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**Structures of 3,6-Dimethoxy-1,2,4,5-tetrazine (V) and 3,6-Bis(1-aziridinyl)-1,2,4,5-tetrazine (VI)**

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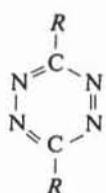
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**Abstract.** (V):  $C_4H_6N_4O_2$ ,  $M_r = 142.12$ , ortho-rhombic,  $Pbca$ ,  $a = 6.865$  (3),  $b = 13.192$  (5),  $c = 7.013$  (3) Å,  $V = 635.1$  (7) Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.486$  g cm<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.71069$  Å,  $\mu = 1.139$  cm<sup>-1</sup>,  $F(000) = 296$ ,  $T = 295$  K,  $R = 0.043$  for 589 unique observed reflections [ $I \geq 1.96\sigma(I)$ ]. (VI):  $C_6H_8N_6$ ,

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$M_r = 164.18$ , monoclinic,  $C2/m$ ,  $a = 9.660(2)$ ,  $b = 9.077(1)$ ,  $c = 4.294(1)$  Å,  $\beta = 91.07(1)^\circ$ ,  $V = 376.5(2)$  Å<sup>3</sup>,  $Z = 2$ ,  $D_x = 1.448$  g cm<sup>-3</sup>,  $\lambda(\text{MoK}\alpha) = 0.71069$  Å,  $\mu = 0.952$  cm<sup>-1</sup>,  $F(000) = 172$ ,  $T = 295$  K,  $R = 0.037$  for 405 unique observed reflections [ $I \geq 1.96\sigma(I)$ ]. (V) and (VI) are centrosymmetric, with planar 1,2,4,5-tetrazine rings slightly compressed in the C...C direction (N—C—N  $\approx 126^\circ$ ). The remarkably short exocyclic C—O [1.328(2) Å] and C—N [1.385(1) Å] bond distances indicate that the methoxy and aziridinyl substituents act as  $\pi$  donors to the electron-deficient 1,2,4,5-tetrazine system.

**Introduction.** In the evaluation of spectroscopic results concerning the triplet state,  $T_1$ , in single crystals of various 1,2,4,5-tetrazines (Gückel, Schweitzer, Hausser & Neugebauer, 1982), the crystal structures, particularly the molecular packing, were required for the compounds studied. Structures are already known for the parent compound 1,2,4,5-tetrazine (I) (Bertinotti, Giacomello & Liquori, 1956) and for three 3,6-disubstituted derivatives [(II), Huffman, 1981; (III), Ahmed & Kitaigorodsky, 1972; (IV), Krieger, Fischer & Neugebauer, 1987]. This paper reports the crystal structures of 3,6-dimethoxy-1,2,4,5-tetrazine (V) (Neugebauer & Fischer, 1982) and 3,6-bis(1-aziridinyl)-1,2,4,5-tetrazine (VI) (Fischer & Neugebauer, 1987, unpublished results). Compound (VI) shows substantial cytotoxic activity which attracts further specific interest.



	(I)	(II)	(III)	(IV)	(V)	(VI)
R	H	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	NH <sub>2</sub>	OCH <sub>3</sub>	N $\triangleleft$

**Experimental.** (V): Needle-shaped red crystals grown from ligroin by slow evaporation at room temperature; approximate crystal dimensions 0.2 × 0.85 × 0.4 mm. Syntex P2<sub>1</sub> four-circle diffractometer, graphite-monochromated Mo K $\alpha$  radiation;  $\theta/2\theta$  scanning technique. Lattice parameters determined from least-squares fit with 15 reflections ( $\theta$  range: 10–12.5°); 794 unique reflections measured in the range  $2 \leq \theta \leq 28.6^\circ$ , max.  $(\sin\theta)/\lambda = 0.676$  Å<sup>-1</sup>,  $0 \leq h \leq 8$ ,  $0 \leq k \leq 17$ ,  $0 \leq l \leq 9$ ; 589 [ $I \geq 1.96\sigma(I)$ ] used for structure solution and refinement. Three standard reflections, 3% intensity variation. Lorentz and polarization corrections were applied. The structure was solved by direct methods using MULTAN80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). Full-matrix least squares minimized  $\sum w(\Delta F)^2$ . H atoms refined with isotropic temperature factors, all other atoms refined anisotropically for 58 variables.  $R = 0.043$ ,  $wR = 0.042$ ,  $w = [\sigma^2(F) + 0.005\sigma(F^2)]^{-1}$ ,

