Crystal and Molecular Structure of 1,3,6,8-Tetra-azatricyclo$[4.4.1.1^{3,8}]$-dodecane, the 2:1 Condensation Product of Formaldehyde and 1,2-Diaminoethane, and the Conformation of this System

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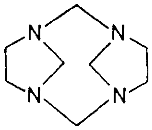
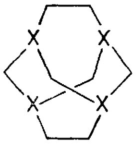
X-Ray structure analysis of the 2:1 condensation product of 1,2-diaminoethane and formaldehyde has shown it to be (II; X = N) 1,3,6,8-tetra-azatricyclo$[4.4.1.1^{3,8}]$dodecane, which contains only seven-membered rings. The unit cell is tetragonal, space group $I\bar{4}2m$, $Z = 2$ with $a = b = 767(2)$, $c = 743(2)$ pm. The structure was solved by Patterson and Fourier methods and refined by full-matrix least-squares to R 0·079 for 178 photographic data. The structure consists of a close-packed lattice of ellipsoidal molecules with unexpectedly high symmetry (D_{2d}). Bond lengths are as expected (C–N 146, C–C 154 pm) but the molecule has a large degree of angle strain as bond angles are distorted outwards by 10°. The conformation of the molecule is shown to be mainly governed by bond torsion energies and intramolecular non-bonded repulsions, but vibrational motion in the solid suggests that less-symmetrical conformations, with S_4 symmetry, may also be possible.

CONDENSATION of ethylenediamine with formaldehyde occurs easily and yields a crystalline product $C_8H_{16}N_4$.[1] This was originally thought to have the structure (I), but n.m.r. evidence suggested that there were only two different types of hydrogen atom and that the structure was (II; X = N).[2,3] This has a close relationship with the structure of hexamethylenetetramine (III), being a dihomologue. In addition to verifying structure (II; X = N), an *X*-ray analysis of the compound is important, since a molecule of this structure presents a very interesting conformational problem.



(I)



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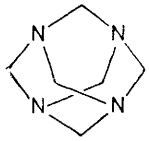

(III)

If a Dreiding model is constructed with rigid bonds and angles it takes up the conformation shown in Figure 1(a); this has $\bar{4}$ symmetry (S_4) and appears to be energetically

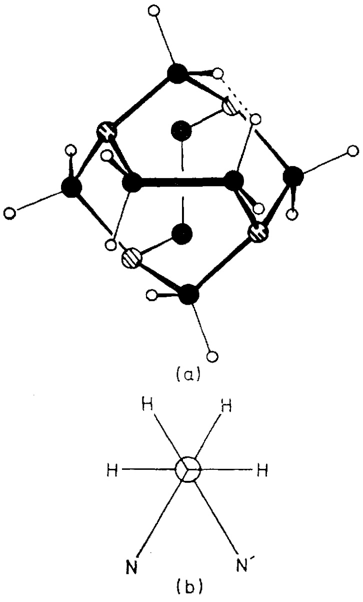

FIGURE 1 The almost stain-free conformation (structure A) of $C_8N_4H_{16}$ adopted by a Dreiding model: (a) plane of molecule down S_4 axis showing shortest non-bonded H · · · H interactions, and (b) Newman projection of the C–C bond

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[1] C. A. Bischoff, *Ber.*, 1898, **31**, 3248.

[2] G. Volpp, *Chem. Ber.*, 1962, **95**, 1493.

[3] F. G. Riddell and P. Murray-Rust, *Chem. Comm.*, 1970, 1075.

satisfactory without much strain in the angles, the conformation about the C–C bonds being almost exactly *gauche* [Figure 1(b)]. This conformation can also exist as a mirror image and the Dreiding model can be twisted and ' flipped ' from one to the other in a way analogous to the inversion of cyclohexane. (The mirror images are superimposable, as the molecule has S_4 symmetry.) In changing from one mirror image to the other the molecule must almost certainly pass through an intermediate conformation with $\bar{4}2m$ (D_{2d}) symmetry, Figure 2(a). At first sight this arrangement would appear to be highly unfavourable, as a Dreiding model with tetrahedral angles for carbon and nitrogen has a large amount of strain and appears to be at a potential maximum. Moreover the N–C–C–N system in the ethylene bridge is planar, so that around the C–C bond the C–N and C–H bonds are exactly eclipsed [Figure 2(b)].

