.7 (1 H, s) and 12.05 (1 H, br s).

5-Amino-3-phenoxy-1,2,4-triazole 6

Hydrazine hydrate (5 cm^3, 0.1 mol) was added to a stirred suspension of diphenyl *N*-cyanocarbonimidate (24 g, 0.1 mol) in absolute ethanol (500 cm^3) and the resulting solution was stirred at ambient temperature for 2 h. The solvent was evaporated off under reduced pressure and the residue was chromatographed on silica, and eluted with ethyl acetate, to give the compound **6** as a solid (15 g, 85%); an aliquot was crystallised from *tert*-butyl acetate to give title compound **6** as prisms, mp 118–120 °C (Found: C, 54.5; H, 4.7; N, 32.1. $C_8H_8N_4O$ requires C, 54.5; H, 4.6; N, 31.8%); δ 6.0 (2 H, br s), 7.0–7.2 (3 H, m), 7.2–7.4 (2 H, m) and 11.45 (1 H, br s); *m/z* 177 (MH^+).

7-Amino-2-(2-furyl)-5-methylsulfanyl[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine 8 (Method A)

An intimate mixture of 5-amino-3-(2-furyl)-1,2,4-triazole **5** (342 g, 2.28 mol) and dimethyl *N*-cyanodithio(imino)carbonate (367.6 g, 2.52 mol) was heated with mechanical stirring at 180 °C in a stream of argon for 1 h. The reaction mixture was cooled, ground up, and refluxed in a mixture of dichloromethane (4 dm^3) and methanol (1.5 dm^3) for 0.5 h. The suspension was then filtered through a bed of Celite, and silica gel (1.6 kg) was added to the filtrate. The solvent was removed under reduced pressure and the resulting solid was chromatographed batchwise, with elution with dichloromethane containing increasing amounts (0–50%) of ethyl acetate. This gave compound **8** as a pale yellow solid (200 g, 35%); an aliquot was crystallised from ethanol to give title compound **8** as prisms, mp 238–240 °C (Found: C, 44.0; H, 3.3; N, 33.7; S, 13.1. $C_9H_8N_6OS$ requires C, 43.6; H, 3.2; N, 33.9; S, 12.9%); δ 2.5 (3 H, s), 6.7 (1 H, dd), 7.2 (1 H, d), 7.7 (1 H, d) and 8.7–9.0 (2 H, br d); *m/z* 248 and 249 (M^+ and MH^+).

5-Amino-2-(2-furyl)-7-methylsulfanyl[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine 9 (Method A)

Further elution of the above column with dichloromethane containing ethyl acetate (30–50%) gave compound **9** as a pale yellow solid (30 g, 7%); crystallisation from methanol gave title compound **9** as pale yellow prisms containing methanol of crystallisation (0.125 mol equiv.), mp 254–257 °C (Found: C, 43.25; H, 3.3; N, 33.0; S, 12.4. $C_9H_8N_6OS$·0.125 MeOH requires C, 43.4; H, 3.6; N, 33.3; S, 12.7%); δ2.7 (3 H, s), 3.2 (s, MeOH), 6.7 (1 H, dd), 7.15 (1 H, d), 7.65 (2 H, s) and 7.9 (1 H, d); *m/z* 248 (M^+).

5-Amino-2-(2-furyl)-7-methylsulfanyl[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine 9 (Method B)

To a solution of compound **5** (1.5 g, 0.01 mol) in dimethylformamide (DMF) (25 cm^3) was added sodium hydride (550 mg of a 50% dispersion, 0.011 mol), and the mixture was stirred at room temp. for 1 h. The suspension was then cooled to −40 °C and dimethyl *N*-cyanodithio(imino)carbonate (1.6 g, 0.011 mol) was added in one portion. The solution was stirred for 3 h, warmed to room temp., and quenched with water (200 cm^3) and HCl (1 mol dm^{-3}; 10 cm^3, 1 mol equiv.). The suspension was extracted with ethyl acetate (2 × 50 cm^3) and the extracts were dried ($MgSO_4$), and evaporated under reduced pressure to give a yellow gum (1.5 g). Chromatography on silica and elution with dichloromethane containing methanol (2.5%) gave the title compound 9 (500 mg, 20%), identical in every respect with that prepared by Method A.

