The Crystal and Molecular Structures of 1-(p-Bromophenyl)-5-bromopyridazine-3,6-dione and 1-(p-Bromophenyl)-4-diethylaminopyridazine-3,6-dione (1)

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The structure of 1-(p-bromophenyl)-5-bromopyridazine-3,6-dione was unequivocally establish-
ed by means of an X-ray crystal structure determination. By the same means its reaction product
with diethylamine was proved to be 1-(p-bromophenyl)-4-diethylaminopyridazine-3,6-dione.

Introduction.

The bromine atom of 1-aryl-2-methyl-5-bromopyri-
dazine-3,6-diones easily undergoes cine-substitution (2-4),
leading to a 4-substituted compound (2). Druey and
coworkers have shown that the mechanism of substitution
involves two subsequent stages: a primary addition of
the nucleophilic reagent at position 4, followed by
elimination of hydrogen bromide (2). This mechanism
was based on the result of the reaction of 1-phenyl-2-
methyl-5-bromopyridazine-3,6-dione (1a) with ammonia
in methanol at 25°, yielding a mixture of 1-phenyl-2-
methyl-4-amino-5-bromopiperidazine-3,6-dione (2a) and
1-phenyl-2-methyl-4-aminopyridazine-3,6-dione (3a) (2).

Picture A

a : X = H; b : X = Br
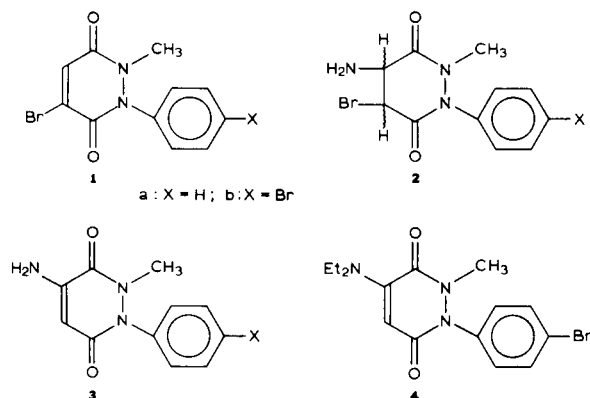
However, we observed that the addition product 2a is
quite stable under basic conditions and could not be
transformed to the compound 3a under the very mild
conditions mentioned above. This somewhat surprising
result induced us to establish unequivocally whether the
product obtained on reaction of a 5-bromopyridazine-3,6-
dione with amines has indeed the structure of a 4-
substituted derivative.

Therefore, a crystal structure determination of the

reaction product of 1-(p-bromophenyl)-2-methyl-5-bromo-
pyridazine-3,6-dione (1b) with diethylamine was under-
taken, which confirmed that compound 1b indeed gave
the 4-substituted product, i.e., the 1-(p-bromophenyl)-2-
methyl-4-diethylaminopyridazine-3,6-dione (4). Since
compound 1b is obtained by dehydrobromination of
1-(p-bromophenyl)-2-methyl-4,5-dihydro-4,5-dibromopyri-
dazine-3,6-dione the crystal structure of 1b was also
determined to make sure that the bromine atom in 1b
is indeed located on position 5 and not on position 4.

1-(p-Bromophenyl)-2-methyl-5-bromopyridazine-3,6-dione
(1b).

Crystal and Intensity Data.

Crystals of 1-(p-bromophenyl)-2-methyl-5-bromopyri-
dazine-3,6-dione (1b) are triclinic with space group $P\bar{1}$ and
four molecules in a unit cell of the following dimensions:
a = 8.198(1), b = 11.335(2), c = 13.826(2) Å α = 105.08(1),
β = 96.08(2), γ = 95.87(2)°. A number of 2167 in-
dependent reflexions were collected by means of a
NONIUS CAD4 single crystal diffractometer using graphite
monochromatised CuKα radiation, 717 of which were
below the 2σ-level and were treated as unobserved. The
intensities were corrected for absorption (μ = 88.0
cm^{-1}; crystal dimensions 0.25x0.18x0.11 mm).

Structure Determination and Refinement.