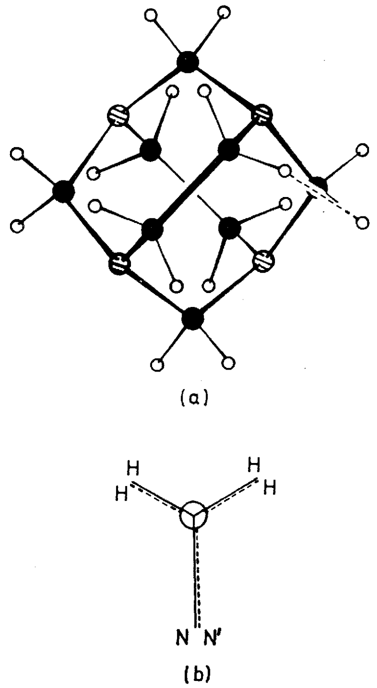

FIGURE 2 The symmetrical (D_{2d}) conformation (structure B) of $C_8N_4H_{16}$ from *X*-ray structure analysis: (a) plane of molecule down S_4 axis, and (b) Newman projection of C–C bond

The n.m.r. spectrum in various solvents at room temperature, however, shows only two singlets at τ 6·0—6·2 and 6·8—7·1.[3] This can be explained in two ways: (i) the molecule exists in two equivalent conformations (structure A, Figure 1) but interconversion between them is rapid on the n.m.r. time-scale; or (ii) the preferred conformation of the molecule is structure B, Figure 2.

To investigate this problem the crystal structure was determined. This can only give information about the conformation in the solid state, but may be of help in suggesting the conformation in solution.

EXPERIMENTAL

Preparation. The compound was prepared by the method of Bischoff,[1] and recrystallised (×2) from chloroform as square prismatic needles formed by (110) capped by (101) faces, and thus having morphology of overall $\bar{4}2m$ symmetry. Crystals for *X*-ray examination were thinly coated with Perspex to prevent sublimation in the *X*-ray beam.

Crystal Data.—$C_8H_{16}N_4$, $M = 168·1$. Tetragonal, $a = b = 767(2)$, $c = 743(2)$ pm, $U = 0·435$ nm^3. $D_m = 1·29$, $Z = 2$, $D_c = 1·28$ g cm^{-3}. Space group $I\bar{4}2m$ from structure analysis; systematic absences hkl, $h + k + l = 2n + 1$. Cu-K_α radiation, $\lambda = 154·18$ pm; μ(Cu-K_α) = 10·3 cm^{-1}. Crystal dimensions 0·5 × 0·5 × 0·5 mm.

Crystallographic Examination.—A particularly noticeable feature of the rotation and Weissenberg photographs is strong thermal diffuse reflection associated with many of the reciprocal lattice points. Those close to the c^* axis were particularly strongly affected and most of the diffuse scattering lay in a cone of semi-angle 45° about this axis. The shape of an individual region close to a reciprocal lattice point was approximately that of an hour-glass highly elongated along the c^* axis. The magnitude of the effect was greater than for the very similar molecule hexamethylenetetramine which has been investigated in some detail.[4]

Cell dimensions and diffraction symmetry were determined from Weissenberg photographs. Levels 0—5*kl* were collected by the multiple-film equi-inclination Weissenberg technique, and intensities estimated visually by comparison with a calibrated strip. Lorentz and polarisation, but not absorption or spot-shape, corrections were made, and layer scale-factors determined by comparison of reflections *hkl* and *khl*. A unique set of 178 reflections was produced.

