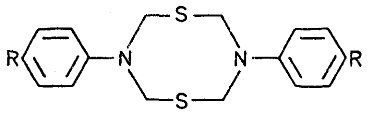
Stereochemistry. Part III.† Conformation of Eight-membered Heterocyclic Rings. Conformation of *NN*-Diphenyl-3,7-diaza-1,5-dithiacyclo-octane in Dioxan Solution

By **M. Vivekananda Bhatt** * and **Shiravante Atmaram,** Department of Organic Chemistry, Indian Institute of Science, Bangalore 560012, India
Vuppalapatty Baliah, Department of Chemistry, Annamalai University, Annamalainagar, India

A general method for defining the geometry of non-rigid ring systems has been developed by a modification of literature methods. Using this method, the resultant moments of different conformers of *NN*-diphenyl-3,7-diaza-1,5-dithiacyclo-octane have been calculated. These compounds prefer a crown conformation in dioxan solution with a diequatorial disposition of the substituents on nitrogen.

WHEREAS conformational analysis of eight-membered alicyclic systems has received considerable attention [1-12] substituted and heterocyclic eight-membered ring systems present a more complex picture.[13] With a view to studying their conformation and stereochemistry, we have prepared *NN*-diphenyl-3,7-diaza-1,5-dithiacyclo-octane (1a) and its *p*-bromo and *p*-methyl derivatives. We have measured the dipole moments of these compounds. Molecules with many polar bonds may be expected to have different resultant moments in different conformations. We thought a comparison of the experimental resultant moment with that calculated for different conformations might give definitive information about the conformational preference in solution. The experimental values of the dipole moments are given in Table 1.



(1) a; R=H
b; R=Br
c; R=CH$_3$

TABLE 1

Experimental dipole moments

Compound	μ/D
(1a)	2.92
(1b)	4.61
(1c)	2.54

RESULTS AND DISCUSSION

Three conformations, crown (I), boat-chair (II) and (III), and saddle (IV) and (V) were considered (Scheme 1). Two different approaches were made to interpret the results. (1) The first method involves the calculation of variation of dipole moment resulting from changes in the substituents and the angle at which they are disposed to each other in different conformations. (2) The second method involves computation of the resultant moment of the molecule by vector addition of group moments.

(1) *First Method.*—The angle between the two N–Ph bonds at opposite sides of the ring was evaluated using the differences in dipole moments of the substituted (1b and c) and unsubstituted compound (1a). If X is the resultant moment of the unsubstituted molecule and $(X + Y)$ the resultant moment of the substituted molecule, the substituents with group moment M must be oriented such that they produce an additional moment of Y. The angle θ between the two dipoles which produce the additional moment of Y is given by equation (1). In case (1b) assuming a C–Br group

$$2M \cos \theta_4 2 = Y \qquad (1)$$

moment of 1.5 D, 2(1.5cosθ/2 = 1.69 or θ = 112°. Similarly for (1c), with a C–Me group moment of —0.35 D, 2(—0.35)cosθ/2 = —0.38 or θ = 114°. Thus the angle θ between the two N–Ph bonds is evaluated as **113 ± 1°.**

The evaluation of this angle θ between the two N–Ph bonds in various possible conformers could be made using models. An *X*-ray analysis of a similar compound *NN*-dimethyl-3,7-diaza-1,5-dithiacyclo-octane has been reported [14] and showed the orientation of *N*-methyl groups to be axial,‡ *i.e.* almost perpendicular to the plane passing through the four carbon atoms of the ring.

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‡ The terms axial and equatorial do not have the same significance as in cyclohexane. 'Axial' refers to the bond that makes the smaller angle with vertical symmetry axis of the ring and 'equatorial' refers to the bond that makes the larger angle.

