# The Conformation of Some Di-, Tetra-, and Hexa-hydropyridazines in the Solid State

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The conformations of five hydropyridazines in the solid state have been determined from their crystal structures. The results are compared with the conformations of these compounds in solution as analysed by interpretation of their $^1H$ and $^{13}C$ n.m.r. spectra Dihydropyridazine (**1**) adopts the twist-boat conformation in the solid state however, in accordance with the interpretation of $^1H$ n.m.r. spectra tetrahydropyridazines, (**2**) and (**3**) adopt the half-chair conformation in agreement with that found for (**2**) and in contrast to that found for (**3**) in solution. Hexahydropyridazine (**4**) was found to adopt the chair conformation both in solution and in the solid state.

The question as to whether the conformation of a molecule in the crystalline phase is identical with or similar to the stable conformation of that molecule in solution arises quite often. It is clear that the stable conformation of rigid molecules (which lack any degree of freedom) as well as of very crowded molecules (where the degrees of freedom are reduced or blocked by the crowding) will be identical in both phases. However, molecules which do not belong to the two classes mentioned above can easily adopt different conformations in the solution and in the solid state.

The conformations of molecules in solutions are generally studied by n.m.r. methods. The interpretation of the n.m.r. spectra sometimes leads to ambiguous results. In cases where there are several interpretations of the n.m.r. spectra it is possible that the molecular conformation observed in the solid state is either identical with one of the conformations as interpreted from the spectra or different from all interpreted conformations. In the first case it is correct to assume that the conformation of the molecule is identical in both phases. In the second case there are two possible explanations, either the molecular conformation in both phases is different or it is identical and the interpretations of the n.m.r. spectra are wrong. We are not in a position to argue about the main question of the similarity of the molecular conformation in both phases and we are not claiming that they are always identical but we have to remember that the unambiguous interpretation of stereochemistry using n.m.r. spectra is limited and we sometimes failed in assigning the correct molecular conformation. In this paper we present examples in which $^1H$ and $^{13}C$ n.m.r.[1] studies on the conformations of hydropyridazines (**1**)-(**4**) in solution were interpreted differently and compare the results with the molecular conformations implied by the crystal structures of these compounds [(**1**), (**2d**), (**3a,b**), (**4b**)] The details of preparation and assignment of correct configurations are referred to in the Experimental of ref. 1. We will first give some details of the molecular structure and then compare the results concerning the conformations found in the two different phases.

## Results and Discussion

*Molecular Structure.*—Stereoscopic drawings of molecules (**1**), (**2d**), (**3a**), (**3b**), and (**4b**) are shown in Figures 1-5 respectively.† See Tables 1-5 also. Three of the compounds studied have two ethoxycarbonyl ($CO_2Et$) groups each, which gives a total of six. Comparison of the conformation of these moieties reveals some striking similarities with regard to the differences between the conformations of the individual $CO_2Et$ groups in each molecule. The similarities between the various molecules and the differences within each molecule is best seen by comparing the torsion angles C–O–C–C (*T*1), O=C–O–C (*T*2), and N–C–O–C (*T*3). Schweizer and Dunitz[2] have studied the geometry of carboxylic ester groups by analysing data from many crystal structures retrieved from the Cambridge Struc

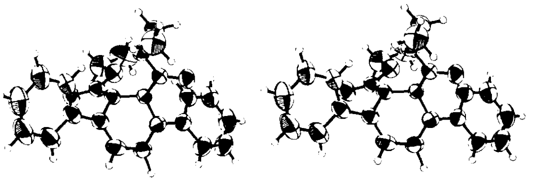

Figure 1. Stereoscopic drawing of (**1**).

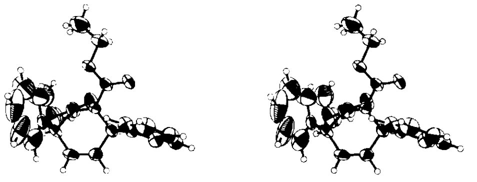

Figure 2. Stereoscopic drawing of (**2d**).

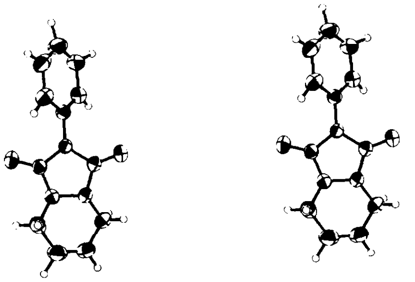

Figure 3. Stereoscopic drawing of (**3a**).

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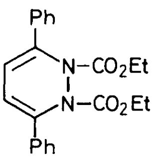
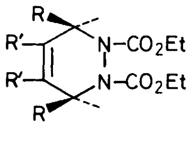
† Tables of atomic co-ordinates, bond lengths and angles, atomic displacement parameters, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre [see Section 5.6.3 of 'Instructions for Authors (1989)', in the January issue of *J. Chem. Soc., Perkin Trans. 2*].