Structure Determination and Refinement.—The systematic absences do not determine the space group uniquely; it may be $I\bar{4}2m$, $I\bar{4}m2$, $I4/mmm$, $I4mm$, or $I422$. As $Z = 2$, the molecule must lie at the origin and have the whole point-group symmetry of the space group *i.e.* $\bar{4}2m$, $4/mmm$, $4mm$, or 422. The last three cannot apply to a single molecule, and could only be produced by a highly disordered arrangement, although this possibility cannot be completely rejected, since the molecule is probably globular (egg-shaped) and might well pack in a disordered fashion. Strong evidence for $\bar{4}2m$ symmetry comes from the morphology of the crystals, which is highly suggestive of $\bar{4}2m$ or $\bar{4}m2$ for the symmetry group of the crystal.

There are two ways in which the molecule can fit into $I\bar{4}2m$ or $I\bar{4}m2$. Model (i): the molecule has structure B ($\bar{4}2m$ symmetry). Model (ii): although a single molecule of $\bar{4}$ symmetry (structure A) cannot be fitted into the space group, if two mirror images are placed on the origin, with equal occupancies, the requisite symmetry results. This might imply that the molecules were statistically disordered throughout the crystal or that they were undergoing conformational changes in the solid state.

The sharpened Patterson function for the structure was calculated. This could be completely interpreted in terms of N · · · N, C · · · N, and C · · · C intramolecular vectors originating from a molecule of $\bar{4}2m$ symmetry. The orientation of the vectors showed clearly that the space group was $I\bar{4}2m$ and not $I\bar{4}m2$. Trial positions for the atoms were obtained and this structure gave R 0·28 for the observed reflections. Two cycles of full-matrix least squares refinement with isotropic temperature factors and unit weights

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[4] G. N. Ramachandran and W. A. Wooster, *Acta Cryst.*, 1951, **4**, 335.

reduced R to 0·184. The weighting scheme was then changed to: $w = 1$ if $F_o < 9·0$ and $w = 1/[1 + (F_o - 9·0)^2]$ for $F_o > 9·0$, and hydrogen atoms were introduced. Two cycles of least-squares refinement converged at R 0·169.

This is very poor agreement, and so a difference-Fourier synthesis was calculated. The most noticeable features of this were close to the C–C bond, and a section is shown in Figure 3. This strongly suggested that considerable anisotropic vibration was occurring, and refinement was continued with anisotropic temperature factors for carbon and nitrogen atoms. Three cycles of least-squares refinement led to convergence at R 0·079; the parameters for this model are given in Table 1. This is a remarkable increase in agreement and suggests that the atomic vibrations are strongly anisotropic, a phenomenon which is analysed and discussed later.

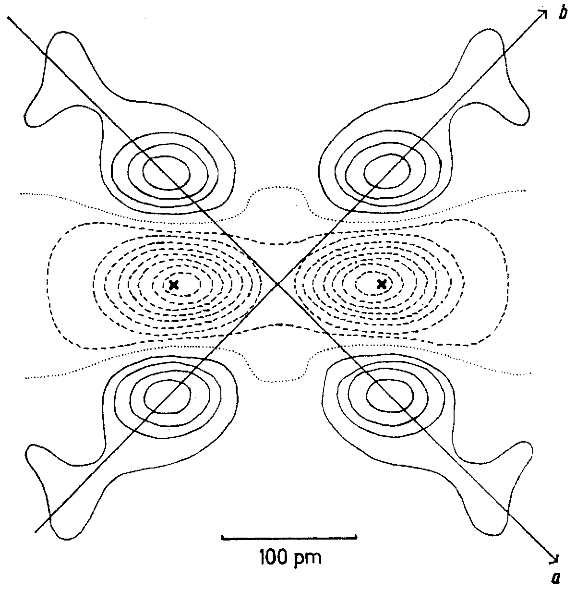

FIGURE 3 Difference-Fourier synthesis at the limit of isotropic refinement in the xy plane through the C(2)–C(2′) bond. Carbon atoms are marked by crosses and contours are at intervals of 200 e nm^{-3}, the negative ones being represented by dashes

TABLE 1

Final positional and thermal parameters,* with estimated standard deviations in parentheses

Atom	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	0·2339(8)	0	0	165(11)	191(10)	344(16)	0	0	27(16)
C(2)	0·0707(7)	0·0707(7)	0·2688(7)	402(18)	402(18)	214(9)	−196(13)	5(10)	5(10)
N(1)	0·1339(5)	0·1339(5)	0·0969(5)	201(7)	201(7)	275(8)	−52(7)	12(7)	12(7)
H(1)	0·0304(100)	0·1748	0·3342(100)	340	340	362	0	0	0
H(2)	0·3173(100)	−0·0665	0·969(100)	340	340	362	0	0	0

* The temperature factor is given by $\exp[-10^{-4}(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2kl\beta_{13} + 2kl\beta_{23})]$.