max.  $\Delta/\sigma = 0.05$ ; residual electron density in final difference map  $-0.14 < \Delta\rho < 0.15$  e Å<sup>-3</sup>. Atomic scattering factors and anomalous-dispersion corrections taken from *International Tables for X-ray Crystallography* (1974); programs used were those of B. A. Frenz & Associates Inc. (1982). (VI): Red needles from methanol approximately 0.08 × 0.10 × 0.30 mm. Enraf-Nonius CAD-4 four-circle diffractometer, graphite-monochromated Mo K $\alpha$  radiation;  $\theta/2\theta$  scanning technique. Lattice parameters determined from least-squares fit with 30 reflections ( $\theta$  range: 12–15°); 530 unique reflections measured in the range  $1.5 \leq \theta \leq 29^\circ$ , max.  $(\sin\theta)/\lambda = 0.682$  Å<sup>-1</sup>,  $0 \leq h \leq 13$ ,  $0 \leq k \leq 12$ ,  $-5 \leq l \leq 5$ ; 405 [ $I \geq 1.96\sigma(I)$ ] used for structure solution and refinement. Three standard reflections, 2% intensity variation. Lorentz and polarization corrections were applied. The structure was solved by direct methods (MULTAN80). Full-matrix least squares minimized  $\sum w(\Delta F)^2$ . H atoms refined with isotropic temperature factors, all other atoms refined anisotropically for 39 variables.  $R = 0.037$ ,  $wR = 0.038$ ,  $w = [\sigma^2(F) + 0.003\sigma(F^2)]^{-1}$ , max.  $\Delta/\sigma < 0.001$ ;  $-0.09 < \Delta\rho < 0.08$  e Å<sup>-3</sup>. For further details see compound (V).

**Discussion.** Final atomic and isotropic thermal parameters are listed in Table 1, and bond distances and angles are presented in Table 2.\* Views of the molecules (V) and (VI) with the chosen atom-numbering schemes are presented in Figs. 1 and 2, respectively.

(V) shows  $C_i$  symmetry. The ring is exactly planar. The attached O atoms deviate from the ring plane by 0.020 Å. The methyl groups are more displaced (0.153 Å) due to some distortion about C(3)—O(3') [N(2)—C(3)—O(3')—C(3'') = 8.8°]. (VI) has  $C_{2h}$  symmetry with the mirror plane bisecting the molecule through N(3), C(2), C(2<sup>III</sup>) and N(3<sup>III</sup>) orthogonal to the planar 1,2,4,5-tetrazine ring. The N atoms of the 1-aziridinyl substituents deviate to some extent from the tetrazine ring plane [N(3): -0.109 Å] yielding 184.3° for the angle between the ring plane and the C(2)—N(3) bond. The angle between this bond and the aziridine ring plane was found to be 124.5°. The slight bending of the aziridinyl N out of the 1,2,4,5-tetrazine plane is apparently caused by intramolecular van der Waals interactions of the aziridinyl methylene groups with C(2) as indicated by the C(4)···C(2) distance of 2.452 Å and the H(4A)···C(2) distance of 2.54 Å.

Bond distances and bond angles in the 1,2,4,5-tetrazine rings in (V) and (VI) agree with those of (I)–(IV) (Table 3). Different N—N—C ( $\approx 117^\circ$ ) and

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43875 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Fractional atomic coordinates and isotropic (for H) or equivalent isotropic (for C,N,O) thermal parameters (Å<sup>2</sup>) with e.s.d.'s in parentheses