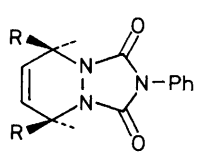


**(1)**



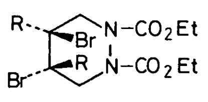
**(2)**

**a**; R = R' = H
**b**; R = Me R' = H
**c**; R = H R' = Me
**d**; R = Ph R' = H



**(3)**

**a**; R = H
**b**; R = Me
**c**; R = Ph



**(4)**

**a**; R = H
**b**; R = Me

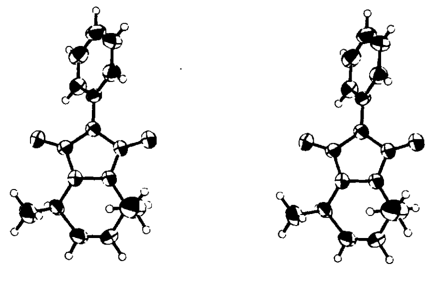


**Figure 4.** Stereoscopic drawing of (**3b**).

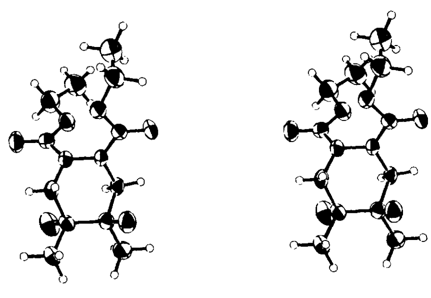


**Figure 5.** Stereoscopic drawing of (**4b**).

tural Database. It was found that esters of primary alcohols usually have the *T*1 torsion angle close to 180°, *i.e.* the ethyl C–C bond is antiperiplanar to the acyl C–O bond. It was found that the exceptions are numerous enough to indicate that the preference for this conformation can easily be outweighed by other factors. We have found, in this study, that each molecule possesses one $CO_2Et$ group of this preferred conformation (*T*1 166.5–177.9°), while the other $CO_2Et$ group in each molecule adopts a different conformation in which *T*1 is in the range 79.5–96.1°. Values of *T*2 were found to be 1.3–8.7° in all six ethoxycarbonyl groups, *i.e.* the O=C bond is synperiplanar to the alkyl C–O bond. The N–C bond is antiperiplanar to the alkyl C–O bond in each as the *T*3 values (170.5–178.7°) indicate. Another difference which should be mentioned is that in (**1**) and (**4b**) the carbonyl bond is antiperiplanar to the N–N bond in each of the $CO_2Et$ groups [N–N–C=O (*T*4) lies in the range 160.9–178.3°)] while in (**2d**) one is anti- and the other is syn-periplanar (*T*4 14.6°). None of these conformations are stable in solution because of single-bond rotation.

The effect of the pyramidality of the nitrogen atoms in acylated hydrazines has recently been studied[3] in connection with the double nitrogen inversion process. It was pointed out that upon flattening, the degree of conjugation with neighbouring carbonyl groups increases which causes shortening of bonds involving nitrogen atoms. This effect is also seen in the present work. The best examples are compounds (**3b**) and (**4b**), where both the adjacent nitrogen atoms have a different degree of pyramidality. In (**3b**) the $\alpha_{avg}$* is 116.5 and 119.2° at N-3 and N-1 respectively; the N–N bond length is 1.398(5) Å [compared with 1.409(4) Å in (**3a**) where the values of $\alpha_{avg}$ are 114.9, and 116.3°); the N–C(=O) bond length is 1.347(6) Å ($\alpha_{avg}$ 119.2°) which is shorter than 1.377(6) Å for the nitrogen with $\alpha_{avg}$ 116.5°. Similarly the N–N bond length in (**4b**) is 1.383(6) Å; which is shorter than, for example, 1.411(6) Å observed in (**2d**) where the $\alpha_{avg}$ values are 115.4 and 116.5°; the N–C(=O) bond lengths in (**4b**) are 1.361(6) ($\alpha_{avg}$ 119.9°) and 1.380(6) Å ($\alpha_{avg}$ 118.7°). Moreover, the N–N–C=O torsion angle in (**4b**) where the central N atom is the planar one ($\alpha_{avg}$ 119.9°) is 0.9° compared with 4.6–28.2°, for the more pyramidal nitrogens, this implies a higher degree of conjugation with the coplanar carbonyl group.

*Conformations of the Hydropyridazine Ring.*—The conformations of the hydropyridazine ring in the five compounds were analysed by the RING program,[4a] which evaluates the degree and type of puckering in a ring system as well as defining the ring-substituent positions.[4b] The torsion angles of the hydropyridazine ring as well as the puckering parameters are summarized in Table 6. There are three puckering degrees of freedom, which are described by a single-amplitude phase pair ($q_2$, $\varphi$) and a single puckering co-ordinate ($q_3$). The displacement expression is given by equation (1). The parameters

$$Z_j = \left(\frac{2}{6}\right)^{1/2} q_2 \cos[\varphi + 4\pi(j - 1)/6] + q_3[(-1)^{j-1}6^{\frac{1}{2}} \quad (1)$$

$q_2$, $q_3$, and $\varphi$ are conveniently replaced by a 'spherical polar set' ($Q$, $\Theta$, $\varphi$) where $Q$ is the total puckering amplitude and $\Theta$ is an angle ($0 < \Theta < \pi$) such that $q_2 = Q \sin \Theta$ and $q_3 = Q \cos \Theta$.

*Diethyl* 3,6-*Diphenyl*-1,2-*dihydropyridazine*-1,2-*dicarboxylate* (**1**).—Anderson and Lehn[5] postulated—on the basis of a variable-temperature $^1H$ n.m.r. study—that (**1**) is in a dynamic cyclohexadiene-like ring inversion or ring-twist conformational process with $\Delta G^\ddagger$ = 23 kcal $mol^{-1}$.† The presence of only eight peaks in the $^{13}C$ n.m.r. spectrum of (**1**) led Fisher *et al.*[1] to conclude that the dihydropyridazine ring of (**1**) is in a symmetrical twist conformation. The crystal structure of (**1**) shows that the dihydropyridazine ring adopts the same stable conformation of cyclohexadiene (see Table 6), namely a twist-boat conformation. The two phenyl rings at positions 3 and 6 are in the plane of the ring. It seems that if this conformation is the stable one then Anderson and Lehn's interpretation is correct.