7-Amino-5-methylsulfanyl-2-phenoxy[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine 10 (Method A)

An intimate mixture of compound **6** (15.8 g, 0.09 mol) and dimethyl *N*-cyanodithio(imino)carbonate (14.6 g, 0.1 mol) was fused at 140 °C; work-up identical with that for compound **8** followed by chromatography (silica; dichloromethane–ethyl acetate 5%) gave compound **10** as a solid (3.5 g, 14%). Crystallisation from ethanol gave title compound **10** as prisms, mp 227–229 °C (Found: C, 48.6; H, 3.7; N, 30.4; S, 11.7. $C_{11}H_{10}N_6OS$ requires C, 48.2; H, 3.7; N, 30.6; S, 11.7%); δ 2.5 (3 H, s), 7.2–7.5 (5 H, m) and 8.3–8.9 (2 H, br d); *m/z* 275 (MH^+).

5-Amino-7-methylsulfanyl-2-phenoxy[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine 11 (Method A)

Further elution of the above column with dichloromethane–ethyl acetate 10% gave compound **11** as a pale yellow solid (4.85 g, 20%); crystallisation from ethanol gave title compound **11** as needles, mp 172–174 °C (Found: C, 48.2; H, 3.7; N, 30.6; S, 11.7. $C_{11}H_{10}N_6OS$ requires C, 48.2; H, 3.7; N, 30.6; S, 11.7%); δ2.6 (3 H, s), 7.2–7.3 (3 H, m), 7.4–7.5 (2 H, m) and 7.65 (2 H, br s); *m/z* 275.

7-Amino-2-(2-furyl)-5-phenoxy[1,2,4]triazolo[1,5-*a*][1,3,5]-triazine 12a (Method C)

A solution of compound **5** (7.5 g, 0.05 mol) and diphenyl *N*-cyanocarbonimidate (13.6 g, 0.06 mol) in acetonitrile (250 cm^3) was stirred at ambient temperature for 3 days; some starting

material remained so the mixture was refluxed for 15 min. The solvent was evaporated off under reduced pressure and the residue was chromatographed on silica, and eluted with dichloromethane–ethyl acetate 5%. After removal of some unchanged diphenyl *N*-cyanocarbonimidate, compound **12a** was isolated as a solid (1.85 g, 12.5%); crystallisation from ethanol gave title compound **12a** as prisms containing ethanol of crystallisation (0.67 mol equiv.), mp 250–252 °C (Found: C, 57.1; H, 4.6; N, 25.8. $C_{14}H_{10}N_6O_2 \cdot 0.67\ C_2H_6O$ requires C, 56.7; H, 4.3; N, 25.9%); δ 1.1 and 3.5 (t and q, solvent), 6.7 (1 H, dd), 7.3 (1 H, d), 7.2–7.3 (3 H, m), 7.4–7.5 (2 H, m), 7.9 (1 H, d) and 8.8–9.2 (2 H, br d); *m/z* 294 (MH^+).

X-Ray structure determination of compound 12a

A sample of the compound was recrystallised from ethyl acetate, to give crystals of suitable dimensions free of solvent of crystallisation.

Crystal data. $C_{14}H_{10}N_6O_2$, M = 294.27. Monoclinic, space group *C*2/*c*, *a* = 17.106(3), *b* = 8.540(2), *c* = 21.135(4) Å; β = 119.92(2), *V* = 2676.10 Å^3, *F*(000) = 1216, μ(Mo-Kα) = 0.65 cm^{-1}, *Z* = 8, D_c = 1.461 g cm^{-3}; final *R* 0.0829 (R_w 0.0725) for 1029 data with $I/\sigma(I) > 2.0$.