The four Br atoms in the asymmetric unit were
located from an (E^2-1) Patterson synthesis. A subsequent
Patterson minimum function based on the positions of
the eight Br atoms in the unit cell revealed the remaining
non-hydrogen atoms. Refinement proceeded by aniso-
tropic block-diagonal least-squares calculations, during
the course of which the H atoms were found from a
difference fourier synthesis. They were introduced in the
final refinement cycles with fixed parameters. The
anomalous contribution to the scattering of Br was taken

into account. The final R-value was 4.1% for the 1450 observed reflexions. The final parameters are listed in Table 1.

Discussion.

The bromo substituent in the pyridazine ring is in the *meta* position with respect to the *p*-bromophenyl group. The two independent molecules A and B in the asymmetric unit are very similar, the only real difference being in the angle between the planes of the benzene ring and the pyridazine ring, 70° for molecule A and 102° for molecule B. The bond lenghts and interbond angles for both molecules are listed in Table 2 (for the atomic numbering see Figure 1a). From the differences between the corresponding values it is clear that the calculated standard deviations are somewhat underestimated. The average values are indicated in Figure 1. These compare very well with those reported for 1,2-dimethylpyridazine-3,6-dione (5), listed in column 4 of Table 2. The normal valence structure I of Figure 2a for pyridazine-3,6-dione cannot account for the bond lengths as found in the two compounds under consideration. The shortening of N(1)-C(4) and N(2)-C(1) relative to the single bond value of 1.48 Å requires considerable contributions from resonance structures II, III, IV and V of Figure 2a. The pyridazine

Figure 1. Average bond length (a) and interbond angles (b) in compound **1b** (The molecule depicted is molecule A projected onto the plane of the pyridazine ring).
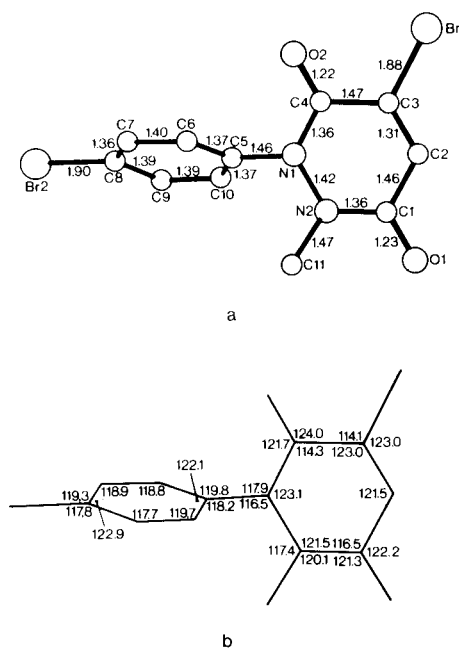