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* $\alpha_{avg}$ Is one of the parameters used to describe the pyramidality of an atom. It is defined as the average of the bond angles around this atom. $\alpha_{avg}$ Is 109.5° for a tetrahedral atom and 120.0° for a trigonal one.
† 1 cal = 4.184 J.

**Table 1.** Final atomic co-ordinates for (**1**) ( × $10^4$).

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O(1) | 7 806(2) | 696(2) | 9 840(2) |
| O(2) | 8 412(2) | −720(2) | 9 908(2) |
| O(3) | 8 236(2) | −2 119(2) | 12 973(2) |
| O(4) | 9 497(2) | −990(2) | 12 961(2) |
| N(1) | 7 750(2) | −215(2) | 11 279(2) |
| N(2) | 7 598(3) | −1 099(2) | 11 509(2) |
| C(1) | 7 099(4) | 394(2) | 11 733(3) |
| C(2) | 6 006(4) | 96(3) | 11 734(3) |
| C(3) | 5 539(3) | −746(3) | 11 232(3) |
| C(4) | 6 309(3) | −1 362(3) | 11 113(3) |
| C(5) | 7 731(4) | 1 216(2) | 12 237(3) |
| C(6) | 9 019(4) | 1 296(3) | 12 636(3) |
| C(7) | 9 613(4) | 2 054(3) | 13 185(4) |
| C(8) | 8 937(7) | 2 738(3) | 13 345(4) |
| C(9) | 7 654(6) | 2 682(3) | 12 921(4) |
| C(10) | 7 044(4) | 1 941(3) | 12 360(4) |
| C(11) | 5 991(3) | −2 236(3) | 10 594(3) |
| C(12) | 4 989(4) | −2 699(3) | 10 664(4) |
| C(13) | 4 668(5) | −3 508(4) | 10 122(5) |
| C(14) | 5 311(6) | −3 866(3) | 9 496(5) |
| C(15) | 6 299(5) | −3 418(3) | 9 416(4) |
| C(16) | 6 640(4) | −2 621(3) | 9 969(4) |
| C(17) | 7 962(3) | −21(3) | 10 266(3) |
| C(18) | 8 591(4) | −622(3) | 8 798(4) |
| C(19) | 7 377(5) | −726(3) | 7 777(4) |
| C(20) | 8 454(4) | −1 457(3) | 12 550(3) |
| C(21) | 10 433(4) | −1 301(3) | 14 079(3) |
| C(22) | 11 380(4) | −594(4) | 14 543(4) |

Bond lengths (Å) and angles (°) for (**1**).

| | | | |
|---|---|---|---|
| O(1)–C(17) | 1.193(4) | C(4)–C(11) | 1.460(5) |
| O(2)–C(17) | 1.331(4) | C(5)–C(6) | 1.387(6) |
| O(2)–C(18) | 1.466(5) | C(5)–C(10) | 1.402(6) |
| O(3)–C(20) | 1.204(4) | C(6)–C(7) | 1.378(5) |
| O(4)–C(20) | 1.324(4) | C(7)–C(8) | 1.363(8) |
| O(4)–C(21) | 1.462(4) | C(8)–C(9) | 1.377(9) |
| N(1)–N(2) | 1.400(3) | C(9)–C(10) | 1.368(6) |
| N(1)–C(1) | 1.436(5) | C(11)–C(12) | 1.389(6) |
| N(1)–C(17) | 1.389(5) | C(11)–C(16) | 1.394(6) |
| N(2)–C(4) | 1.439(4) | C(12)–C(13) | 1.381(7) |
| N(2)–C(20) | 1.392(4) | C(13)–C(14) | 1.373(9) |
| C(1)–C(2) | 1.348(6) | C(14)–C(15) | 1.368(8) |
| C(1)–C(5) | 1.462(5) | C(15)–C(16) | 1.371(5) |
| C(2)–C(3) | 1.434(5) | C(18)–C(19) | 1.488(5) |
| C(3)–C(4) | 1.340(6) | C(21)–C(22) | 1.485(6) |

| | | | |
|---|---|---|---|
| C(17)–O(2)–C(18) | 116.1(2) | C(6)–C(7)–C(8) | 120.1(5) |
| C(20)–O(4)–C(21) | 115.1(3) | C(7)–C(8)–C(9) | 119.8(5) |
| N(2)–N(1)–C(1) | 114.5(2) | C(8)–C(9)–C(10) | 121.0(5) |
| N(2)–N(1)–C(17) | 117.7(2) | C(5)–C(10)–C(9) | 119.8(5) |
| C(1)–N(1)–C(17) | 120.8(3) | C(4)–C(11)–C(12) | 120.8(3) |
| N(1)–N(2)–C(4) | 113.2(3) | C(4)–C(11)–C(16) | 121.6(3) |
| N(1)–N(2)–C(20) | 117.4(3) | C(12)–C(11)–C(16) | 117.6(3) |
| C(4)–N(2)–C(20) | 118.9(2) | C(11)–C(12)–C(13) | 120.0(4) |
| N(1)–C(1)–C(2) | 114.8(3) | C(12)–C(13)–C(14) | 121.2(5) |
| N(1)–C(1)–C(5) | 117.6(3) | C(13)–C(14)–C(15) | 119.6(5) |
| C(2)–C(1)–C(5) | 127.3(3) | C(14)–C(15)–C(16) | 119.6(4) |
| C(1)–C(2)–C(3) | 120.0(3) | C(11)–C(16)–C(15) | 122.0(3) |
| C(2)–C(3)–C(4) | 120.9(4) | O(1)–C(17)–O(2) | 126.8(3) |
| N(2)–C(4)–C(3) | 114.8(3) | O(1)–C(17)–N(1) | 122.4(3) |
| N(2)–C(4)–C(11) | 117.1(3) | O(2)–C(17)–N(1) | 110.7(3) |
| C(3)–C(4)–C(11) | 128.1(4) | O(2)–C(18)–C(19) | 110.1(3) |
| C(1)–C(5)–C(6) | 121.4(3) | O(3)–C(20)–O(4) | 126.6(4) |
| C(1)–C(5)–C(10) | 120.4(4) | O(3)–C(20)–N(2) | 121.9(4) |
| C(6)–C(5)–C(10) | 118.2(4) | O(4)–C(20)–N(2) | 111.4(3) |
| C(5)–C(6)–C(7) | 120.9(3) | O(4)–C(21)–C(22) | 107.4(3) |