It is possible, although unlikely in view of the good agreement, that the above model is incorrect and that the structure is composed of a disordered array of molecules of $\bar{4}$ symmetry. Two approaches were attempted. (i) Positional parameters for conformation A were obtained from a Dreiding model, and two enantiomorphic molecules of this type, each with occupancy 0·5, were placed at the origin. Their rotational orientation was determined such that the atoms were as close as possible to the (110) mirror plane. This model gave R 0·47 and failed to refine further; it is clearly totally incorrect. (ii) Instead of the atoms vibrating anisotropically it is possible that there is a disordered arrangement of two structures with atoms very close to the (110) mirror plane. Accordingly these atoms were introduced into the calculation and four cycles of full-matrix least-squares refinement with isotropic temperature factors was carried out, the final R being 0·121. There are 29 variable parameters in this model, compared with 26 in the model of $\bar{4}2m$ symmetry with R 0·079. Since an increase in the number of parameters would be expected to lead to a lower R factor, the $\bar{4}2m$ model with anisotropic vibrations is more satisfactory than the disordered structure; the latter also gave poor bond lengths for the molecule.

There is one other possibility, which is that the crystal is a twin composed of two individuals of lower symmetry, *e.g.* $I\bar{4}$. This would be extremely difficult to detect in the tetragonal system, but the morphology of the crystal and the good final agreement make twinning rather unlikely in this case.

Computations were carried out on an Elliott 4130 computer using the CRYSTAL 69 set of programs.[5] X-Ray scattering factors were taken from ref. 6. Structure factors are listed in Supplementary Publication No. SUP 20900 (2 pp.).*

DISCUSSION

The overall structure consists of globular ' eggs ' in an approximately close-packed lattice (Figure 4). The molecules are well separated and close intermolecular contacts are few (Table 2). It seems likely that the intermolecular forces are not highly directional and also that they will be fairly small. This is confirmed by the observation that the crystals sublimed slowly at room temperature. For this reason the conformation is unlikely to be greatly influenced by intermolecular forces in the solid state.

The molecule has exact $\bar{4}2m$ symmetry and bond lengths and angles are given in Tables 3 and 4 (uncorrected for thermal motion, since this correction depends on the model adopted for the vibration). As the discussion later shows, there are several possible ways of interpreting the anisotropic vibrations, which are given in Table 5. The bond lengths lie in the expected range (*cf.* C–N 147·7 pm hexamethylenetetramine[7,8] and

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1973, Index issue.

[5] A. Griffiths and M. T. G. Powell, CRYSTAL 69, System of programs, Portsmouth Polytechnic, 1969.

[6] ' International Tables for X-Ray Crystallography, 1962, vol. III, Kynoch Press, Birmingham.

[7] L. N. Becka and D. W. Cruickshank, *Proc. Roy. Soc.*, 1963, *A*, **273**, 435.

[8] F. Hanic and V. Subrtova, *Acta Cryst.*, 1969, **B25**, 405.

147 pm in triethylenediamine[9]) but all the bond angles are substantially greater than tetrahedral, implying considerable strain in the molecule.

The conformation of this and similar ring systems is of considerable interest and depends on three main factors: angle strain, torsional strain, and interactions between non-bonded atoms. Calculations of the most stable conformation of some hydrocarbon systems have been made,[10] based mainly on estimated potential functions for these effects, but relatively few confirmatory structural data exist. A close approximation to (II; X = N) would be the corresponding hydrocarbon (II; X = CH) and this, together with derivatives, has recently been prepared,[11,12] although no structural data are yet available. The homoadamantane system (IV) has been more extensively investigated and its structure is helpful to an understanding of the conformation of the present compound.