Data collection and refinement. Data were collected on a Phillips PW 1100 diffractometer in the θ-range 3–21°, using Mo-Kα radiation, using a scan width of 0.90° and a θ–2θ scan mode, with a crystal of dimensions 0.24 × 0.20 × 0.13 mm^3. A total of 6250 reflections were recorded (positive and negative values of both *h* and *k* were scanned) and the structure was solved by direct methods.[19] The phenyl ring was treated as a rigid group of idealised geometry {C–C 1.395 and C–H 1.08 Å}. The two H-atoms of the amino group were directly located in a difference-Fourier synthesis and allowed to refine without constraint; all other H-atoms were included in calculated positions with fixed *U*-values of 0.10 Å^2. In the final cycles of full-matrix refinement anisotropic thermal parameters were assigned to the oxygen and nitrogen atoms, and individual reflections were assigned weights of $1/[\sigma 2(F) + 0.000\,0254F^2]$.[20] The final atom coordinates have been deposited with the Cambridge Crystallographic Data Centre.‡

5-Amino-3-(2-furyl)-7-phenoxy[1,2,4]triazolo[4,3-*a*][1,3,5]-triazine 13 (Method C)

Elution of the above column with dichloromethane–methanol 5% gave compound **13** as a solid (1.7 g, 12%); crystallisation from acetonitrile gave title compound **13** as prisms, mp 195–197 °C, which resolidified, and remelted at 250–255 °C (Found: C, 57.3; H, 3.0; N, 28.3. $C_{14}H_{10}N_6O_2$ requires C, 57.1; H, 3.4; N, 28.6%); δ 6.7 (1 H, dd), 7.1 (1 H, d), 7.1–7.3 (3 H, m), 7.4–7.5 (2 H, m), 8.0 (1 H, d) and 9.0–10.0 (2 H, br s); *m/z* 294 (MH^+) and 226 (base peak). Attempts to crystallise from ethanol resulted in rearrangement to compound **12a**.

5-Amino-3-methylsulfanyl-7-phenoxy[1,2,4]triazolo[4,3-*a*]-[1,3,5]triazine 15 (Method C)

A solution of compound **7** (1.3 g, 0.01 mol) and diphenyl *N*-cyanocarbonimidate (2.4 g, 0.01 mol) in DME (50 cm^3) was stirred at ambient temperature for 3 h. The solvent was evaporated off under reduced pressure and the residue was chromatographed on silica, and eluted with dichloromethane–methanol 5%, to give compound **15** as a solid (500 mg, 18%). (*NB:* a significant amount of unidentifiable polymeric material was also isolated); crystallisation from ethanol gave title compound **15** as prisms, mp 196–197 °C (Found: C 48.5; H, 3.5; N, 30.8; S, 11.3. $C_{11}H_{10}N_6OS$ requires C, 48.2; H, 3.7; N, 30.6; S, 11.7%); δ 2.6 (3 H, s), 7.1–7.3 (3 H, m), 7.4–7.5 (2 H, m) and 8.3–9.0 (2 H, br s); *m/z* 274 (M^+) and 206 (base peak).

7-Amino-2-methylsulfanyl-5-phenoxy[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine 14 (Method D)

A solution of compound **7** (1.3 g, 0.01 mol) and diphenyl *N*-cyanocarbonimidate (2.4 g, 0.01 mol) in DME (50 cm^3) was refluxed for 3 h. The solvent was evaporated off under reduced pressure and the residue was chromatographed on silica, and eluted with dichloromethane–methanol 2%, to give compound **14** as a solid (430 mg, 16%) (*NB:* a significant amount of unidentifiable polymeric material was also isolated); crystallisation from benzene gave title compound **14** as prisms containing a small amount of benzene (0.05 mol equiv.), mp 187–189 °C (Found: C, 49.2; H, 3.6; N, 30.4; S, 11.4. $C_{11}H_{10}N_6OS \cdot 0.05\ C_6H_6$ requires C, 48.8; H, 3.7; N, 30.2; S, 11.5%); δ 2.6 (3 H, s), 7.2–7.3 (3 H, m), 7.35 (sharp s, benzene), 7.4–7.5 (2 H, m) and 8.5–9.1 (2 H, br d); *m/z* 274 (M^+) and 206 (base peak).

***N*^{1}[2-(4-Hydroxyphenyl)ethyl]-O-phenylisourea-*N*^{3}-carbonitrile 17**

A solution of tyramine (2.75 g, 0.02 mol) and diphenyl *N*-cyanocarbonimidate (4.75 g, 0.02 mol) in acetonitrile (30 cm^3) was stirred for *ca.* 4 h, during which time a copious precipitate appeared. This was filtered off and dried to give compound **17** as a solid (4.2 g, 75%); crystallisation from ethyl acetate gave title compound **17** as prisms, mp 169–171 °C; δ 2.6–2.9 (2 H, m), 3.3–3.6 (2 H, m), 6.7 (2 H, d), 6.9–7.2 (4 H, m), 7.2–7.5 (3 H, m), 8.3–8.9 (1 H, br s) and 9.2 (1 H, s); *m/z* 282 (MH^+).