**Table 2.** Atomic co-ordinates for (**2d**) ( × $10^4$).

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O(1) | 6 191(3) | 3 514(6) | 904(2) |
| O(2) | 6 093(3) | 6 291(6) | 1 133(2) |
| O(3) | 5 035(3) | 106(5) | 1 037(2) |
| O(4) | 5 340(2) | 1 722(5) | 1 672(2) |
| N(1) | 5 144(3) | 4 552(5) | 1 203(2) |
| N(2) | 4 815(3) | 3 007(6) | 1 048(2) |
| C(1) | 4 596(3) | 2 975(8) | 553(2) |
| C(2) | 4 341(4) | 4 775(9) | 409(2) |
| C(3) | 4 343(4) | 6 110(9) | 694(3) |
| C(4) | 4 662(3) | 6 061(7) | 1 178(3) |
| C(5) | 4 003(3) | 1 693(8) | 454(2) |
| C(6) | 4 012(4) | 765(10) | 38(3) |
| C(7) | 3 475(5) | −377(9) | −77(3) |
| C(8) | 2 925(4) | −553(10) | 232(4) |
| C(9) | 2 907(4) | 334(11) | 645(3) |
| C(10) | 3 448(4) | 1 498(9) | 760(2) |
| C(11) | 4 131(4) | 6 057(8) | 1 579(3) |
| C(12) | 3 510(5) | 6 946(13) | 1 533(3) |
| C(13) | 3 043(6) | 6 935(22) | 1 901(5) |
| C(14) | 3 137(7) | 6 187(21) | 2 305(5) |
| C(15) | 3 781(9) | 5 340(14) | 2 352(4) |
| C(16) | 4 240(5) | 5 243(12) | 1 993(4) |
| C(17) | 5 844(4) | 4 698(9) | 1 059(3) |
| C(18) | 6 848(4) | 6 651(11) | 963(4) |
| C(19) | 7 275(5) | 6 403(14) | 1 370(4) |
| C(20) | 5 071(4) | 1 480(9) | 1 241(3) |
| C(21) | 5 631(4) | 143(10) | 1 883(3) |
| C(22) | 6 043(6) | 666(12) | 2 297(4) |

Bond lengths (Å) and angles (°) for (**2d**).

| | | | |
|---|---|---|---|
| O(1)–C(17) | 1.205(8) | C(4)–C(11) | 1.51(1) |
| O(2)–C(17) | 1.330(8) | C(5)–C(6) | 1.375(9) |
| O(2)–C(18) | 1.530(9) | C(5)–C(10) | 1.364(9) |
| O(3)–C(20) | 1.207(8) | C(6)–C(7) | 1.38(1) |
| O(4)–C(20) | 1.331(8) | C(7)–C(8) | 1.36(1) |
| O(4)–C(21) | 1.461(8) | C(8)–C(9) | 1.35(1) |
| N(1)–N(2) | 1.412(6) | C(9)–C(10) | 1.40(1) |
| N(1)–C(4) | 1.478(7) | C(11)–C(12) | 1.36(1) |
| N(1)–C(17) | 1.388(9) | C(11)–C(16) | 1.34(1) |
| N(2)–C(1) | 1.458(8) | C(12)–C(13) | 1.36(1) |
| N(2)–C(20) | 1.383(8) | C(13)–C(14) | 1.29(2) |
| C(1)–C(2) | 1.521(8) | C(14)–C(15) | 1.39(2) |
| C(1)–C(5) | 1.519(8) | C(15)–C(16) | 1.34(1) |
| C(2)–C(3) | 1.304(9) | C(18)–C(19) | 1.41(1) |
| C(3)–C(4) | 1.49(1) | C(21)–C(22) | 1.46(1) |

