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1,2,3,5-Tetrazines and 1,2,3-Triazaspiro[4.4]nonanes: Remarkable Products from 1,3-Dipolar Cycloadditions of *N*-Sulphinylamines with Substituted Triazolium Imides

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Cycloadditions of aryl-*N*-sulphinylamines with substituted triazolium imides gave new 8π-2,4,5,6-tetrasubstituted-1,2,3,5-tetrazines, the *X*-ray crystal structure of one of which is reported; strained tricyclic tetra-aza tetracyclo[4.3.1.0^{1,6}]decenes are suspected as intermediates and attempts to intercept them led to new substituted 1,2,3-triazaspiro[4.4]nonanes, the *X*-ray crystal structure of one of which is reported.

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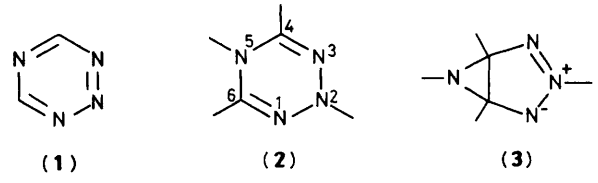
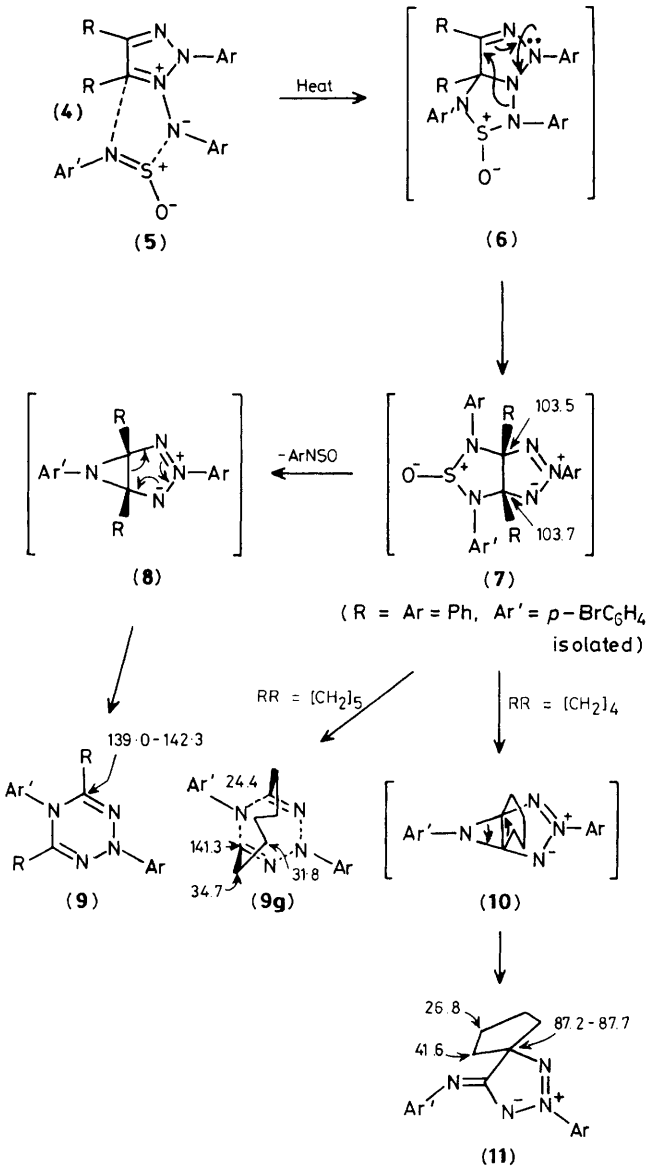
Of the three possible tetrazine systems, the 1,2,3,5-tetrazines (**1**) are by far the rarest and least studied class.[1] Few derivatives are known[2,3] and most involve condensed forms of the ring.[4] The 2,5-disubstituted derivatives (**2**) were previously unknown and their stable existence was considered unlikely since they constitute an 8π-*as*-tetrazine ring. Herein we report a reaction which gives rise to high yields of compounds with the structure(**2**). The novel structure (**3**) is the likely precursor to (**2**) and attempts to intercept it led to the isolation of new 1,2,3-triazaspiro[4.4]nonanes (**11**).

When substituted 1,2,3-triazolium imides (**4**) were treated† with aryl-*N*-sulphinylamines (**5**) in benzene, the tetrazines (**9**) were obtained in high yields (see Table 1). The reaction occurred *via* a cycloaddition giving rise to the sequence of intermediates (**6**)→(**7**)→(**8**) (Scheme 1). *N*-Sulphinylamines readily undergo 1,3-dipolar cycloadditions[5] and we have previously[6] isolated products similar to (**7**) (with N–S replaced by C–C) in reactions of compounds (**4**) with other dipolarophiles. Loss of a molecule of *N*-sulphinylamine from (**7**) may occur in either of two ways when the Ar and Ar′ substituents are different; both expected products (**9**) were obtained, but PhNSO was lost preferentially (Table 1). In one case it proved possible to isolate compound (**7**) (R = Ar = Ph; Ar′ = *p*-BrC$_6$H$_4$) in *ca.* 10% yield along with the other products. When this sample was heated separately in benzene the expected mixture of the products (**9**) was obtained in a ratio identical to that reached by the direct reaction. The ring expansion of (**8**) is a disrotatory outward electrocyclic process. In theory, this could be sterically constricted by bridging the two R substituents. When RR = [CH$_2$]$_5$ the ring expansion