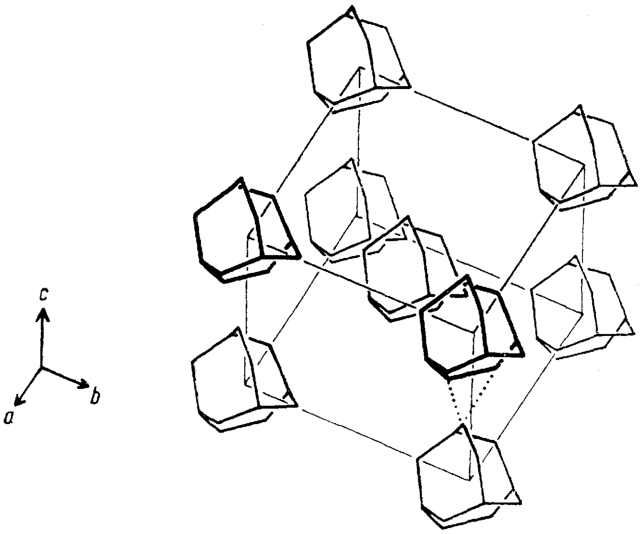


FIGURE 4 The structure of one unit cell of the crystal, showing the shortest C · · · C intermolecular contact

TABLE 2

Shortest intermolecular contacts (pm)

(*a*) C · · ·C, C · · · N, N · · ·N <400 pm
C(3) · · · C(3^{I}) 360
(*b*) C · · · H, N · · · H <320 pm
C(3) · · · H(4^{II}) 308
(*c*) H · · · H <300 pm
H(1) · · · H(3^{III}) 236

Equivalent positions: I $x, y, 1 - z$; II $\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} - z$; III $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$.

TABLE 3

Intramolecular bond lengths (pm), with standard deviations in parentheses

C(2)–C(2′)	153·4(8)	C(1)–H(1)	98(3)
C(2)–N(1)	145·0(7)	C(2)–H(2)	109(3)
C(1)–N(1)	147·0(7)	H(1) · · · H(2)	220(5)

TABLE 4

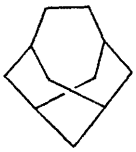
Intramolecular bond angles (deg.), with estimated standard deviations in parentheses

C(1)–N(1)–C(1′)	119·3(3)	N(1)–C(1)–N(1′)	116·9(3)
C(1)–N(1)–C(2)	111·9(2)	C(2)–C(2′)–N(1)	118·0(2)

TABLE 5

Root-mean-square vibration amplitudes (pm), with direction cosines of the principal axes of the vibration ellipsoids

	$\sqrt{\overline{U^2}}$	l_1	l_2	l_3
N(1)	27·7	0	0	1
	25·6	0·707	−0·707	0
	21·1	0·707	0·707	0
C(1)	31·0	0	0	1
	23·8	0	0	0
	22·2	1	0	0
C(2)	42·2	0·707	−0·707	0
	24·8	0·707	0·707	0
	24·5	0	0	0



(IV)

The same conformational problem exists in homoadamantane but is confined to a small part of the molecule. There are two possible conformations: C_{2v}, with a planar ethylene bridge, and C_2, with a twisted *gauche* bridge. Calculations[10] and spectroscopic data[13] have been invoked to suggest the former, but the only structural data are for the 4,5-dione,[14] which has a definitely twisted bridge. A recent *X*-ray structural investigation of a derivative of the hydrocarbon[15] showed an almost planar ethylene bridge with large angle distortions but no abnormal vibrations in the molecule. The conformation is most easily rationalised in terms of the torsional interactions in the three bonds of the ethylene bridge, but there is a considerable likelihood that there is a range of conformations in solution.

In the tricyclo[4.4.1.1^{3,8}]decane system however, the whole molecule must be considered.* If the compound consists of two interconverting S_4 conformations, it will be found that one ethylene bridge cannot invert by itself; both bridges must ' flip ' at the same time. In doing so

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* At this stage a Dreiding model will help in the following discussion. In ' flipping ' the molecule from one S_4 conformation to the other, it should be noted that both ethylene bridges rotate in the same direction.