| | | | |
|---|---|---|---|
| C(17)–O(2)–C(18) | 116.5(5) | C(6)–C(7)–C(8) | 118.2(7) |
| C(20)–O(4)–C(21) | 113.5(5) | C(7)–C(8)–C(9) | 121.5(7) |
| N(2)–N(1)–C(14) | 112.1(4) | C(8)–C(9)–C(10) | 120.3(7) |
| N(2)–N(1)–C(17) | 113.4(4) | C(5)–C(10)–C(9) | 119.0(6) |
| C(4)–N(1)–C(17) | 120.6(4) | C(4)–C(11)–C(12) | 119.9(6) |
| N(1)–N(2)–C(1) | 115.9(4) | C(4)–C(11)–C(16) | 123.4(7) |
| N(1)–N(2)–C(20) | 116.1(4) | C(12)–C(11)–C(16) | 116.6(7) |
| C(1)–N(2)–C(20) | 117.5(4) | C(11)–C(12)–C(13) | 118.8(9) |
| N(2)–C(1)–C(2) | 109.2(4) | C(12)–C(13)–C(14) | 126(1) |
| N(2)–C(1)–C(5) | 113.2(5) | C(13)–C(14)–C(15) | 114(1) |
| C(2)–C(1)–C(5) | 108.1(5) | C(14)–C(15)–C(16) | 122(1) |
| C(1)–C(2)–C(3) | 123.6(6) | C(11)–C(16)–C(15) | 122.4(9) |
| C(2)–C(3)–C(4) | 123.0(6) | O(1)–C(17)–O(2) | 124.3(6) |
| N(1)–C(4)–C(3) | 108.1(5) | O(1)–C(17)–N(1) | 124.2(6) |
| N(1)–C(4)–C(11) | 111.8(5) | O(2)–C(17)–N(1) | 111.4(5) |
| C(3)–C(4)–C(11) | 114.7(5) | O(2)–C(18)–C(19) | 104.6(7) |
| C(1)–C(5)–C(6) | 118.9(5) | O(3)–C(20)–O(4) | 125.4(6) |
| C(1)–C(5)–C(10) | 121.4(5) | O(3)–C(20)–N(2) | 122.6(6) |
| C(6)–C(5)–C(10) | 119.6(6) | O(4)–C(20)–N(2) | 112.0(5) |
| C(5)–C(6)–C(7) | 121.4(6) | O(4)–C(21)–C(33) | 107.3(6) |

*Diethyl* 1,2,3,6-*Tetrahydropyridazine*-1,2-*dicarboxylates* (**2a**–**d**).—Earlier studies of the conformations of (**2a**),[6] (**2d**),[7,8] and (**2c**),[9] using $^1H$ n.m.r. spectroscopy suggest that the hydropyridazine ring adopts the half-chair conformation in all three compounds. From a $^{13}C$ n.m.r. study it was found that the two *cis*-methyl groups of (**2b**) and the two *cis*-phenyl groups of (**2d**)

**Table 3.** Atomic co-ordinates for (**3a**) ( × $10^4$).

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O(1) | 2 311(1) | 942(4) | 5 401(4) |
| O(2) | 3 593(1) | 2 939(4) | 10 398(4) |
| N(1) | 2 086(1) | 2 335(4) | 8 214(4) |
| N(2) | 3 138(1) | 1 793(4) | 7 607(4) |
| N(3) | 2 468(1) | 3 104(4) | 9 589(4) |
| C(1) | 1 421(2) | 3 134(6) | 7 775(6) |
| C(2) | 1 123(2) | 3 801(6) | 9 557(8) |
| C(3) | 1 439(2) | 3 865(6) | 11 205(7) |
| C(4) | 2 157(2) | 3 303(6) | 11 454(5) |
| C(5) | 2 479(2) | 1 603(4) | 6 882(5) |
| C(6) | 3 124(2) | 2 645(4) | 9 342(5) |
| C(7) | 3 734(2) | 1 135(4) | 6 732(5) |
| C(8) | 4 171(2) | 138(5) | 7 801(7) |
| C(9) | 4 755(2) | −463(6) | 6 950(8) |
| C(10) | 4 903(2) | −88(6) | 5 090(8) |
| C(11) | 4 462(2) | 896(7) | 4 029(7) |
| C(12) | 3 870(2) | 1 496(5) | 4 850(6) |

Bond lengths (Å) and angles (°) for (**3a**).

|  |  |  |  |
|---|---|---|---|
| O(1)–C(5) | 1.205(4) | C(1)–C(2) | 1.474(6) |
| O(2)–C(6) | 1.207(4) | C(2)–C(3) | 1.310(7) |
| N(1)–N(3) | 1.409(3) | C(3)–C(4) | 1.498(6) |
| N(1)–C(1) | 1.456(4) | C(7)–C(8) | 1.389(5) |
| N(1)–C(5) | 1.367(4) | C(7)–C(12) | 1.370(5) |
| N(2)–C(5) | 1.405(4) | C(8)–C(9) | 1.383(5) |
| N(2)–C(6) | 1.387(4) | C(9)–C(10) | 1.363(7) |
| N(2)–C(7) | 1.427(4) | C(10)–C(11) | 1.384(6) |
| N(3)–C(4) | 1.444(4) | C(11)–C(12) | 1.388(5) |
| N(3)–C(6) | 1.372(4) |  |  |