a

b

Table 1

Final Coordinates with their Estimated Standard Deviations of Compound **1b**

	molecule A			molecule B		
	x	y	z	x	y	z
Br(1)	.32070(12)	1.17283(10)	.24547(8)	-.37126(12)	.14190(11)	-.04920(8)
Br(2)	.65126(18)	.45763(10)	.38605(11)	.19568(17)	.78146(11)	.48282(9)
C(1)	.8116(10)	1.1036(8)	.2380(7)	.1478(11)	.1933(9)	-.0147(7)
C(2)	.6553(11)	1.1513(8)	.2241(7)	-.0268(11)	.1407(9)	-.0430(7)
C(3)	.5246(10)	1.1114(8)	.2603(7)	-.1451(10)	.2029(8)	-.0119(6)
C(4)	.5225(10)	1.0121(8)	.3094(6)	-.1133(10)	.3273(8)	.0606(7)
C(5)	.6692(11)	.8460(8)	.3367(7)	.0951(10)	.4713(8)	.1828(6)
C(6)	.6535(12)	.8330(9)	.4307(7)	.1510(13)	.5898(9)	.1806(7)
C(7)	.6482(13)	.7162(9)	.4461(8)	.1825(14)	.6839(9)	.2726(8)
C(8)	.6600(12)	.6183(9)	.3664(8)	.1577(13)	.6553(9)	.3591(7)
C(9)	.6775(13)	.6299(9)	.2709(7)	.1034(13)	.5349(9)	.3622(7)
C(10)	.6805(13)	.7462(9)	.2558(7)	.0733(13)	.4429(9)	.2706(7)
C(11)	.9718(12)	.9834(10)	.3259(9)	.3472(12)	.3762(10)	.0715(8)
N(1)	.6687(9)	.9670(7)	.3191(6)	.0513(9)	.3726(7)	.0884(6)
N(2)	.8145(8)	1.0167(6)	.2885(6)	.1801(8)	.3068(7)	.0531(6)
O(1)	.9392(8)	1.1448(6)	.2101(6)	.2579(8)	.1408(7)	-.0524(5)
O(2)	.3978(8)	.9682(6)	.3364(5)	-.2194(8)	.3850(7)	.0947(6)
H(2)	.660	.204	.175	.060	.954	.078
H(6)	.632	.896	.485	.144	.607	.113
H(7)	.632	.693	.513	.232	.764	.275
H(9)	.692	.546	.200	.108	.511	.438
H(10)	.696	.875	.183	.032	.329	.270
H(11A)	1.048	1.025	.298	.340	.436	.028
H(11B)	.972	.921	.275	.364	.393	.145
H(11C)	.960	.936	.380	.420	.321	.033

Table 2

Bond Lenghts and Interbond Angles

a. Molecule A, b. Molecule B, c. 1,2-Dimethylpyridazine-3,6-dione (5)

	a	b	c		a	b	c
N(1)-N(2)	1.421(12)Å	1.411(12)Å	1.406Å	N(2)N(1)C(4)	122.7(8)°	123.5(7)°	122.3
N(1)-C(4)	1.358(12)	1.370(11)	1.369	N(2)N(1)C(5)	116.5(8)	116.4(7)	117.0
N(1)-C(5)	1.454(13)	1.464(10)	1.467	C(4)N(1)C(5)	119.0(8)	116.7(8)	119.3
N(2)-C(1)	1.348(13)	1.362(11)	1.369	N(1)N(2)C(1)	121.5(7)	121.4(7)	122.3
N(2)-C(11)	1.460(13)	1.470(12)		N(1)N(2)C(11)	117.5(9)	117.2(7)	117.0
C(1)-C(2)	1.454(13)	1.464(12)	1.465	C(1)N(2)C(11)	120.5(8)	119.7(8)	119.3
C(1)-O(1)	1.241(12)	1.220(12)	1.239	N(2)C(1)C(2)	116.7(8)	116.2(8)	116.0
C(2)-C(3)	1.317(14)	1.301(13)	1.337	N(2)C(1)O(1)	120.9(9)	121.7(8)	121.4
C(3)-C(4)	1.457(15)	1.482(11)	1.465	C(2)C(1)O(1)	122.3(10)	122.1(8)	122.7
C(3)-Br(1)	1.887(9)	1.879(8)		C(1)C(2)C(3)	121.0(10)	121.9(8)	121.4
C(4)-O(2)	1.227(11)	1.204(12)	1.239	C(2)C(3)C(4)	123.1(9)	122.8(8)	121.4
C(5)-C(6)	1.363(15)	1.383(14)		C(2)C(3)Br(1)	122.2(8)	123.7(6)	
C(5)-C(10)	1.387(13)	1.359(14)		C(4)C(3)Br(1)	144.7(6)	113.5(6)	
C(6)-C(7)	1.392(16)	1.411(11)		C(3)C(4)N(1)	114.7(8)	113.9(8)	116.0
C(7)-C(8)	1.365(14)	1.348(16)		C(3)C(4)O(2)	123.4(8)	124.6(8)	122.7
C(8)-C(9)	1.381(16)	1.405(15)		N(1)C(4)O(2)	121.9(10)	121.5(8)	121.4
C(8)-Br(2)	1.905(12)	1.895(9)		N(1)C(5)C(6)	119.5(8)	120.1(9)	
C(9)-C(10)	1.386(16)	1.395(12)		N(1)C(5)C(10)	118.5(9)	117.8(8)	
				C(6)C(5)C(10)	122.0(10)	122.1(8)	
				C(5)C(6)C(7)	119.1(9)	118.5(9)	
				C(6)C(7)C(8)	118.7(11)	119.1(7)	
				C(7)C(8)C(9)	122.9(11)	122.8(8)	
				C(7)C(8)Br(2)	119.2(9)	119.4(7)	
				C(9)C(8)Br(2)	117.9(8)	117.7(8)	
				C(8)C(9)C(10)	118.0(9)	117.4(10)	
				C(9)C(10)C(5)	119.2(10)	120.2(9)	

