Crystal Structure of 5,10-(Diphenyl)-5,10-dihydrophenarsazine

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The crystal structure of the title compound **1**, the first phenarsazine possessing a 10-phenyl substituent to be synthesized, has been determined by single crystal x-ray methods. The crystals are monoclinic, space group $P2_1/c$ with four molecules in a cell of dimensions a = 10.737(3), b = 8.561(4), c = 20.523(7)Å, β = 91.91(3)° and V = 1885(1)Å^3. The structure has been refined by full matrix least-squares to R = 0.046 using 2087 observed reflections. The folding angle between the two benzo planes is 151.7(4)° indicating that **1** is significantly more puckered than phenarsazines substituted with 5-aryl groups. Moreover, although both phenyl groups adopt a boat-axial conformation, the planes of the aryl rings are nearly perpendicular to each other with the 10-phenyl group adopting the usual conformation (*i.e.* in the plane bisecting the phenarsazine ring which contains As(5) and N(10)) and the 5-phenyl group assuming the a typical conformation (*i.e.* very nearly perpendicular to the plane bisecting phenarsazine ring). The bond distance between As and the carbon atom of the 5-phenyl ring is approximately the same as that found in other 5-arylphenarsazine compounds indicating little resonance interactions between As and the aromatic ring in **1**.

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Introduction.

Over the past several years, we have been studying the effect of 10-aryl and 10-heteroaryl substitutents on the structure of phenothiazines [1-9] and pyrido[3,2-*b*][1,4]benzothiazines [10-14]. From these studies, we showed that the electronic nature and location of groups on the 10-aromatic moiety influence strongly 1) the conformation that the aromatic ring assumes relative to the plane bisecting the ring containing the two heteroatoms of the tricyclic ring and 2) the folding angle of the tricyclic ring [15]. For example, 10-aryl rings possessing electron-releasing groups, such as 4'-OMe [13] and 4'-Br [10], adopt conformations in which the 10 aryl ring lies nearly in the plane bisecting the central ring of the tricyclic compound. 10-Aryl rings substituted with electron-attracting groups, *e.g.* 2'-NO_2 group, that are prevented sterically from interacting by resonance with the lone electron pair on N-10, adopt similar conformations. The folding angles of these tricyclic compounds lie in the range of 145-166° [1,3,5-14].

On the other hand, 10-aryl rings substituted with electron-attracting groups, such as 4'-NO_2 [2] or the 2-pyrazyl heterocyclic ring [4,12], which do interact directly with the lone electron pair on N-10 by resonance, adopt conformations in which the 10-aryl ring is nearly perpendicular to the plane bisecting the ring containing the two heteroatoms of the tricyclic ring. Because of the mutual resonance interactions of the 10-aryl group and the N-10 electron pair, the folding angles of these compounds range between 120-133° [2,4], which are significantly lower than those of 10-aryl substituted phenothiazines in which these resonance interactios are absent.

Knowledge of the folding angles of these tricyclic compounds is important since they appear, in part, to influence the pharmacological activity of several important neuroleptic phenothiazine derivatives. For example, the increased planarity resulting from replacement of the 2-chloro group of phenothiazine (folding angle = 139.0°) [16] with a 2-methoxy substituent (folding angle = 157.4) [17] is accompanied with complete loss of pharmacological activity [18].

We recently turned our direction to obtaining structural information on 5,10-dihydrophenarsazines. This ring system is interesting in that it allows one to assess the influence of aromatic rings substituted on both heteroatoms in the central tricyclic ring in contrast to phenothiazine ring system which allow only 10-aryl intereacts to be ascertained. 3'-Methoxy-5-phenyl-5,10-dihydrophenarsazine was the first in this series to be prepared and its crystal structure revealed that the 5-aryl group existed in the plane bisecting the phenarsazine ring and the folding angle of the compound was 164.6° [19]. This paper reports on the preparation and crystal structure of 5,10-diphenyl-5,10-dihydrophenarsazine (**1**).