[9] G. S. Weiss, A. S. Parkes, R. E. Nixon, and R. E. Hughes, *J. Chem. Phys.*, 1964, **41**, 3759.

[10] E. M. Engler, L. Chang, and P. v. R. Schleyer, *Tetrahedron Letters*, 1972, 2525.

[11] F. N. Stepanov, M. I. Nowikowa, and A. G. Jurtschenko, *Synthesis*, 1971, 653.

[12] D. Skare and Z. Majerski, *Tetrahedron Letters*, 1972, 4887.

[13] S. H. Liggero, P. v. R. Schleyer, and K. C. Ramey, *Spectroscopy Letters*, 1969, **2**, 197.

[14] P. B. Braun, J. Hornstra, and J. I. Leenhouts, *Acta Cryst.*, 1970, **B26**, 1802.

[15] R. Henry, J. Murray-Rust, P. Murray-Rust, and W. Parker, to be published.

the molecule goes through an intermediate with D_{2d} symmetry, where all the atoms have moved sizeable distances from their original positions. (In homoadamantane the inversion only involves movement of the four bridge atoms.) In the [4.4.1.1^{3,8}] system it is therefore more difficult to estimate the relative effects of the three types of strain. Angle-strain clearly favours the S_4 conformation since this is what is found in a model with tetrahedral carbon atoms, whereas a D_{2d} system must have angles approaching 120°. This strain is, however, overemphasised by Dreiding models (the angles in homoadamantane are distorted by up to 10°). It would appear that in the D_{2d} conformation the angle deformations are more than compensated by the relief of torsional and non-bonded interactions. In the extreme case of conformation A (representing minimum angle strain) there is a very short $H \cdots H$ contact of 120 pm whereas in the D_{2d} arrangement this is increased to 220 pm. Relatively small distortions of A towards B would, however, greatly decrease this interaction and might suggest an energy minimum at a conformation halfway between A and B.

The most significant feature appears to be the torsional arrangements about the bonds. There are 14 bonds in the molecule and all undergo considerable rotation in the change from A to B. Although the ethylene bridges change by the greatest amount, they are outnumbered by the C–N bonds and these can be seen to have the greatest effect (Table 6). This Table outlines an approximate calculation of the torsional contribution to the energies of structures A and B. If it is assumed that the torsional energy of a bond varies sinusoidally with the torsional angle τ (where $0° < \tau < 60°$), the total torsional strain for each conformation can be calculated. The torsional energy of a bond has been taken as zero when $\tau = 60°$ and E_{CC} (or E_{CN}) when τ 0°. Accurate values of these energies are not known, and the sinusoidal function is unlikely to be exact, but the results can still be used semiquantitatively. Values of E_{CC} and E_{CN} are related to the barriers to rotation about C–C and C–N bonds which have been estimated[16] to be *ca.* 3·8 (n-butane) and 4·4 kcal mol^{-1} (trimethylamine). These values suggest that $E_{CN} \approx E_{CC}$ and thus that conformation A has considerably more torsional strain than conformation B.

TABLE 6

Approximate torsional energies for conformations A and B

Bond	No. per mol	Torsion angles/deg.	Calc. energy
(*a*) Confirmation A (S_4)			
C(1)–N(1)	4	52, 66	0·12E_{CN}
C(1)–N(1′)	4	28, 99	2·52E_{CN}
C(2)–N(1)	4	20, 102	3·00E_{CN}
C(2)–C(2′)	2	60, 60	0
Total torsional energy: 5·64 E_{CN}			
(*b*) Conformation B (D_{2d})			
C(1)–N(1)	8	55, 75	0·48E_{CN}
C(2)–N(1)	4	62, 62	0
C(2)–C(2′)	2	0, 120	2·00E_{CC}
Total torsional energy: 0·48 E_{CN} + 2·0 E_{CC}			