Figure 2. a) Resonance structures for pyridazine-3,6-dione b) Additional resonance structures for 4-aminopyridazine-3,6-dione.

I	II	III	IV	V

a

VI	VII

b
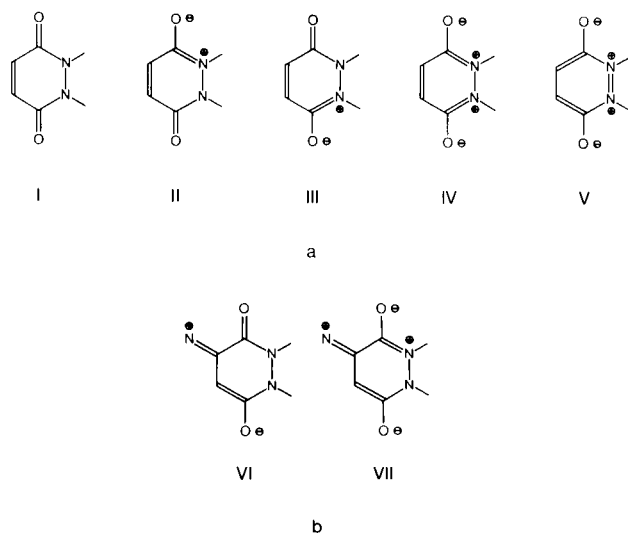
ring is not exactly planar. The deviations from the best plane through the atoms of the pyridazine ring are listed in Table 3 for a number of atoms. As can be seen from this table the bonds issuing from the N atoms are not coplanar; the angles around N(1) add up to 358.2 and 356.6°.

Those around N(2) to 359.5 and 358.2° for molecules A and B respectively. The benzene rings are planar within the limits of accuracy with Br(2) and N(1) at 0.024 and -0.043 Å from the ring for molecule A and at -0.040 and at -0.040 and 0.092 Å for molecule B.

1-(p-Bromophenyl)-2-methyl-4-diethylaminopyridazine-3,6-dione (4).

Crystal and Intensity Data.

Crystals of 1-(p-bromophenyl)-2-methyl-4-diethylamino-pyridazine-3,6-dione (4) are monoclinic with space group C2/c and eight molecules in a unit cell of dimensions: a = 27.504(3), b = 9.470(3), c = 12.539 Å and β = 102.60(1).

A number of 1824 reflexions above the 2σ-level were collected by means of a NONIUS CAD4 single crystal diffractometer using graphite monochromatised CuKα radiation. No absorption correction was applied (μ= 38.2 cm⁻¹; crystal dimensions 0.28x0.25x0.13 mm).

Structure Determination and Refinement.

The position of the Br atom in the asymmetric unit was derived from an (E²-1) Patterson synthesis. A Patterson minimum function based on four translation independent Br positions in the unit cell enabled the remaining non-hydrogen atoms to be found. Anisotropic

Table 3

Deviations from the Best Planes Through the Pyridazine Rings

	Molecule A	Molecule B
N(1)	-.03 Å	.00 Å
N(2)	.04	.01
C(1)	-.01	-.02
C(2)	-.02	.03
C(3)	.03	-.01
C(4)	.00	.00
O(1)	.02	-.14
O(2)	-.06	.03
C(5)	-.48	.47
C(11)	.35	-.28
Br(1)	.05	-.01