EXPERIMENTAL

Title compound **1** was prepared in the following way. Sodamide (0.02 mole) was prepared from 0.46 g (0.02 mole) of sodium in liquid ammonia (50 ml) containing 0.01 g of ferric nitrate. After the discharge of the initial blue solution to gray, indicating the conversion of the sodium to sodamide, 2.19 g (0.01 mole) of 5-phenyl-5,10-dihydrophenarsazine was added over a period of 5 minutes. After the addition was complete, the mixture was stirred for 10 minutes then 0.79 g (0.005 mole) of bromobenzene was added. The mixture was then stirred for 1 hour, quenched with ammonium chloride, and the ammonia evaporated. The residue was extracted with methylene chloride (3 × 25 ml), and the combined extracts were washed with brine, dried (sodium sulfate), and concentrated under reduced pressure to yield an oil. Compound **1** was obtained by flash chromatography of the oil using a mixture of hexane/ethyl acetate [9:1] as the eluent. Suitable crystals in the shape of transparent colorless cubes were obtained by recrystallizing **1** with solvent mixture containing hexane and ethyl acetate.

Data Collection and Reduction.

A crystal of approximate size 0.60 × 0.50 × 0.40 mm was mounted with an epoxy resin and used for the determination of unit cell parameters and intensity measurements. Unit cell parameters were obtained from a least-squares fit to the 2θ values of 25 reflections centered in the range $10 < 2\theta < 25$ measured on a Nicolet R_3m/V automatic diffractometer with graphite monochromatazized MoKα radiation. The crystal data are summarized in Table 1.

Table 1

Summary of Parameters in the X-ray Structure Determination

Chemical formula	$C_{24}H_{18}NAs$
Formula weight	395.35
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 10.737(3) Å b = 8.561(4) Å c = 20.523(7) Å β = 91.91(3)° V = 1885(1) Å^3
Number of molecules per unit cell	4
Density calculated	1.39 g cm^{-3}
X-ray radiation used for data collection	λ(MoKα) = 0.71069
Linear absorption coefficient	μ(MoKα) = 18.02 cm^{-1}
Total number of independent reflections with $2\theta < 50°$	2950
Number of reflections with $I > 3\sigma(I)$	2087
R-indexes for 2087 observed reflections	R = 0.046, Rw = 0.0038
Maximum residual electron density	0.25 e/Å^3

Solution and Refinement of the Structure.

The space group $P2_1/c$ (#15) was determined from the systematic absences (*hOl, l* odd, *OkO, k* odd). There was no significant change in the intensities of 3 standard reflections remeasured after every 100 reflections which indicated crystal and electronic stability. The data were collected in the $\theta/2\theta$ scan mode with a variable scan rate 3.00-14.7°/minute. A total of 2950 independent reflections was collected in the range $3 < 2\theta < 50°$, out of which, 2087 were considered observed based on $I > 3\sigma(I)$, where $\sigma(I)$ was determined from counting statistics. The intensity data were reduced to structure amplitudes by application of the Lorentz and Polarization corrections. No correction for absorption was applied.

The structure was solved by direct methods, using SHELXTL-Plus [20] which showed the positions of all non hydrogen atoms. All non-hydrogen atoms were refined anisotropically. Hydrogen positions were calculated using the constraint as phenyl hydrogen and included in the refinement with isotropic temperature factors. The quantity minimized in the least-squares refinement was $\Sigma w(|Fo|-|Fc|)^2$. In the final stages of refinement, a weight $w = 1/\sigma^2(F) + 0.000202\ F^2$) was used. The final R indexes are R = 0.046 and wR = 0.038 for 2087 observed reflections. Maximum shift/deviation ratio was 0.06. The atomic scattering factors for C, H, N and As and the effect of anomalous dispersion for As used were those stored in SHELXTL-Plus. The final atomic parameters are given in Table 2. A list of structure factors and anisotropic thermal parameters have been deposited [21].

Table 2

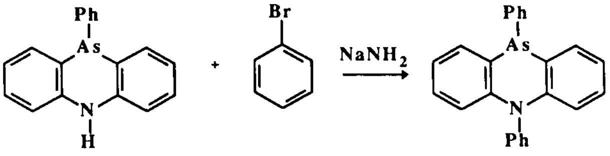
Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($A^2 \times 10^3$)