|  |  |  |  |
|---|---|---|---|
| N(3)–N(1)–C(1) | 115.8(2) | O(1)–C(5)–N(2) | 127.7(3) |
| N(3)–N(1)–C(5) | 108.8(2) | N(1)–C(5)–N(2) | 105.3(2) |
| C(1)–N(1)–C(5) | 124.4(2) | O(2)–C(6)–N(2) | 127.7(3) |
| C(5)–N(2)–C(6) | 110.4(2) | O(2)–C(6)–N(3) | 126.4(3) |
| C(5)–N(2)–C(7) | 125.0(2) | N(2)–C(6)–N(3) | 105.9(2) |
| C(6)–N(2)–C(7) | 124.6(2) | N(2)–C(7)–C(8) | 119.5(3) |
| N(1)–N(3)–C(4) | 114.2(2) | N(2)–C(7)–C(12) | 119.7(3) |
| N(1)–N(3)–C(6) | 108.0(2) | C(8)–C(7)–C(12) | 120.8(3) |
| C(4)–N(3)–C(6) | 122.6(2) | C(7)–C(8)–C(9) | 119.0(4) |
| N(1)–C(1)–C(2) | 109.1(3) | C(8)–C(9)–C(10) | 120.9(4) |
| C(1)–C(2)–C(3) | 124.4(4) | C(9)–C(10)–C(11) | 119.8(4) |
| C(2)–C(3)–C(4) | 122.8(4) | C(10)–C(11)–C(12) | 120.2(4) |
| N(3)–C(4)–C(3) | 108.8(3) | C(7)–C(12)–C(11) | 119.3(3) |
| O(1)–C(5)–N(1) | 127.0(3) |  |  |

**Table 4.** Atomic co-ordinates for (**3b**) ( × $10^4$).

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O(1) | 3 367(4) | 4 558(0) | 7 409(4) |
| O(2) | 2 174(4) | −179(7) | 3 887(4) |
| N(1) | 2 427(4) | 1 786(7) | 7 571(4) |
| N(2) | 2 891(3) | 2 484(7) | 5 271(4) |
| N(3) | 1 929(3) | 427(7) | 6 472(4) |
| C(1) | 2 063(5) | 1 876(9) | 9 126(5) |
| C(2) | 2 040(5) | −9(10) | 9 750(5) |
| C(3) | 1 946(5) | −1 435(9) | 8 826(6) |
| C(4) | 1 795(5) | −1 427(8) | 7 035(5) |
| C(5) | 803(10) | 2 836(14) | 9 014(12) |
| C(6) | 545(7) | −2 205(11) | 6 202(8) |
| C(7) | 2 948(5) | 3 117(8) | 6 835(5) |
| C(8) | 2 330(4) | 781(8) | 5 066(5) |
| C(9) | 3 434(4) | 3 415(8) | 4 095(4) |
| C(10) | 4 272(5) | 2 507(10) | 3 333(6) |
| C(11) | 4 777(5) | 3 386(11) | 2 187(6) |
| C(12) | 4 481(5) | 5 191(11) | 1 817(6) |
| C(13) | 3 670(6) | 6 077(10) | 2 587(7) |
| C(14) | 3 133(5) | 5 197(9) | 3 725(6) |

**Table 5.** Atomic co-ordinates for (**4b**) ( × $10^4$).

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| Br(1) | 18 370(4) | 36 218(8) | 38 299(4) |
| Br(2) | 23 637(5) | −16 905(10) | 35 023(4) |
| O(1) | −190(2) | 2 333(5) | 3 343(2) |
| O(2) | 156(3) | 1 006(6) | 4 302(2) |
| O(3) | 1 350(3) | −3 062(6) | 4 467(3) |
| O(4) | 305(2) | −2 244(5) | 3 627(2) |
| N(1) | 780(3) | 609(6) | 3 652(2) |
| N(2) | 1 214(3) | −477(6) | 4 122(3) |
| C(1) | 1 022(4) | 956(8) | 3 136(3) |
| C(2) | 1 837(4) | 1 507(8) | 3 404(3) |
| C(3) | 2 334(3) | 3 65(8) | 3 945(3) |
| C(4) | 1 989(4) | −35(9) | 4 435(3) |
| C(5) | 2 095(4) | 1 827(11) | 2 854(4) |
| C(6) | 3 149(4) | 913(10) | 4 312(4) |
| C(7) | 212(3) | 1 402(7) | 3 744(3) |
| C(8) | −505(5) | 1 581(10) | 4 396(4) |
| C(9) | −1 091(6) | 378(14) | 4 151(6) |
| C(10) | 987(4) | −2 048(8) | 4 100(3) |
| C(11) | −8(5) | −3 823(9) | 3 577(5) |
| C(12) | −732(5) | −3 817(10) | 3 024(5) |

Bond lengths (Å) and bond angles (°) for (**4b**).

|  |  |  |  |
|---|---|---|---|
| Br(1)–C(2) | 2.004(6) | N(1)–C(7) | 1.361(8) |
| Br(2)–C(3) | 1.991(6) | N(2)–C(4) | 1.445(8) |
| O(1)–C(7) | 1.212(6) | N(2)–C(10) | 1.380(8) |
| O(2)–C(7) | 1.328(9) | C(1)–C(2) | 1.536(9) |
| O(2)–C(8) | 1.46(1) | C(2)–C(3) | 1.546(8) |
| O(3)–C(10) | 1.198(7) | C(2)–C(5) | 1.51(1) |
| O(4)–C(10) | 1.346(6) | C(3)–C(4) | 1.52(1) |
| O(4)–C(11) | 1.440(9) | C(3)–C(6) | 1.548(8) |
| N(1)–N(2) | 1.382(6) | C(8)–C(9) | 1.46(1) |
| N(1)–C(1) | 1.448(9) | C(11)–C(12) | 1.47(1) |