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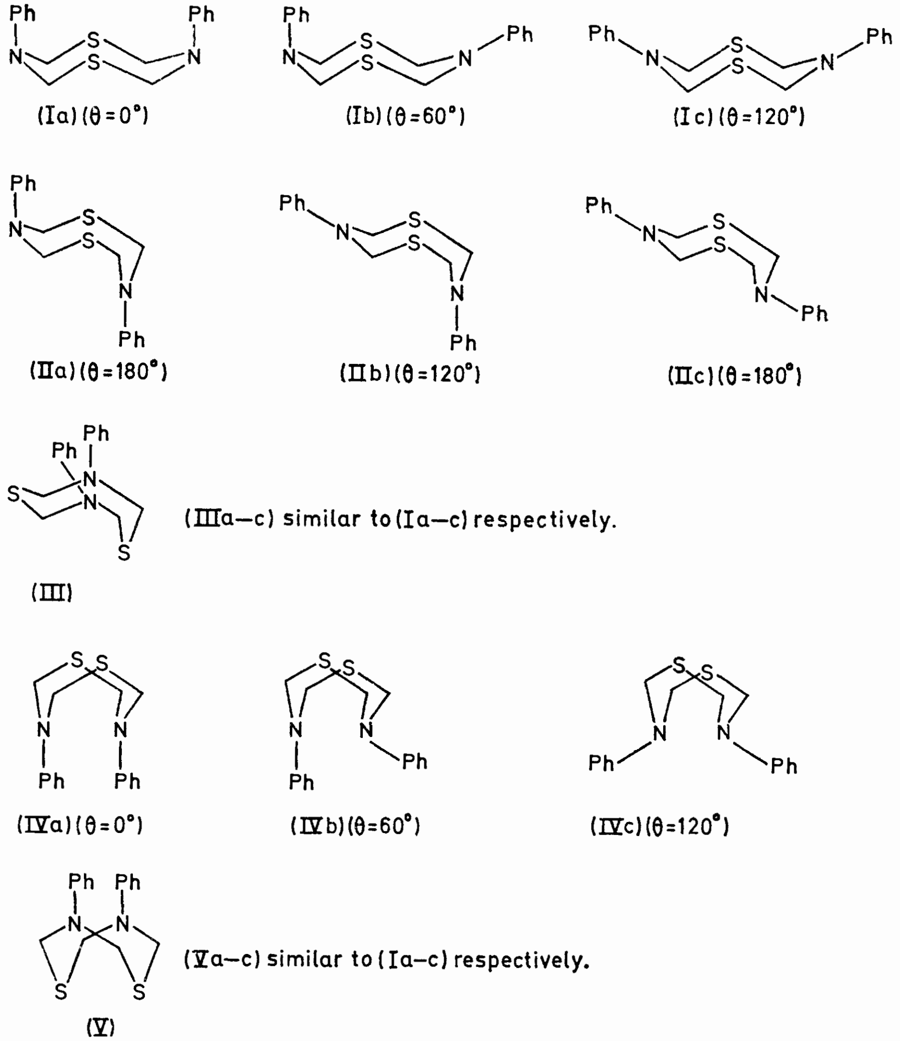
A similar situation for the *NN*-diphenyl compound is assumed. To account for other possible orientations of the N–Ph bond (equatorial), we have calculated the angle between the axial and equatorial bonds on nitrogen using the equation given by Hendrickson[15] for an irregular tetrahedron. Thus when $H_2C\widehat{N}CH_2$ and $H_2C\widehat{N}C_6H_5$ are 118 and 116° respectively (from *X*-ray analysis of the *NN*-dimethyl compound) the angle between the two possible bonds at nitrogen is calculated to be 63° 18′. When the axial bond on nitrogen is assumed to be almost perpendicular to the plane passing through the four carbon atoms of the ring, the possible structures with the eight-membered ring in different conformations are those given in Scheme 1. In each structure the angle between the two N–Ph bonds on opposite sides of the ring can be evaluated using simple principles of geometry. Though the exact value of this angle depends on the orientation of the N–Ph bonds (the dihedral angle of the ring) an approximation can be made to ±10° for each structure. The value of θ in each structure is also given in Scheme 1. A comparison of this angle with that calculated on the basis of experimental data reduces the possibility to only five structures, *viz.* (Ic), (IIb), and (IIIc)—(Vc).



SCHEME 1

Structure (Vc) can be eliminated due to the close proximity of the bulky sulphur atoms. Conformers (IVc) and (IIIc) have polar bonds opposite to each other [two pairs of C–S and C–N bonds in (IIIc) and C–S and N–Ph bonds in (IVc)]. Consequently these structures are not expected to have a dipole moment of the order of 3 D. In structure (IIb), the two N–Ph bonds are oriented such that the substitution of an electronegative group at the *para*-position of the phenyl ring should decrease the resultant moment of the molecule. The resultant moment of two N–Ph bonds act in a direction opposite to the resultant moment of the ring. Experimentally, however, it is found that the *p*-bromo-compound (1b) has a moment much higher than the

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[15] J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1967, **89**, 7036.

unsubstituted molecule. The low temperature n.m.r. data[16] also do not support a boat-chair form.

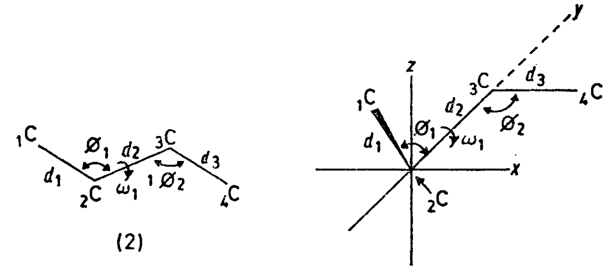
In structure (Ic) the value of the angle between the two N–Ph bonds agrees fairly well with that evaluated from dipole moment data. The small difference may be due to the difference between the actual dihedral angle and that of the model.