5-Amino-*N*^{2}-cyano-3-(2-furyl)-*N*^{1}-[2-(4-hydroxyphenyl)ethyl]-1,2,4-triazole-1-carboximidamide 18

A solution of compound **5** (0.75 g, 5 mmol) and the isourea **17** (1.4 g, 5 mmol) in acetonitrile (20 cm^3) was refluxed for 3.5 h; the solvent was evaporated off under reduced pressure and the residue was chromatographed on silica, and eluted with dichloromethane–methanol 2%, to give compound **18** as a solid (150 mg, 10%). Crystallisation from ethanol gave title compound **18** as prisms, mp 218–220 °C (Found: C, 56.7; H, 4.5; N, 28.7. $C_{16}H_{15}N_7O_2$ requires C, 57.0; H, 4.5; N, 29.1%); δ 2.9 (2 H, t), 3.85 (2 H, br t), 6.7 (3 H, m), 7.0 (1 H, d), 7.1 (2 H, d), 7.6 (2 H, s) 7.85 (1 H, d), 9.1 (1 H, s) and 9.15 (1 H, s); *m/z* 338 (MH^+).

5-Amino-2-(2-furyl)-7-[2-(4-hydroxyphenyl)ethylamino]-[1,2,4]triazolo[1,5-*a*][1,3,5]triazine 19a

Elution of the above column with dichloromethane–methanol 5% gave compound **19a** as a pale yellow solid (450 mg, 27%); crystallisation from methanol gave title compound **19a** as pale yellow plates, mp > 280 °C (Found: C, 56.6; H, 4.5; N, 28.8. $C_{16}H_{15}N_7O_2$ requires C, 57.0; H, 4.5; N, 29.1%); δ 2.85 (2 H, t), 3.6 (2 H, m), 6.7 (1 H, dd and 2 H, d), 7.0 (5 H, m), 7.85 (1 H, d), 8.5 (1 H, t) and 9.2 (1 H, br s); *m/z* 338 (MH^+).

Reaction of 7-methylsulfanyl compounds 9 and 11 with amines

In a typical experiment the 7-methylsulfanyl compound was refluxed in ethanol with a 2–5 molar excess of propylamine or cyclohexylamine until no starting material remained (TLC). The solvent was evaporated off under reduced pressure and the residue was crystallised to give: 5-*amino*-2-(2-*furyl*)-7-*propylamino*[1,2,4]*triazolo*[1,5-a][1,3,5]*triazine* **19b** as prisms (95%), mp > 260 °C (from propan-2-ol) (Found: C, 51.2; H, 5.5; N, 35.5. $C_{11}H_{13}N_7O \cdot 0.25\ C_3H_8O$ requires C, 51.4; H, 5.5; N, 35.8%); δ 0.9 (3 H, t), 1.6 (2 H, sext), 3.4 (2 H, q), 6.7 (1 H, dd), 7.0 (2 H, br s), 7.1 (1 H, d), 7.8 (1 H, d), 8.5 (1 H, t) and 1.1, 3.8 and 4.3 (0.25 mol equiv., solvent); *m/z* 259 (M^+); 5-*amino*-7-*cyclohexylamino*-2-(2-*furyl*)[1,2,4]*triazolo*[1,5-a][1,3,5]*triazine*

‡ See Instructions for Authors, in the January issue.