	x	y	z	U(eq)
C(1)	650(4)	−1685(5)	8853(2)	52(2)
C(2)	974(5)	−3204(6)	8734(2)	66(2)
C(3)	2202(5)	−3667(7)	8743(2)	69(2)
C(4)	3108(5)	−2571(6)	8857(2)	61(2)
C(4a)	2828(4)	−1009(5)	8973(2)	47(2)
As(5)	4140(1)	518(1)	9033(1)	55(1)
C(5a)	3233(3)	1934(5)	9571(2)	49(2)
C(6)	3884(4)	2965(6)	9982(2)	64(2)
C(7)	3298(5)	4100(6)	10327(2)	65(2)
C(8)	2017(5)	4218(6)	10267(2)	62(2)
C(9)	1347(4)	3203(5)	9874(2)	52(2)
C(9a)	1930(3)	2035(5)	9524(2)	42(1)
N(10)	1222(3)	1005(4)	9125(2)	42(1)
C(10a)	1567(3)	−560(5)	8983(2)	42(1)
C(11)	−10(3)	1491(5)	8905(2)	42(1)
C(12)	−138(4)	2164(5)	8301(2)	62(2)
C(13)	−1299(5)	2598(7)	8057(3)	83(2)
C(14)	−2323(5)	2350(6)	8429(3)	77(2)
C(15)	−2207(4)	1709(6)	9029(3)	68(2)
C(16)	−1039(4)	1258(5)	9274(2)	54(2)
C(17)	3753(3)	1590(5)	8201(2)	47(2)
C(18)	4111(4)	3126(6)	8124(3)	65(2)
C(19)	3884(5)	3885(8)	7539(3)	86(3)
C(20)	3311(5)	3122(8)	7023(3)	85(3)
C(21)	2957(5)	1595(8)	7095(3)	88(3)
C(22)	3175(4)	861(6)	7681(2)	71(2)
H(1)	−213	−1385	8845	41(11)
H(2)	331	−3961	8645	76(16)
H(3)	2418	−4739	8670	66(15)
H(4)	3966	−2887	8857	60(13)
H(6)	4774	2876	10024	58(12)
H(7)	3766	4799	10607	71(14)
H(8)	1590	5015	10501	60(14)
H(9)	457	3302	9839	55(12)
H(12)	582	2337	8045	47(11)
H(13)	−1402	3066	7633	73(15)
H(14)	−3134	2638	8258	83(15)
H(15)	−2925	1563	9289	66(14)
H(16)	−936	786	9696	58(13)
H(18)	4522	3671	8479	114(22)
H(19)	4125	4958	7493	126(24)
H(20)	3162	3651	6616	74(15)
H(21)	2560	1043	6738	120(23)
H(22)	2912	−203	7728	74(15)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

Results and Discussion.

The title compound **1** was prepared by treating 5-phenyl-5,10-dihydrophenarsazine with bromobenzene in the presence of sodamide in liquid ammonia. Although 5-aryl substituted phenarsazines are readily prepared by a Grignard reaction involving the appropriate 5-chloro-5,10-dihydrophenarsazine and aryl magnesium halide [22], to our knowledge no synthesis of 10-aryl derivatives have been reported.



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The identification of the atoms and the configuration of the **1** are shown in the ORTEP [23] drawing in Figure 1. The dihydrophenarsazine ring is folded (the folding angle between the two benzo planes is 151.7(4)° with the central ring in a flattened boat conformation as shown in the front view of the molecule in Figure 1 and by the torsion angles (Table 5) around the central ring and $q_2 = 0.474(4)$, $q_3 = 0.112(4)$, $\Phi_2 = 358.39(51)$, $Q = 0.487$ and $\theta = 76.76$ of the Cremer and Pople [24] puckering parameters. The near perpendicularity of 5-aryl and 10-aryl groups is shown in Figure 2. Selected bond lengths, bond angles and the atomic displacements from the least-squares planes and the dihedral angles are given in Tables 3, 4 and 6, respectively. The two phenyl groups occupy axial positions of the flattened boat central ring. Moreover, the aryl rings are nearly perpendicular (dihedral angle 107.3(4)) to each other and to the least-squares plane of the phenarsazine ring (dihedral angles 92.0(4) and 97.7(5)). The 10-phenyl group adopts the usual conformation (*i.e.* in the plane bisecting the phenarsazine ring) and the 5-phenyl group assumes the conformation (*i.e.* very nearly perpendicular to the plane bisecting the phenarsazine ring) observed only for