Second Method.—Dipole moment of any molecule can be evaluated by adding up all the group and bond moments vectorially. The resultant moment of the molecule projected onto a co-ordinate system is given by equation (2) where μ_x, μ_y, and μ_z are total projections

$$\mu^2 = (\Sigma\mu_x)^2 + (\Sigma\mu_y)^2 + (\Sigma\mu_z)^2 \qquad (2)$$

of all group and bond moments on the *x*, *y*, and *z* axes respectively. A molecule in a particular conformation is conveniently placed on the co-ordinate system and the co-ordinates of all skeletal atoms and unit vectors in the direction of the substituents are calculated. The direction cosine of each bond and its bond moment give its projection on each of the three axes. The resultant moment of the molecule is calculated according to equation (2).

This method of defining the geometry of ring systems using vector algebra, proposed by Corey and Sneen[17] and also by Wilcox,[18] could not be reproduced here as the eight-membered ring system is not rigid like cyclohexane. For non-rigid ring systems where dihedral angles vary widely, a different method was used to obtain the co-ordinates of skeletal atoms. In a system such as (2), the distance between C-1 and -4 is obtained as a function of dihedral angle ω_1 as shown in Scheme 2.



Co-ordinates of C-1

$x_1 = 0$

$y_1 = d_1\sin(\phi_1 - 90°)$

$z_1 = d_1\cos(\phi_1 - 90°)$

Co-ordinates of C-4

$x_4 = d_3\sin(180 - \phi_2)\sin\omega_1$

$y_4 = d_2 + d_3\cos(180 - \phi_2)$

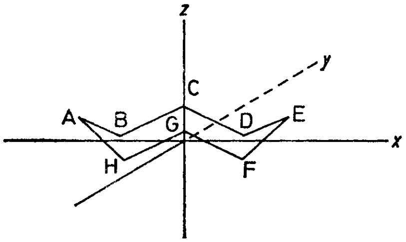
$z_4 = d_3\sin(180 - \phi_2)\cos\omega_1$

$$\text{C-1–C-4} = [(x_1 - x_4)^2 + (y_4 - y_1)^2 + (z_4 - z_1)^2]^{1/2}$$

SCHEME 2

Two other equations were obtained using simple vector algebra and solving for *x*, *y*, and *z* gave the co-ordinates of skeletal atoms.

In a non-rigid cyclo-octane system dihedral angles are variable in all conformations. A regular, crown conformation has all dihedral angles the same (96°),[19] but a skewed crown formed by expanding one pair of dihedral angles to 120°, the other pair diminishing to 60°, represents a minimum energy conformation.[20] Hence we examined different conformations obtained by variation of ω_1 from 120 to 60° which gave two extremes of a skewed crown conformation. A molecule in the crown conformation was placed on the co-ordinate system as shown in Scheme 3. Physical parameters, bond angles and lengths, were obtained from the *X*-ray analysis of the *NN*-dimethyl compound.[14]



SCHEME 3

During our calculations we observed that when ω_1 = 120—110 the *z* co-ordinates of point A becomes imaginary. Consequently, these conformations are ignored. When ω_1 = 100° the two sulphur atoms on the opposite side of the ring approach each other more closely than is allowed by their van der Waals radii, so also do the two nitrogens when ω_1 = 60° [when ω_1 = 100 CG = 3.56 Å (van der Waals radius of sulphur = 1.85 Å); when ω_1 = 60° AE = 2.9 Å (van der Waals radius of N = 1.5 Å)]. These conformations are energetically unfavourable. Saddle conformations have both the N and S atoms too close to each other to permit detailed examination. Structures (I)—(III) were considered (Scheme 1).

The co-ordinates of unit vectors in the direction of substituents were calculated using a simple method developed by Mckenzie.[21] Axial protons of ring methylene were considered to be perpendicular to the *xy* plane and equatorial protons at 109° to axial ones. Models show that it is almost the case. The effect due to lone pair electrons is neglected. Standard values for group and bond moments were used.[22]

TABLE 2

Calculated dipole moments for various dihedral angles

Structure	μ/D		
	$\omega_1 = 90°$	$\omega_1 = 80°$	$\omega_1 = 70°$
(Ia)	2.1	1.9	1.72
(Ib)	2.57	2.23	1.92
(Ic)	3.03	2.56	2.1
(IIa)	2.2	1.94	1.80
(IIb)	2.7	2.26	1.89
(IIc)	2.2	1.94	1.80
(IIIa)	0.91	11.10	1.12
(IIIb)	0.9	0.98	1.01
(IIIc)	0.9	0.98	1.1

Calculated dipole moments for various structures with different dihedral angles are given in Table 2. A comparison of the experimental dipole moment of 2.92 D

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[16] J. M. Lehn and F. G. Riddell, *Chem. Comm.*, 1966, 803.