(**1**) (**2**) (**3**)



(**4**) (**5**) (**6**) (**7**) (**8**) (**9**) (**9g**) (**10**) (**11**)

Scheme 1. [Some ^{13}C n.m.r. ($CDCl_3$) shifts shown].

† *Typical procedures:* Compound (**4**) (R = Ar = Ph) (2.6 mmol) in dry benzene (10 ml) was treated with a solution of (**5**; Ar = Ph) (2.9 mmol) in dry benzene (2 ml). The mixture heated under reflux (48 h), then evaporated under reduced pressure. The residue in dichloromethane was placed on a flash column of silica gel (230—400 mesh ASTM) and eluted with mixtures of petroleum spirit (b.p. 40—60 °C) and dichloromethane (9:1 to 1:1 v/v) to give compound (**9a**). Unchanged (**5**) was subsequently recovered as aniline from the column, along with traces of (**4**). [When a mixture of products was expected the reaction residue was initially passed through the column quickly with dichloromethane to give first fractions containing the products (**9**) which were subsequently re-chromatographed as described.]

Compound (**4**) (RR = [CH$_2$]$_4$) (2.6 mmol) in dry benzene (15 ml) was treated with a solution of (**5**; Ar′ = *p*-NO$_2$C$_6$H$_4$) (22 mmol) [use of excess favoured cycloaddition against competitive fragmentation of (**4**)] in dry benezne (5 ml), heated under reflux (48 h), and evaporated. The residue was placed on a column as described above and eluted with dichloromethane to remove excess of *p*-nitroaniline and thermal degradation products of compound (**5**). The product (**11a**) was removed from the column with ethanol, re-chromatographed with toluene–ethanol (9:1 v/v) and recrystallised from n-propanol.

All compounds reported gave satisfactory microanalyses (C, H, and N).

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Table 1. Products.

Substituents					
RR	Ar	Ar′	Product	Yield %	M.p./°C
Ph, Ph	Ph	Ph	(**9a**)	83	196—197[d]
Ph, Ph	Ph	*p*-BrC_6H_4	(**9b**)	71[a]	206—207[d]
Ph, Ph	Ph	*p*-$NO_2C_6H_4$	(**9c**)	78[a]	245—246[d]
Ph, Ph	Ph	5-Methyloxazol-3-yl	(**9d**)	75[a]	191—192[e]
Ph, Ph	*p*-$NO_2C_6H_4$	*p*-$NO_2C_6H_4$	(**9e**)	83	235—236[d]
Ph, Ph	*p*-$NO_2C_6H_4$	5-Methyloxazol-3-yl	(**9f**)	75[b]	217—218[d]
$-[CH_2]_5-$	*p*-$NO_2C_6H_4$	*p*-$NO_2C_6H_4$	(**9g**)	84	216—217[e]
$-[CH_2]_4-$	*p*-$NO_2C_6H_4$	*p*-$NO_2C_6H_4$	(**11a**)	47	208—209[d]
$-[CH_2]_4-$	*p*-$NO_2C_6H_4$	5-Methyloxazol-3-yl	(**11b**)	10	181—182[f]
Ph, Ph	Ph	*p*-BrC_6H_4	(**7**)	10[c]	181—182[g]

[a] (**9a**) (10—12%) was also isolated. [b] (**9e**) (18.5%) was also isolated. [c] Isolated along with (**9b**) (71%) and (**9a**) (10%). When (**7**) was heated under reflux in benzene (12 h), (**9b**) and (**9a**) were obtained in a ratio of 7:1. [d] From n-propanol. [e] From ethanol. [f] From hexane. [g] Purified by careful rapid recrystallization from ethanol (labile, may fragment during attempted purification).

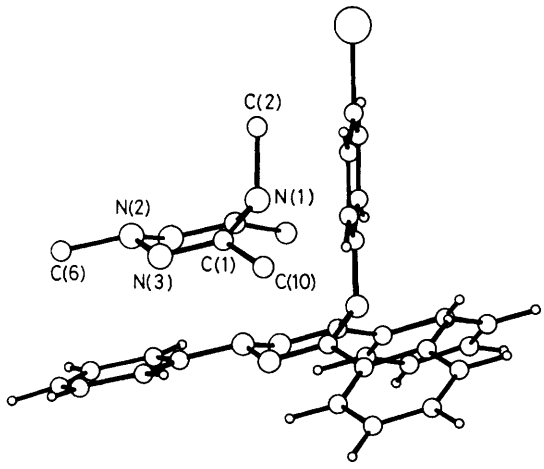

Figure 1. *X*-Ray crystal structure of (**9b**) and (inset) detail of 8π-tetrazine ring.