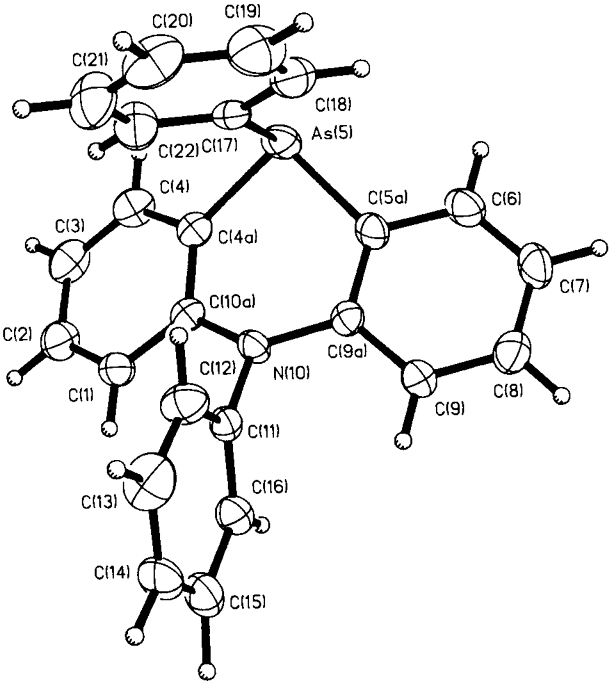

Figure 1. Ortep drawing of the molecule. Thermal Ellipsoids are scaled at 35% probability level. Hydrogen atoms are represented as spheres of arbitrary radii.

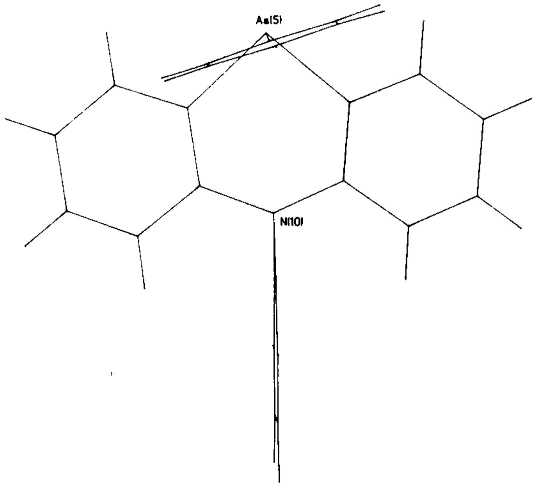

Figure 2. The view of the molecule showing the near perpendicularity of phenyl and phenarsazine rings.

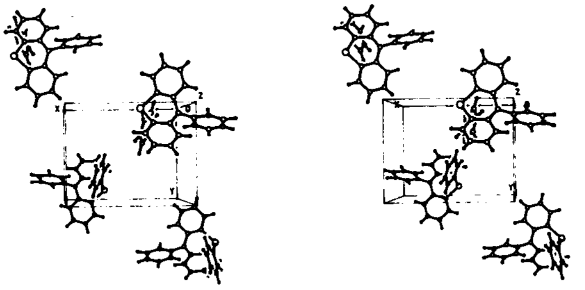

Figure 3. Stereoscopic drawing showing the packing of the molecules in the cell.

Table 3

Selected Bond Lengths (A)

C(4a)-As(5)	1.923 (4)	C(4a)-C(10a)	1.408 (5)
As(5)-C(5a)	1.926 (4)	As(5)-C(17)	1.970 (4)
C(5a)-C(9a)	1.402 (5)	C(9a)-N(10)	1.409 (4)
N(10)-C(10a)	1.423 (5)	N(10)-C(11)	1.445 (4)

electron-withdrawing aryl groups that mutually engage in resonance with the lone pair of electrons on N(10). The bond distance between As and the carbon atom of the 5-phenyl ring is approximately the same as that found in other 5-arylphenarsazine compounds indicating little resonance intereactions between As and the aromatic ring in **1** as would be expected because of the vast difference in size of the participating orbitals of arsenic and carbon. Apparently for steric reasons, the two phenyl groups avoid occupying the same plane; the rather large folding angle of **1** allows the 5-phenyl group to twist away from the 10-phenyl substituent.