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[19] L. Pauling, *Proc. Nat. Acad. Sci. U.S.A.*, 1949, **35**, 495.

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[22] V. Minkin, O. A. Osipov, and Y. A. Zhadnov, 'Dipole Moments in Organic Chemistry,' Plenum Press, New York, 1970, ch. III.

with that calculated for different possible isomers leaves only two structures worthy of consideration, *viz.* (IIb) and (Ic).

Boat-chair (IIb). The boat-chair conformation was discarded in our first method of calculation. The results from low temperature n.m.r. spectroscopy also do not favour a boat-chair conformation. The AB quartet observed for the ring methylene protons at lower temperatures does not show any change in $\Delta\nu$ or J over a range of temperatures. Though a rapidly equilibrating boat-chair can explain the AB quartet, the fact that $\Delta\nu$ and J remain unaltered over a range of temperatures is clearly not consistent with this conformation.

Structure (Ic). Only this structure appears to satisfy the experimental results. The angle between the two N–Ph bonds also agrees well with that method (1). The ring methylene protons being of one type only, the low-temperature n.m.r. spectra is also explained. The crystallographic analysis of the *NN*-dimethyl compound shows that the ring has a crown conformation. The two *N*-methyl groups appear to be axial, but our calculations favour an equatorial orientation of the N–Ph groups. In the solid state, crystal lattice forces influence the conformational preference. Such forces are not operative in solution. Also an axial orientation of the phenyl rings is not consistent with the variation of dipole moment on substitution. These axial bonds being almost perpendicular to the plane of the ring (*xy* plane, Scheme 3) a polar substituent at the *para*-position of the ring should increase the moment of the ring. When a C–Br bond with a group moment of 1.5 D is considered, the resultant moment would be expected to increase by *ca.* 3.0 D, but the increase found experimentally was only 1.7 D. Although a small distortion of the ring may change the orientation of the N–Ph bonds, it is difficult to bend the ring to the extent of producing an angle of 110° between the N–Ph bonds as required by experimental observation.

The dipole moment data on *NN*-diphenyl-3,7-diaza-1,5-dithiacyclo-octane favour a crown conformation for the ring. A number of other unsymmetrical conformers of approximately equal energy might contribute to equilibria in solution. A detailed computer examination of structures with different dihedral angles is being carried out.

EXPERIMENTAL

Measurement of Dipole Moments.—Dipole moments were calculated from measurement of the dielectric constant and specific volume of solvent and solution. All the measurements were made in dioxan solution at 30 ± 0.05°. Dielectric constants were measured with a DMO1 dipolmeter (Wiessenschaftlisch-Technische Werkstatten). Densities were measured with 10 ml pyknometer and refractive indices with a Ballingham–Stanley refractometer of the Pulfrich type. The dipole moments were evaluated by standard methods.[23]

Compounds (1a—c) were prepared by reacting thioformaldehyde with the corresponding aniline. *N*-Benzylideneaniline derivatives react with thioformaldehyde to give compounds (1a—c).[24] We also found that they can be obtained directly from formaldehyde, aniline, and hydrogen sulphide. Compounds prepared by both methods were found identical (i.r., mixed m.p., *etc.*).

Compound (Ia).—Hydrogen sulphide (0.5 g) was dissolved in formalin and a solution of aniline (2.5 ml) in ethanol (10 ml) was added. On keeping overnight material precipitated and this was filtered and purified by refluxing in absolute methanol for *ca.* 1 h. Crystallization from chloroform gave the pure compound (3 g, 75%), m.p. 184—186° (lit.,[24] 184—185°), $\delta(CDCl_3)$ 6.8—7.2 (10 H, m, Ph) and 4.8 (8 H, s, ring CH_2).

Compound (Ib).—This had m.p. 161—162°, $\delta(CDCl_3)$ 6.8—7.2 (8 H, m, ArH) and 4.92 (8 H, s, CH_2).

Compound (Ic).—This had m.p. 170—171°, $\delta(CDCl_3)$ 6.8—7.2 (8 H, m, ArH), 4.9 (8 H, s, CH_2), and 2.12 (6 H, s, $ArCH_3$).

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