Table 4

Final Coordinates with their Estimated Standard Deviations
of the Atoms in Compound 4

	x	y	z
Br	.50554(3)	.34040(12)	.41366(8)
C(1)	.2054(2)	.4009(7)	.2968(5)
C(2)	.1871(2)	.4836(6)	.3830(4)
C(3)	.2188(2)	.4893(7)	.4841(4)
C(4)	.2684(3)	.4402(6)	.5079(5)
C(5)	.3380(2)	.3781(7)	.4223(4)
C(6)	.3712(3)	.3055(7)	.5036(5)
C(7)	.4203(3)	.2974(8)	.5022(6)
C(8)	.4376(2)	.3616(7)	.4684(6)
C(9)	.4056(2)	.4355(7)	.3370(5)
C(10)	.3558(2)	.4442(7)	.3389(5)
C(11)	.2672(3)	.2435(7)	.2529(5)
C(12)	.1086(2)	.5555(8)	.2503(5)
C(13)	.0694(3)	.4438(12)	.2186(7)
C(14)	.1210(2)	.6004(8)	.4485(5)
C(15)	.1355(3)	.7528(8)	.4667(6)
N(1)	.2863(2)	.3791(6)	.4228(4)
N(2)	.2531(2)	.3583(5)	.3202(3)
N(3)	.1406(2)	.5333(5)	.3598(4)
O(1)	.1780(2)	.3669(5)	.2105(3)
O(2)	.2973(2)	.4541(5)	.5972(3)
H(3)	.211(3)	.531(7)	.548(5)
H(6)	.361(4)	.255(10)	.552(7)
H(7)	.439(3)	.242(10)	.548(6)
H(9)	.420(2)	.471(6)	.276(5)
H(10)	.336(3)	.510(8)	.291(5)
H(11A)	.231(3)	.196(10)	.201(6)
H(11B)	.287(3)	.288(7)	.202(6)
H(11C)	.294(3)	.197(8)	.291(5)
H(12A)	.130(3)	.567(7)	.197(5)
H(12B)	.092(3)	.661(7)	.248(5)
H(13A)	.048(3)	.437(8)	.257(6)
H(13B)	.053(3)	.477(10)	.173(7)
H(13C)	.085(3)	.346(8)	.215(7)
H(14A)	.133(2)	.541(6)	.512(5)
H(14B)	.083(3)	.590(6)	.426(5)
H(15A)	.174(2)	.767(6)	.487(4)
H(15B)	.115(3)	.795(8)	.524(5)
H(15C)	.122(3)	.815(8)	.401(6)

Table 5

Bond Distances and Interbond Angles in Compound 4

N(1)-N(2)	1.420(6)Å	N(2)N(1)C(4)	119.1(5)°
N(1)-C(4)	1.395(9)	N(2)N(1)C(5)	116.2(5)
N(1)-C(5)	1.423(8)	C(4)N(1)C(5)	121.7(5)
N(2)-C(1)	1.342(8)	N(1)N(2)C(1)	124.1(5)
N(2)-C(11)	1.479(9)	N(1)N(2)C(11)	115.0(5)
C(1)-C(2)	1.507(9)	C(1)N(2)C(11)	117.5(5)
C(1)-O(1)	1.219(7)	N(2)C(1)C(2)	117.6(5)
C(2)-C(3)	1.374(7)	N(2)C(1)O(1)	120.0(6)
C(2)-N(3)	1.334(8)	C(2)C(1)O(1)	122.4(6)
C(3)-C(4)	1.410(10)	C(1)C(2)C(3)	116.0(5)
C(4)-O(2)	1.231(8)	C(1)C(2)N(3)	118.8(5)
C(5)-C(6)	1.393(9)	C(3)C(2)N(3)	124.9(5)
C(5)-C(10)	1.396(9)	C(2)C(3)C(4)	124.9(6)
C(6)-C(7)	1.357(12)	C(3)C(4)N(1)	117.5(5)
C(7)-C(8)	1.385(11)	C(3)C(4)O(2)	124.1(7)
C(8)-C(9)	1.384(9)	N(1)C(4)O(2)	118.3(7)
C(8)-Br	1.893(6)	N(1)C(5)C(6)	119.7(6)
C(9)-C(10)	1.378(9)	N(1)C(5)C(10)	121.0(5)
N(3)-C(12)	1.475(8)	C(6)C(5)C(10)	119.3(6)
C(12)-C(13)	1.501(12)	C(5)C(6)C(7)	120.9(7)
N(3)-C(14)	1.481(9)	C(6)C(7)C(8)	119.5(6)
C(14)-C(15)	1.501(11)	C(7)C(8)C(9)	120.9(6)
		C(7)C(8)Br	118.8(5)
		C(9)C(8)Br	120.3(6)
		C(8)C(9)C(10)	119.5(6)
		C(9)C(10)C(5)	119.9(5)
		C(2)N(3)C(12)	127.0(6)
		C(2)N(3)C(14)	118.4(5)
		C(12)N(3)C(14)	113.4(5)
		N(3)C(12)C(13)	113.2(6)
		N(3)C(14)C(15)	113.5(6)