19c as prisms (quantitative), mp 258–260 °C (from EtOH) (Found: C, 56.4; H, 6.0; N, 32.7. $C_{14}H_{17}N_7O$ requires C, 56.2; H, 5.7; N, 32.8%); δ 1.0–1.4 (3 H, m), 1.4–1.7 (3 H, m), 1.7–2.0 (4 H, m), 4.0 (1 H, m), 6.7 (1 H, dd), 7.0 (2 H, br s), 7.1 (1 H, d), 7.8 (1 H, d) and 8.3 (1 H, br d); *m/z* 299 (M^+); *5-amino-2-phenoxy-7-propylamino*[1,2,4]*triazolo*[1,5-a][1,3,5]*triazine* **19d** as prisms (53%), mp 180–182 °C (from *tert*-butyl acetate) (Found: C, 54.9; H, 5.7; N, 34.4. $C_{13}H_{15}N_7O$ requires C, 54.7; H, 5.3; N, 34.4%); δ 0.9 (3 H, t), 1.6 (2 H, sext), 3.4 (2 H, q), 6.95 (2 H, br s), 7.2–7.3 (3 H, m), 7.4–7.5 (2 H, m) and 8.2 (1 H, t); *m/z* 285 (M^+); *5-amino-7-cyclohexylamino-2-phenoxy*[1,2,4]*triazolo*[1,5-a]-[1,3,5]*triazine* **19e** as a hydrate, prisms (35%), mp 142–144 °C (from toluene) (Found: C, 56.8; H, 6.2; N, 29.0; H_2O, 4.9. $C_{16}H_{19}N_7O{\cdot}0.85\ H_2O$ requires C, 56.4; H, 6.1; N, 28.8; H_2O, 4.5%); δ 1.0–1.4 (3 H, m), 1.4–1.7 (3 H, m), 1.8 (4 H, m), 3.8–4.0 (1 H, br m), 7.0 (2 H, br s), 7.2 (3 H, m), 7.4 (2 H, m) and 8.1 (1 H, d); *m/z* 325 (M^+).

7-Amino-2-(2-furyl)-5-methylsulfonyl[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine 20

A solution of MCPBA (50% strength; 45 g, 0.13 mol, 4 mol equiv.) in dichloromethane (300 cm^3) was added to a stirred, ice-cooled suspension of sulfide **8** (8.0 g, 0.03 mol) in dichloromethane (300 cm^3). The resulting solution was stirred overnight, the solvent was evaporated off under reduced pressure, and ethanol (150 cm^3) added to the residue. The solid was collected by filtration, washed with ethanol, and dried to give the title compound **20** as a solid (6.6 g, 75%), mp 238–240 °C (Found: C, 38.8; H, 2.8; N, 30.0. $C_9H_8N_6O_3S$ requires C, 38.6; H, 2.9; N, 30.0%); δ 3.3 (3 H, s), 6.7 (1 H, q), 7.3 (1 H, q), 7.9 (1 H q) and 9.4–9.8 (2 H, br d); *m/z* 281 (M^+).

In order to reduce the risk of using excessive amounts of oxidant, 2.5 mol equiv. were routinely used, resulting in incomplete oxidation; the product so formed could be used without detriment.

7-Amino-2-(2-furyl)-5-phenoxy[1,2,4]triazolo[1,5-*a*][1,3,5]-triazine 12a

Phenol (6.4 g, 0.07 mol) and DBU (3.8 cm^3, 0.03 mol) were added to a suspension of sulfone **20** (6.4 g, 0.02 mol) in DME (150 cm^3), and the resulting mixture was refluxed for 1 h. After removal of the solvent under reduced pressure and chromatography of the residue on silica, the title compound was obtained, identical in all respects with that prepared previously.

2-Hydrazino-4,6-diphenoxy-1,3,5-triazine 22

To a solution of 2,4,6-triphenoxy-1,3,5-triazine (36 g, 0.1 mol) in dichloromethane (500 cm^3) was added hydrazine hydrate (5 cm^3, 0.1 mol) and the solution was left overnight. The solvent was then evaporated off under reduced pressure and the residue was treated with hot propan-2-ol (300 cm^3); this was left overnight and the product was filtered off to give compound **22** as prisms (25 g, 84%). Recrystallisation of a portion from propan-2-ol gave title compound **22** as prisms, mp 106–108 °C (Found: C, 61.0; H, 4.4; N, 23.3. $C_{15}H_{13}N_5O_2$ requires C, 61.0; H, 4.4; N, 23.7%); δ 4.3 (2 H, br s), 7.1–7.3 (6 H, m), 7.3–7.5 (4 H, m) and 9.2 (1 H, br s); *m/z* 296 $(M + H)^+$