$$B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i \cdot a_j$$

	x	y	z	B <sub>eq</sub> or B <sub>iso</sub>
(V) 3,6-Dimethoxy-1,2,4,5-tetrazine				
N(1)	-0.0431 (2)	-0.0991 (1)	0.0327 (2)	3.92 (3)
N(2)	0.1272 (3)	-0.0635 (1)	0.0898 (2)	4.13 (4)
C(3)	0.1637 (3)	0.0343 (1)	0.0546 (2)	3.52 (4)
O(3')	0.3356 (2)	0.0661 (1)	0.1176 (2)	4.83 (3)
C(3'')	0.3983 (3)	0.1671 (2)	0.0644 (3)	5.01 (5)
H(3A)	0.322 (3)	0.217 (2)	0.130 (3)	6.1 (6)
H(3B)	0.386 (2)	0.175 (2)	-0.079 (3)	5.8 (5)
H(3C)	0.524 (3)	0.176 (2)	0.109 (3)	6.3 (6)
(VI) 3,6-Bis(1-aziridinyl)-1,2,4,5-tetrazine				
N(1)	-0.0514 (1)	0.1307 (1)	0.0992 (2)	2.83 (2)
C(2)	-0.0989 (2)	0.0000	0.1906 (4)	2.36 (4)
N(3)	-0.1989 (1)	0.0000	0.4177 (4)	2.83 (4)
C(4)	-0.3276 (1)	0.0806 (2)	0.3616 (4)	3.83 (3)
H(4A)	-0.332 (1)	0.129 (2)	0.161 (3)	5.0 (4)
H(4B)	-0.361 (1)	0.131 (2)	0.542 (4)	5.0 (4)

Table 2. Bond distances (Å), angles (°) and selected torsion angles (°) with e.s.d.'s in parentheses

(V) 3,6-Dimethoxy-1,2,4,5-tetrazine			
N(1)–N(2)	1.322 (2)	N(2)–N(1)–C(3)	117.3 (1)
N(1)–C(3)	1.338 (2)	N(1)–N(2)–C(3)	116.9 (1)
N(2)–C(3)	1.337 (2)	N(1)–C(3)–N(2)	125.8 (1)
C(3)–O(3')	1.328 (2)	N(1)–C(3)–O(3')	120.0 (1)
O(3')–C(3'')	1.450 (2)	N(2)–C(3)–O(3')	114.2 (1)
C(3'')–H(3A)	0.955 (20)	C(3)–O(3')–C(3'')	117.9 (1)
C(3'')–H(3B)	1.016 (19)		
C(3'')–H(3C)	0.925 (21)	N(2)–C(3)–O(3')–C(3'')	8.8 (2)

Symmetry code: (i)  $-x, -y, -z$ .

(VI) 3,6-Bis(1-aziridinyl)-1,2,4,5-tetrazine			
N(1 <sup>ii</sup> )–N(1)	1.320 (1)	N(1 <sup>ii</sup> )–N(1)–C(2)	117.2 (1)
N(1)–C(2)	1.334 (1)	N(1)–C(2)–N(1)	125.6 (1)
C(2)–N(3)	1.385 (1)	N(1)–C(2)–N(3)	117.1 (1)
N(3)–C(4)	1.458 (1)	C(2)–N(3)–C(4)	119.2 (1)
C(4)–C(4')	1.464 (2)	C(4)–N(3)–C(4')	60.2 (1)
C(4)–H(4A)	0.969 (9)	N(3)–C(4)–C(4')	59.9 (1)
C(4)–H(4B)	0.963 (9)		
		N(1 <sup>ii</sup> )–N(1)–C(2)–N(3)	174.9 (1)
		N(1)–C(2)–N(3)–C(4)	57.3 (2)
		C(2)–N(3)–C(4)–C(4')	108.9 (2)

Symmetry code: (i)  $x, -y, z$ ; (ii)  $-x, y, -z$ ; (iii)  $-x, -y, -z$ .

Table 3. Observed bond lengths (Å) and angles (°) for the 1,2,4,5-tetrazine ring in (I) and in the 3,6-disubstituted derivatives (II)–(VI)

	R	N–N	C–N	N–N–C	N–C–N
(I)	H	1.321	1.345	116.2	127.2
			1.323	115.4	
(II)	CH <sub>3</sub>	1.326	1.343	118.2	123.8
			1.335	118.0	
(III)	C <sub>6</sub> H <sub>5</sub>	1.314	1.353	120.6	121.8
			1.338	117.5	
(IV)	NH <sub>2</sub>	1.328	1.348	118.3	123.7
		1.314	1.347	118.0	
(V)	OCCH <sub>3</sub>	1.322	1.338	117.3	125.8
			1.337	116.9	
(VI)	N	1.320	1.334	117.2	125.6

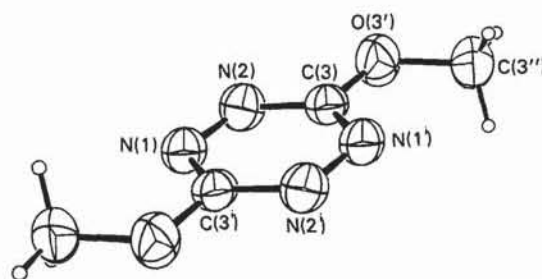


Fig. 1. ORTEP drawing (Johnson, 1976) of (V) with the atom-numbering scheme and thermal ellipsoids at the 50% probability level.