Table 4

Selected Bond Angles (°)

As(5)-C(4a)-C(4)	120.1(3)	C(10a)-C(4a)-C(4)	118.6(4)
C(10a)-C(4a)-As(5)	121.1(3)	C(5a)-As(5)-C(4a)	94.7(2)
C(17)-As(5)-C(4a)	97.4(2)	C(17)-As(5)-C(5a)	96.2(2)
C(6)-C(5a)-As(5)	119.6(3)	C(9a)-C(5a)-As(5)	121.4(3)
N(10)-C(9a)-C(5a)	121.3(4)	N(10)-C(9a)-C(9)	120.4(3)
C(10a)-N(10)-C(9a)	124.7(3)	C(11)-N(10)-C(9a)	118.2(3)
C(11)-N(10)-C(10a)	116.7(3)	N(10)-C(10a)-C(1)	120.0(3)
N(10)-C(10a)-C(4a)	121.1(4)	C(12)-C(11)-N(10)	117.8(4)
C(16)-C(11)-N(10)	122.1(4)	C(18)-C(17)-As(5)	119.5(4)
C(22)-C(17)-As(5)	122.7(4)		

Table 5

Selected Torsion Angles (°)

C(4)-C(4a)-As(5)-C(5a)	−154.5(6)	C(4)-C(4a)-As(5)-C(17)	108.7(6)
C(10a)-C(4a)-As(5)-C(5a)	31.6(7)	C(10a)-C(4a)-As(5)-C(17)	−65.2(7)
C(4a)-As(5)-C(5a)-C(6)	154.3(6)	C(4a)-As(5)-C(5a)-C(9a)	−30.5(8)
C(17)-As(5)-C(5a)-C(6)	−107.8(7)	C(17)-As(5)-C(5a)-C(9a)	67.5(8)
As(5)-C(5a)-C(9a)-C(9)	−173.0(7)	As(5)-C(5a)-C(9a)-N(10)	5.9(6)
C(6)-C(5a)-C(9a)-C(9)	2.3(5)	C(6)-C(5a)-C(9a)-N(10)	−178.9(7)
C(5a)-C(9a)-N(10)-C(10a)	30.6(6)	C(5a)-C(9a)-N(10)-C(11)	−157.4(7)
C(9)-C(9a)-N(10)-C(10a)	−150.6(7)	C(9)-C(9a)-N(10)-C(11)	21.4(6)
C(4)-C(4a)-C(10a)-C(1)	−2.4(6)	C(4)-C(4a)-C(10a)-N(10)	177.5(7)
As(5)-C(4a)-C(10a)-C(1)	171.6(7)	As(5)-C(4a)-C(10a)-N(10)	−8.5(7)
C(9a)-N(10)-C(10a)-C(1)	150.8(7)	C(9a)-N(10)-C(10a)-C(4a)	−29.1(7)
C(11)-N(10)-C(10a)-C(1)	−21.3(7)	C(11)-N(10)-C(10a)-C(4a)	158.7(7)
C(9a)-N(10)-C(11)-C(12)	95.8(6)	C(9a)-N(10)-C(11)-C(16)	−86.0(7)
C(10a)-N(10)-C(11)-C(12)	−91.5(7)	C(10a)-N(10)-C(11)-C(16)	86.7(6)
C(4a)-As(5)-C(17)-C(18)	155.1(6)	C(4a)-As(5)-C(17)-C(22)	−27.2(7)
C(5a)-As(5)-C(17)-C(18)	59.5(7)	C(5a)-As(5)-C(17)-C(22)	−122.7(6)

Table 6

Atomic Displacements(A) from the Least-squares Planes

Plane #1

Atom	Deviation
C(11)	−0.003(4)
C(12)	0.004(5)
C(13)	0.001(4)
C(14)	−0.006(5)
C(15)	0.006(4)
C(16)	−0.002(5)

Plane #2

Atom	Deviation
C(17)	0.001(4)
C(18)	0.003(4)
C(19)	−0.004(5)
C(20)	0.001(5)
C(21)	0.004(4)
C(22)	−0.005(4)

Plane #3

Atom	Deviation
C(1)	−0.039(7)
C(2)	0.305(7)
C(3)	0.460(6)
C(4)	0.235(6)
C(4a)	−0.128(7)
As(5)	−0.628(6)
C(5a)	−0.141(7)
C(6)	0.213(6)
C(7)	0.440(6)
C(8)	0.320(6)
C(9)	−0.005(6)
C(9a)	−0.229(7)
N(10)	−0.560(7)
C(10A)	−0.243(6)

Angle between plane A and B

1	2	107.3(4)
1	3	92.0(4)
2	3	97.7(5)

The packing of the molecules in the unit-cell is shown in the stereoscopic drawing of Figure 3. There are no intermolecular contacts less than van der Waals distances.

Acknowledgements.

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