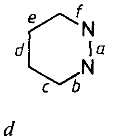
|  |  |  |  |
|---|---|---|---|
| C(7)–O(2)–C(8) | 116.5(6) | Br(2)–C(3)–C(2) | 106.1(4) |
| C(10)–O(4)–C(11) | 115.6(6) | Br(2)–C(3)–C(4) | 105.6(4) |
| N(2)–N(1)–C(1) | 115.4(5) | Br(2)–C(3)–C(6) | 107.1(4) |
| N(2)–N(1)–C(7) | 121.2(5) | C(2)–C(3)–C(4) | 112.1(5) |
| C(1)–N(1)–C(7) | 123.1(5) | C(2)–C(3)–C(6) | 115.6(5) |
| N(1)–N(2)–C(4) | 114.5(4) | C(4)–C(3)–C(6) | 109.6(6) |
| N(1)–N(2)–C(10) | 120.1(6) | N(2)–C(4)–C(3) | 112.4(6) |
| C(4)–N(2)–C(10) | 121.4(6) | O(1)–C(7)–O(2) | 125.6(5) |
| N(1)–C(1)–C(2) | 111.1(6) | O(1)–C(7)–N(1) | 122.9(5) |
| Br(1)–C(2)–C(1) | 104.9(4) | O(2)–C(7)–N(1) | 111.6(6) |
| Br(1)–C(2)–C(3) | 106.9(4) | O(2)–C(8)–C(9) | 109.0(7) |
| Br(1)–C(2)–C(5) | 106.6(4) | O(3)–C(10)–O(4) | 126.1(6) |
| C(1)–C(2)–C(3) | 111.0(5) | O(3)–C(10)–N(2) | 123.4(7) |
| C(1)–C(2)–C(5) | 111.0(6) | O(4)–C(10)–N(2) | 110.4(6) |
| C(3)–C(2)–C(5) | 115.7(6) | O(4)–C(11)–C(12) | 107.6(7) |

are magnetically non-equivalent. Fisher *et al.*[1] concluded that this is clear evidence that both of these compounds are present in their half-chair conformations in the solution. The crystal structure of (**2d**) shows that indeed the molecule adopts the same conformation as in the solution. The hydropyridazine ring is in the half-chair conformation.

N-*Phenyl*-5,8-*dihydro*[1,2,4]*triazolo*[1,2-a]*pyridazine*-1,3-*dione* (**3a**–**c**).—The equivalence of the 3,6-dimethyl groups in the $^{13}C$ n.m.r. spectrum of (**3b**) and the use of the Garbish equation in the $^{1}H$ n.m.r. of (**3c**) led to the conclusion that the stable conformation of the hydropyrazine ring of (**3a**–**c**) is the boat conformation.[1]

The crystal structures of the two compounds (**3a** and **b**) show that the molecules adopt the half-chair conformation [although (**3b**) is somewhat less puckered]. There are reasons to believe that the conformation of a boat is less stable than that of the

**Table 6.** Torsion angles (°) in the hydropyridazine moieties and puckering parameters.



| Compound | *a* | *b* | *c* | *d* | *e* | *f* | Q/Å | angle/° | Θ/° |
|---|---|---|---|---|---|---|---|---|---|
| **(1)** | 54.3 | −33.3 | −4.1 | 22.1 | −0.8 | −36.3 | 0.440 | 206.9 | 110.4 |
| **(2d)** | 63.6 | −35.9 | 1.5 | 6.2 | 17.9 | −50.7 | 0.467 | 192.3 | 124.1 |
| **(3a)** | 61.3 | −39.2 | 8.8 | 1.8 | 15.7 | −45.3 | 0.425 | 201.9 | 128.6 |
| **(3b)** | −40.8 | 41.5 | −20.3 | −2.8 | −7.3 | 13.7 | 0.331 | 71.9 | 60.5 |
| **(4b)** | 57.0 | −54.6 | 48.4 | −46.0 | 47.2 | −52.1 | 0.496 | 258.84 | 177.50 |

half-chair. In the boat conformation the two lone-pair electrons at the N–N atoms are at the same side and will contribute to a repulsion interaction which is not expected in a half-chair conformation. We have no explanation for the differences in the conformation found in the solute and in the solid state.

*Diethyl* 4,5-*Dibromoperhydropyridazine*-1,2-*dicarboxylates* (**4a–b**).—Earlier studies by Price[9] suggested that (**4b**) has a 19.8 kcal mol$^{-1}$ barrier to hindered carbamate rotation, but later studies by Price *et al.*[10] suggested that a chair-boat equilibrium was more likely. The $^{13}$C n.m.r study by Fisher *et al.*[1] suggests that in both (**4a** and **b**) there are similar mixtures of conformers. Consideration of the three conformational processes: hindered carbamate rotation, ring flip, and nitrogen inversion led to the conclusion that the hydropyridazine ring adopts the chair conformation and the mixture of conformers is due to nitrogen inversion. The crystal structure of (**4b**) shows that indeed the conformation of the hydropyridazine ring is a chair. In agreement with Fisher's findings[1] the two $CO_2Et$ groups are inclinal, the two bromines in axial positions, and the two methyls in equatorial positions.

## Experimental

Details of preparation of the five compounds (**1**), (**2d**), (**3a,b**), and (**4b**) are given in ref. 1. Intensity data were measured using a Philips 1100 four-circle computer-controlled diffractometer using the ω–2θ scanning mode with graphite-monochromated Mo-$K_\alpha$ radiation (λ 0.7107 Å). The crystal structures were solved by MULTAN 80[11] and refined by SHELX[12] using a full-matrix least-squares procedure with anisotropic displacement parameters for non-hydrogen atoms, isotropic for H.