N^2-(4,6-Diphenoxy-1,3,5-triazin-2-yl)2-furohydrazide 23a

A solution of 2-furoyl chloride (3.8 g, 0.05 mol) in dichloromethane (50 cm^3) was added dropwise to a stirred, ice-cooled suspension of the hydrazine **22** (15 g, 0.05 mol) in dichloromethane (200 cm^3) containing triethylamine (7.0 cm^3, 0.05 mol). The suspension was stirred for 2 h, a further aliquot of 2-furoyl chloride (0.76 g, 0.01 mol) was added, and the reaction mixture was stirred overnight. The mixture was then washed successively with water (2 × 200 cm^3) and brine (100 cm^3), dried (phase-separating paper) and evaporated under reduced pressure to give a brown oil (20 g). This was purified by chromatography on silica and eluted with dichloromethane–ethyl acetate 5% to give a high-running compound (2.5 g, 10%) which was identified as *N*-(4,6-diphenoxy-1,3,5-triazin-2-yl)-*N*,*N'*-di-(2-furoyl)hydrazine. Further elution gave compound **23a** as a solid (10.5 g, 51%). Crystallisation from propan-2-ol gave title compound **23a** as prisms, mp 182–184 °C (Found: C, 61.4; H, 3.8; N, 17.7. $C_{20}H_{15}N_5O_4$ requires C, 61.7; H, 3.9; N, 18.0%); δ 6.7 (1 H, q), 7.1–7.6 (11 H, m), 7.9 (1 H, d), 10.0 (1 H, br s) and 10.4 (1 H, br s); *m/z* 390 $(M + H)^+$. By a similar method were prepared: N^2-(4,6-diphenoxy-1,3,5-triazin-2-yl)isoxazole-5-carbohydrazide **23b** as pale yellow prisms, mp 162–165 °C (from toluene); δ 7.0–7.5 (11 H, m), 8.8 (1 H, d), 10.3 (1 H, br s) and 10.9 (1 H, br s); N^2-(4,6-*diphenoxy*-1,3,5-*triazin*-2-*yl*)-3-*methylisoxazole*-5-*carbohydrazide* **23c** as pale yellow prisms (55%), mp 195–198 °C (from EtOH) (Found: C, 59.4; H, 3.9; N, 21.0. $C_{20}H_{16}N_6O_4$ requires C, 59.4; H, 4.0; N, 20.8%); δ 2.3 (3 H, s), 6.9 (1 H, s), 7.1–7.4 (10 H, m), 10.2 (1 H, s) and 10.9 (1 H, s); *m/z* 405 $(M + H)^+$; N^2-(4,6-*diphenoxy*-1,3,5-*triazin*-2-*yl*)-2-*methyloxazole*-4-*carbohydrazide* **23d** as a foam (82% after chromatography) which was used without characterisation; N^2-(4,6-*diphenoxy*-1,3,5-*triazin*-2-*yl*)*trifluoroacetohydrazide* **23e** as prisms, (55%), mp 207–208 °C (from toluene) (Found: C, 52.4; H, 3.0; N, 17.9. $C_{17}H_{12}F_3N_5O_3$ requires C, 52.5; H, 3.1; N, 17.9%); δ 7.1–7.6 (10 H, m), 10.4 (1 H, s) and 11.6 (1 H, s); *m/z* 392 $(M + H)^+$.

2-(2-Furyl)-5,7-diphenoxy[1,2,4]triazolo[1,5-*a*][1,3,5]triazine 24a

A mixture of hydrazide **23a** (7.0 g, 0.018 mol) and phosphorus pentaoxide (17 g) in xylene was refluxed and mechanically stirred for 14 h. The solvent was evaporated off under reduced pressure and the residue was dissolved in dichloromethane (200 cm^3); this was washed successively with water and brine, dried, and evaporated to give a brown solid. This was purified by chromatography on silica and elution with dichloromethane–ethyl acetate 2.5%, to give compound **24a** as a solid (3.9 g, 58%). Crystallisation from ethyl acetate gave title compound **24a** as prisms, mp 246–248 °C (Found: C, 64.8; H, 3.3; N, 19.2. $C_{20}H_{13}N_5O_3$ requires C, 64.7; H, 3.5; N, 18.9%); δ 6.7 (1 H, q), 7.2–7.6 (11 H, m) and 8.0 (1 H, d); *m/z* 372 $(M + H)^+$.