Table 6

Deviations from the Best Plane Through
the Pyridazine Ring

N(1)	.04 Å
N(2)	-.01
C(1)	-.04
C(2)	.06
C(3)	-.03
C(4)	-.03
N(3)	.09
C(1)	-.22
O(2)	-.02
C(5)	.58
C(11)	-.51
C(12)	.45
C(14)	.04

least-squares refinement was applied. The H atoms were located in a difference fourier synthesis and included in the refinement with isotropic temperature parameters. The anomalous scattering of Br was taken into account. The final R-value for the 1824 observed reflexions was 5.3%. The final coordinates are listed in Table 4.

Discussion.

The diethylamino group is in the *para* position relative to the p-bromophenyl group. The bond lengths and interbond angles are listed in Table 5 and indicated in Figure 3 where also the atomic numbering is given. Comparison with the results for 1-(p-bromophenyl)-2-methyl-5-bromopyridazine-3,6-dione (Figure 1) shows that the introduction of the diethylamino group has markedly affected the bond lenghts within the pyridazine ring. Judging from the length of the bond C(2)-N(3), considerable interaction of N(3) with the pyridazine ring must exist. In fact the most conspicous changes, shortening of N(2)-C(1) and C(3)-C(4) and lengthening of C(1)-C(2), C(2)-C(3) and C(4)-N(1), can be reasonably accounted for by the additional resonance structures VI and VII of Figure 2b that may be expected to come into play. The pyridazine ring is not completely planar. The deviations from the best plane through the pyridazine ring are given in Table 6 for a number of atoms. The three N atoms are not coplanar with their direct neighbours as can be seen from Table 6 for N(1) and N(2). The angles around the N atoms add up to 357.0, 356.6 and 358.8° for N(1), N(2) and N(3) respectively. The benzene ring is planar within 0.005 Å with Br and N(1) at 0.10 and 0.08 Å from its plane respectively. The angle between the planes of the benzene ring and the pyridazine ring is 53°.

Figure 3. Average bond length (a) and interbond angle (b) in compound **4**.

a

b
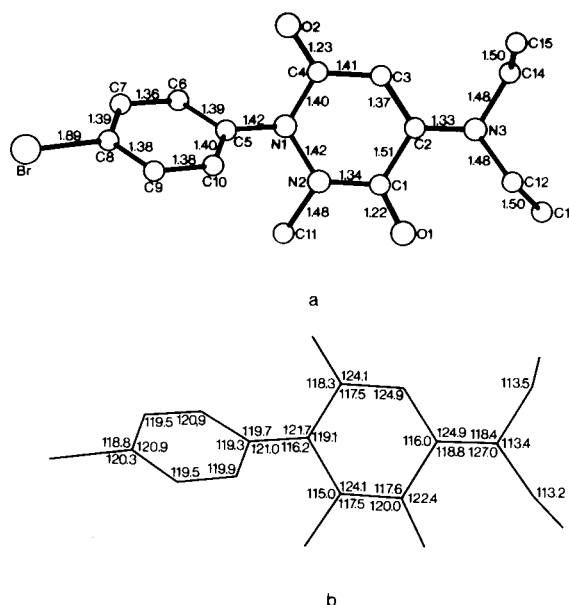
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