*Crystal Structure Data.*—*Diethyl* 3,6-*diphenyl*-1,2-*dihydropyridazine*-1,2-*dicarboxylate* (**1**) $C_{22}H_{22}N_2O_4$. ($M$ 378.428), monoclinic, space group $P2_1/c$, $a$ = 11.601(6), $b$ = 15.213(8), $c$ = 12.276(6) Å, β = 112.66(2)°, $U$ = 1 999.3 Å$^3$, $F$000 = 800, μ = 0.51 cm$^{-1}$. The agreement factors at the end of the refinement are $R$ = 0.073, $R_w$ = 0.063 for 2 208 observed reflections [$F_o$ > 1.5 σ ($F_o$)] (out of 3 146 unique reflections measured). {$w$ = 1.7825/[σ$^2$($F_o$)]}.

*Diethyl* 3,6-*diphenyl*-1,2,3,6-*tetrahydropyridazine*-1,2-*dicarboxylate* (**2d**). $C_{22}H_{24}N_2O_4$. ($M$ = 380.444), orthorhombic, space group $Pbcn$, $a$ = 18.874(9), $b$ = 7.699(4), $c$ = 28.226(14) Å, $U$ = 4 101.5 Å$^3$, $F$000 = 1 616, μ = 0.50 cm$^{-1}$. The agreement factors at the end of the refinement are $R$ = 0.079, $R_w$ = 0.070 for 1 483 observed reflections [$F_o$ > 1.5 σ ($F_o$)] (out of 2 716 unique reflections measured). {$w$ = 2.2719/[σ$^2$($F_o$) + 0.0002 $F_o^2$]}.

N-*Phenyl*-5,8-*dihydro*[1,2,4]*triazolo*[1,2-a]*pyridazine*-1,2,3-*dione* (**3a**). $C_{12}H_{11}N_3O_2$. ($M$ = 229.239), orthorhombic, space group $P2_12_12_1$, $a$ = 19.779(10), $b$ = 7.920(4), $c$ = 6.978(3) Å, $U$ = 1 093.1 Å$^3$, $F$000 = 480, μ = 0.59 cm$^{-1}$. The agreement factors at the end of the refinement are $R$ = 0.055, $R_w$ = 0.054 for 1 139 observed reflections ($F_o$ > 0.0). {$w$ = 0.7790/[σ$^2$($F_o$) + 0.0015 $F_o^2$]}.

cis-5,8-*Dimethyl*-2-*phenyl*-5,8-*dihydro*[1,2,4]*triazolo*[1,2-a]-*pyridazine*-1,3-*dione* (**3b**). $C_{14}H_{15}N_3O_2$. ($M$ = 257.293), monoclinic, space group $P2_1$, $a$ = 10.767(5), $b$ = 7.369(4), $c$ = 8.494(4) Å, β = 101.93(2)°, $U$ = 659.4 Å$^3$, $F$000 = 272, μ = 0.53 cm$^{-1}$. The agreement factors at the end of the refinement are $R$ = 0.064, $R_w$ = 0.060 for 1 238 observed ($F_o$ > 0.0) unique reflections). {$w$ = 0.3999/[σ$^2$($F_o$) + 0.0012 $F_o^2$]}.

*Diethyl*-trans-4,5-*dibromo*-4,5-*dimethylperhydropyridazinedicarboxylate* (**4b**). $C_{12}H_{20}Br_2N_2O_2$. ($M$ = 384.122), monoclinic, space group $C2/c$, $a$ = 19.482(10), $b$ = 8.353(4), $c$ = 22.204(11) Å, β = 112.78(2)°, $U$ = 3 331.5 Å$^3$, $F$000 = 1 664, μ = 47.6 cm$^{-1}$ (during the refinement the positions of the methyl and methylenic groups were calculated and tied to their bonded atoms). The agreement factors at the end of the refinement are $R$ = 0.063, $R_w$ = 0.066 for 2 344 observed reflections [$F_o$ > 1.5 σ ($F_o$)] (out of 2 789 unique reflections measured). {$w$ = 1.2942/[σ$^2$($F_o$) + 0.0014 $F_o$]}.

## References

1 T. H. Fisher, J. C. Crook, and S. Chang, *Tetrahedron*, 1987, **43**, 2443, and references cited therein.

2 W. B. Schweizer and J. D. Dunitz, *Helv. Chim. Acta*, 1982, **65**, 1547.

3 M. Kaftory and I. Agmon, *J. Am. Chem. Soc.*, 1984, **106**, 7785.

4 (*a*) D. Cremer, 'RING,' *QCPE*, Program No. 288, University of Indiana, Bloomington, Indiana; (*b*) D. Cremer, *Isr. J. Chem.*, 1980, **20**, 12.

5 J. E. Anderson and J. M. Lehn, *Tetrahedron*, 1968, **24**, 137.

6 E. W. Bittner and J. T. Gerig, *J. Am. Chem. Soc.*, 1972, **94**, 913.

7 J. C. Breliere and J. M. Lehn, *J. Chem. Soc., Chem. Commun.*, 1965, 426.

8 B. H. Korsch and N. V. Riggs, *Tetrahedron Lett.*, 1966, 5897.

9 B. Price, I. O. Sutherland, and F. G. Williamson, *Tetrahedron*, 1966, **22**, 3477.

10 B. Price and I. O. Sutherland, *J. Chem. Soc. B*, 1967, 573.

11 P. Main, S. J. Fisher, S. E. Hull, L. Lessinger, G. Germain, S. P. Declercq, and M. M. Woolfson, MULTAN 80, 'A System of Computer Programs for the Automatic Solution of Crystal Structures from *X*-Ray Diffraction Data,' Universities of York, England, and Louvain, Belgium.

12 G. M. Sheldrick, SHELX, Program for Crystal Structure determination, University of Cambridge, 1976.

*Received* 13*th February* 1989; *Paper* 9/00763F