By a similar method were prepared: 2-(*isoxazol*-5-*yl*)-5,7-*diphenoxy*[1,2,4]*triazolo*[1,5-*a*][1,3,5]*triazine* **24b** as a pale brown solid essentially pure by TLC, and which was treated directly with ammonia without further characterisation; 5,7-diphenoxy-2-trifluoromethyl[1,2,4]triazolo[1,5-*a*][1,3,5]triazine **24e** as a pale brown oil essentially pure by TLC, and which was treated directly with ammonia without further characterisation.

2-(3-Methylisoxazol-5-yl)-5,7-diphenoxy[1,2,4]triazolo-[1,5-*a*][1,3,5]triazine 24c

A solution of compound **23c** (4.2 g, 10.5 mmol) and toluene-4-sulfonyl chloride (4.0 g, 21 mmol, 2 mol equiv.) in pyridine (80 cm^3) was heated and stirred at 100 °C for 2.5 h. The solvent was evaporated off under reduced pressure and the residue was dissolved in dichloromethane (200 cm^3); this was washed successively with dil. HCl (2 × 100 cm^3 of 2 mol dm^{-3}), water (100 cm^3) and brine (100 cm^3), dried ($MgSO_4$), and evaporated to give a brown gum, essentially pure by TLC, and which was treated directly with ammonia without further characterisation.

By a similar method was prepared: 2-(2-methyloxazol-4-yl)-5,7-diphenoxy[1,2,4]triazolo[1,5-*a*][1,3,5]triazine **24d** as a pale brown foam essentially pure by TLC, and which was treated directly with ammonia without further characterisation.

7-Amino-2-(2-furyl)-5-phenoxy[1,2,4]triazolo[1,5-*a*][1,3,5]triazine 12a

A solution of compound **24a** in saturated ethanolic ammonia was refluxed for 3 h. After removal of the solvent under reduced pressure and crystallisation of the residue from ethanol, the title compound was obtained, identical in all respects with that prepared previously. Recrystallisation from ethyl acetate gave prisms containing no solvent of crystallisation and which were suitable for X-ray crystallographic analysis (*vide supra*).

By a similar method were prepared: 7-*amino*-2-(isoxazol-5-*phenoxy*-1,2,4-*triazolo*[1,5-a][1,3,5]triazine **12b** as prisms containing solvent of crystallisation, mp 255–257 °C (from EtOH) (Found: C, 53.0; H, 4.2; N, 29.3. $C_{13}H_9N_7O_2 \cdot 0.75\ C_2H_6O$ requires C, 52.8; H, 4.1; N, 29.7%); δ 7.1 (1 H, d) 7.2–7.6 (5 H, m), 8.8 (1 H, d) and 9.1 (2 H, br d); signals were also present corresponding to 0.75 mol equiv. of ethanol; *m/z* 296 $(M + H)^+$; 7-*amino*-2-(3-*methylisoxazol*-5-*yl*)-5-*phenoxy*[1,2,4]*triazolo*[1,5-a][1,3,5]*triazine* **12c** as prisms containing solvent of crystallisation, mp 279–281 °C (from EtOH) (Found: C, 54.3; H, 4.6; N, 28.8. $C_{14}H_{11}N_7O_2 \cdot 0.5\ C_2H_6O$ requires C, 54.2; H, 4.3; N, 29.1%); δ 2.3 (3 H, s) 7.0 (1 H, d), 7.2–7.5 (5 H, m) and 9.1 (2 H, br s); signals were also present corresponding to 0.6 mol equiv. of ethanol; *m/z* 310 $(M + H)^+$; 7-*amino*-2-(2-*methyloxazol*-4-*yl*)-5-*phenoxy*[1,2,4]*triazolo*[1,5-a][1,3,5]*triazine* **12d** as prisms, mp 305–307 °C (from EtOH) (Found: C, 54.2; H, 3.5; N, 31.5. $C_{14}H_{11}N_7O_2$ requires C, 54.4; H, 3.6; N, 31.7%); δ 2.5 (3 H, s), 7.2–7.3 (3 H, m), 7.4–7.5 (2 H, m), 8.5 (1 H, d) and 8.9 (2 H, br s); *m/z* 310 $(M + H)^+$; 7-*amino*-5-*phenoxy*-2-*trifluoromethyl*[1,2,4]*triazolo*[1,5-a][1,3,5]*triazine* **12e** as prisms, mp 243–244 °C (from propan-2-ol) (Found: C, 44.8; H, 2.2; N, 28.1. $C_{11}H_7F_3N_6O$ requires C, 44.6; H, 2.4; N, 28.4%); δ 7.2–7.3 (3 H, m), 7.4–7.5 (2 H, m) and 9.0–9.5 (2 H, br s); *m/z* 297 $(M + H)^+$