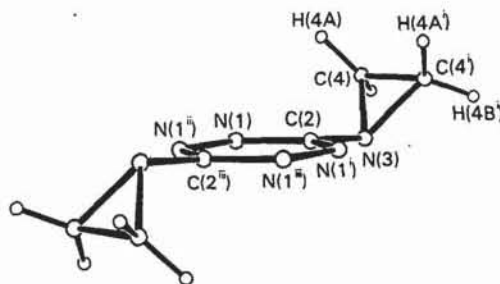


Fig. 2. Perspective view of (VI) with the atom-numbering scheme.

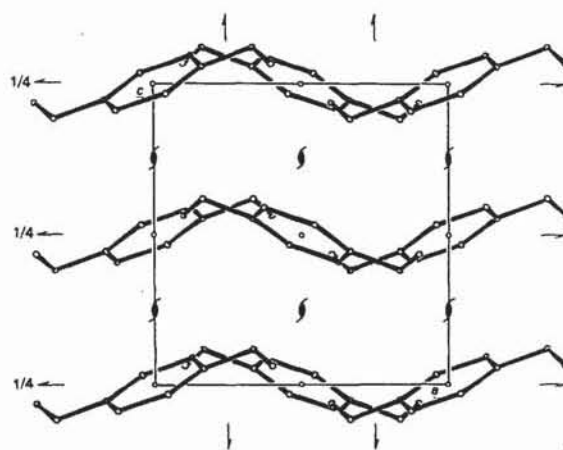


Fig. 3. Packing arrangement of (V) as viewed along *b*.

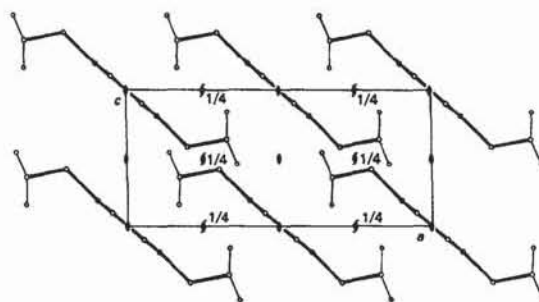


Fig. 4. Packing arrangement of (VI) as viewed along *b*.

N—C—N angles ( $\approx 125^\circ$ ) produce a compressed six-membered ring in which all bonds (N—N  $\approx 1.32$  and C—N  $\approx 1.34$  Å) have partial ( $\approx 50\%$ ) double-bond character consistent with the resonance structure. The exocyclic bonds, C(3)—O(3') = 1.328 (2) Å in (V) and C(2)—N(3) = 1.385 (1) Å in (VI), are also remarkably short. As in the case of (IV) we interpret this finding as a result of the strong electron-acceptor property of the 1,2,4,5-tetrazine system. The methoxy and also, surprisingly, the 1-aziridinyl substituents serve as weak  $\pi$ -electron donors. The interaction of the lone pair of electrons at the exocyclic heteroatoms with the electron-deficient  $\pi$  system of the molecule gives the exocyclic C(3)—O(3') and C(2)—N(3) bonds some double-bond character. Bond distances and angles of the aziridinyl substituents correspond to known data for the aziridine ring (e.g. Boese, Rademacher & Treschanke, 1985; Rudchenko, D'yachenko, Zolotoi, Atovmyan, Chervin & Kostyanovsky, 1982).

The molecular packing of (V) viewed along **b** is shown in Fig. 3. The 1,2,4,5-tetrazine moieties are positioned in a herringbone arrangement. (VI) shows layers in the (201) plane in which each 1,2,4,5-tetrazine unit is surrounded by four neighbouring molecules. The packing arrangement of the layers, separated from each other by 3.18 Å and with the shortest intermolecular contact C(2)···C(2)(-x, y, 1-z) = 3.244 Å, is illustrated in Fig. 4.

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