still occurred giving compound (**9g**) (Table 1), but when the bridging chain was shortened to four carbons, RR = $[CH_2]_4$, the disrotatory outward process was indeed prohibited. The intermediate (**10**), which contains a strained inverted tetrahedral carbon, was either by-passed‡ or reacted instead *via* a ring opening and a 1,2-shift involving contraction of the cyclohexane ring to a spirocyclopentane giving the novel fused products (**11**). An analogous ring opening and 1,2-halogeno shift has been reported[7] on thermal ring opening of dihalogenoaziridines. Accurate Dreiding models showed that the interesting structure (**9g**) was at the limit for bridging the tetrazine carbon atoms with a methylene chain and it was not possible to do so with a chain of four methylene groups without breaking the tetrazine ring. The structures of the products were confirmed by ^1H (270 MHz) and ^{13}C n.m.r. spectra. Compounds (**9**) and (**11**) showed the expected number and chemical shifts of n.m.r. signals (Scheme 1).

The *X*-ray crystal structures§ of compounds (**9b**) and (**11b**) are shown in Figures 1 and 2. The 8π-tetrazine ring is boat shaped with the *N*-5-aryl group axial, and the *N*-2-aryl group

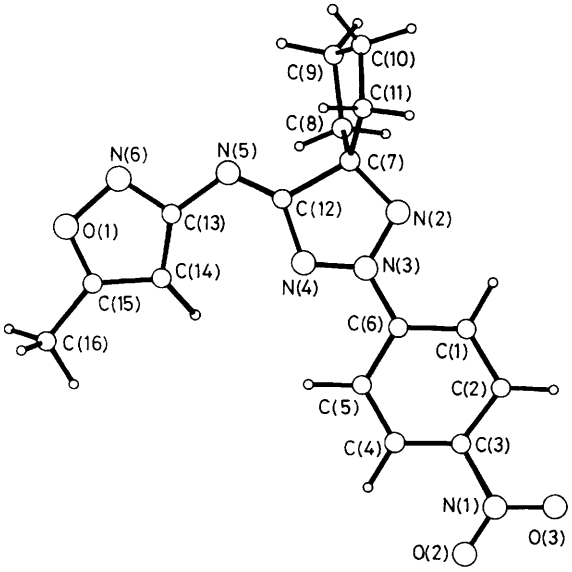

Figure 2. *X*-Ray crystal structure of (**11b**).

‡ The intermediate (**10**) could be by-passed if the 1,2-shift leading to cyclohexane ring contraction occurred during fragmentation of (**7**). However the fused aziridine intermediate (**10**) is a likely common precursor to both compounds (**9**) and (**11**).

§ *Crystal data* for (**9b**): $C_{26}H_{19}BrN_4$, M = 467.35, orthorhombic, space group *Pnma*, a = 11.649(3), b = 13.298(4), c = 13.945(3) Å, U = 2160.2 Å^3, Z = 4, Mo-K_α radiation, λ = 0.71069 Å, μ(Mo-K_α) = 18.57 cm^{-1}, $F(000)$ = 952, $2 < \theta < 24°$. The structure was solved by a combination of Patterson search and direct methods, SHELX 86[8] using 599 reflections with $I > 3\sigma(I)$. Least-squares refinement with anisotropic thermal parameters for Br and hydrogen atoms in calculated positions converged to R = 0.0685 and R_w = 0.0672.

For (**11b**): $C_{16}H_{16}N_6O_2$, monoclinic, space group $P2_1/c$, a = 8.631(4), b = 11.493(7), c = 15.615(5) Å, β = 110.83(3)°, U = 1622 Å^3, Z = 4, μ(Mo-K_α) = 0.62 cm^{-1}, $F(000)$ = 712.00. A Nonius CAD4 diffractometer was used. 408 reflections with $I > 2\sigma(I)$ were observed within the range 2—22°. The crystal, a red needle, had dimensions of 0.07 × 0.09 × 0.35 mm and did not diffract strongly. The structure was solved by direct methods, SHELX 86,[9] and refined by full-matrix least-squares, SHELX 76,[10] to give final R factors R = 0.0642 and R_w = 0.0515. Atoms were refined isotropically and hydrogen atoms were included at calculated positions.

Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

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equatorial, to the average plane. Hence the n-electrons of the two singly bound nitrogens extend from opposite faces of the ring. The bond lengths N(1)–N(2), N(3)–C(4), and C(4)–N(5) were 1.39, 1.28, and 1.43 Å, respectively, which, when compared with the values[8] for individual alternating single and double bonds, N–N (1.41 Å), C=N (1.27 Å), and C–N (1.45 Å), suggest that the ring is composed of two isolated amidine groups with no aromaticity. This is fully consistent with the boat structure since the meeting of two normal planar imino moieties necessitates such a structure. Models show that a chair structure would require severe out of plane rotation of the groups around the imino bonds.

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