It is possible that considerable distortion from the equilibrium D_{2d} arrangement can take place without much change in potential energy. This would imply that the symmetrical structure B represented the bottom of a very broad potential well, or even one with two very shallow minima, where the molecule might be vibrating considerably. This possibility is strongly supported by an analysis of the size and directions of the anisotropic vibrations (Table 5 and Figure 5). The ethylene carbon C(2) has an extremely large vibration perpendicular to the C(2)–C(2′) bond, and C(1) has a significant vibration in the *c* direction. These are not consistent with a rigid-body vibration, such as libration about the *c* axis, but can be explained in terms of vibrations in the molecule. If, in this vibration, C(2) and C(2′) are exactly out-of-phase, a twisting of the planar N–C–C–N system results. The large root-mean-square amplitude of vibration of C(2) implies a large amount of distortion at the extremes of the vibration, particularly in torsional angles. The magnitude of the effect requires the nitrogen atoms to move in a manner which will partially compensate for the distortion and this is confirmed by the significant component of vibration along *c*. At the extreme of the vibration, the torsion angle about C–C can be roughly calculated as 55°, which leads to almost complete removal of strain due to this cause. There is no need for much change in the other torsion angles although there will be a slight increase in strain about N–C(2). It is not necessary for the two ethylene bridges to be vibrating in phase, although if they do, and have the same sense, the geometry at the extreme of vibration will have S_4 symmetry.

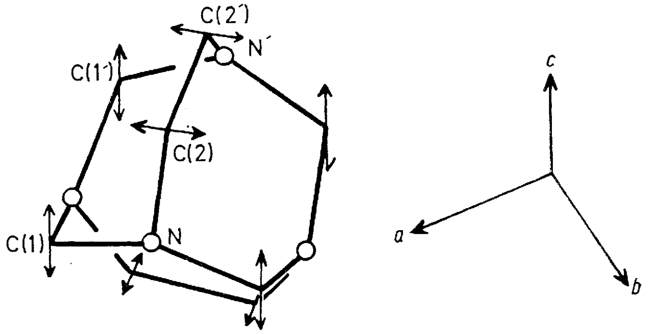

FIGURE 5 The skeleton of the molecule with the directions of the most significant anisotropic vibrations

Two other observations suggest that substantial molecular motion is occurring in the solid state. Strong thermal diffuse *X*-ray reflection is often associated with abnormal molecular motion, and the small, sharp first-order phase transition at 184 K could be due to the onset of motion in the crystal.[3]

Two other molecules in which twisting of ethylene bridges in the crystal has been postulated are bicyclo-[2.2.2]octane-1,8-dicarboxylic acid[17] and tetrahydro-

[16] J. P. Lowe, *Progr. Phys. Org. Chem.*, 1968, **6**, ch. 1.

[17] O. Ermer and J. D. Dunitz, *Helv. Chim. Acta*, 1969, **52**, 1861.

selenophen–iodine complex.[18,19] In the former, Dunitz and Ermer analysed the anisotropic vibrations of the atoms in the ethylene bridges and showed that these were consistent with either a rigid-body libration of the molecule of 6°, or an out-of-phase twisting of the top and bottom halves of the molecule about the triad axis. Because of the symmetry of the molecule it was not possible to decide between the two, but a semi-empirical calculation of the potential energy of the molecule suggested that the twisted conformation was very slightly more stable than the totally eclipsed one. The barrier to interconversion was very low (0·1 kcal mol^{-1}) and the molecule had effectively D_{3h} symmetry at all temperatures. In the tetrahydroselenophen–iodine complex, the crystal structure could be interpreted as a disordered structure with equal amounts of non-planar conformers or as a non-planar molecule undergoing interconversion between two enantiomers in the crystal. Analysis of the temperature-dependence of the solid-state ^1H n.m.r. suggested the latter, and the magnitude of the anisotropic root-mean-square vibration of the ethylene carbon atoms was shown to be 50 pm.

I thank Dr. F. G. Riddell for pointing out the existence and conformational interest of this system.

[3/1630 *Received, 2nd August,* 1973]

[18] H. Hope and J. D. McCullough, *Acta Cryst.*, 1964, **17**, 172.

[19] B. Pedersen and H. Hope, *Acta Cryst.*, 1965, **19**, 473.