N-(4,6-Diphenoxy-1,3,5-triazin-2-yl)-N'-furfurylidenehydrazine 25a

A solution of the hydrazine **22** (15.0 g, 0.05 mol) and 2-furaldehyde (4.2 cm^3, 0.05 mol) in propan-2-ol (300 cm^3) containing a few drops of glacial acetic acid was heated to reflux for 5 min and then left at room temperature overnight. The precipitated solid was filtered off, washed with propan-2-ol, and dried to give pale brown prisms (15.8 g, 85%), which were used without further purification. Crystallisation of a portion from propan-2-ol gave title compound **25a** as very pale yellow prisms, mp 205–207 °C (Found: C, 64.1; H, 3.7; N, 19.2. $C_{20}H_{15}N_5O_3$ requires C, 64.3; H, 4.0; N, 18.8%); δ 6.6 (1 H, q), 6.8 (1 H, d), 7.1–7.3 (6 H, m), 7.3–7.5 (4 H, m), 7.8 (1 H, d) 8.05 (1 H, s) and 11.7 (1 H, br s); *m/z* 374 $(M + H)^+$

N-2-(4,6-Diphenoxy-1,3,5-triazin-2-yl)-*N'*-(3-pyridylmethylene)hydrazine **25f** was prepared similarly in 88% yield, mp 214–215 °C (from propan-2-ol); δ 7.1–7.3 (6 H, m), 7.3–7.6 (5 H, m), 8.0 (1 H, dd), 8.2 (1 H, s), 8.6 (1 H, dd), 8.8 (1 H, d) and 11.95 (1 H, br s); *m/z* 385 $(M + H)^+$.

Oxidative cyclisation of hydrazones 25a, f

A solution of the hydrazone (0.005 mol) in dichloromethane (50 cm^3) was treated with LTA (~ 10% mol excess), and the resulting reaction mixture was stirred for *ca.* 2 h at room temp. It was then washed sequentially with water, dil. aq. sodium hydrogen carbonate, water and brine, dried (Phase Separating paper), and evaporated under reduced pressure. Since all attempts to purify the two-spot mixture by chromatography resulted in decomposition, it was treated directly with a saturated solution of ammonia in ethanol for 2 h at room temp. Evaporation and purification of the residue by chromatography gave: 7-amino-2-(2-furyl)-5-phenoxy[1,2,4]triazolo[1,5-*a*]-[1,3,5]triazine **12a**, identical in all respects with that prepared previously; 7-*amino*-5-*phenoxy*-2-(3-*pyridyl*)[1,2,4]*triazolo*-[1,5-a][1,3,5]*triazine* **12f** as fawn prisms mp > 300 °C (from EtOH) (Found: C, 58.8; H, 3.5; N, 31.7. $C_{15}H_{11}N_7O$ requires C, 59.0; H, 3.6; N, 32.1%); δ 7.2–7.4 (3 H, m), 7.4–7.6 (3 H, m), 8.4 (1 H, dt) 8.7 (1 H, d), 8.7–9.2 (2 H, br d) and 9.3 (1 H, s); *m/z* 306 $(M + H)^+$

Acknowledgements

We thank Dr E. Clayton and Mrs Madeleine Vickers for obtaining and interpreting the mass spectra, Mr H. Beeley and his staff for the NMR data, Mr B. Crookes and his staff for the elemental analyses, and Mr A. Guildford and his staff for the large-scale preparations.

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Paper 4/06782G
Received 7*th November* 1994
Accepted 7*th December* 1994