Tetrahedron Vol. 43, No. 7, pp. 1299 to 1305, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00
Pergamon Journals Ltd.

MODIFICATION OF CRYSTAL PACKING AND MOLECULAR CONFORMATION VIA SYSTEMATIC SUBSTITUTION

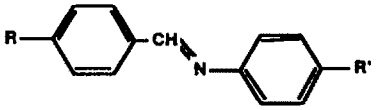
I. Bar and J. Bernstein*

Department of Chemistry
Ben-Gurion University of the Negev
Beersheva, Israel

(*Received in UK* 16 *February* 1987)

Abstract - Variations in molecular conformation and crystal packing are investigated by systematically altering the substitutents on a molecule which has two degrees of conformational freedom. The crystal structures of the heterodisubstituted benzylideneanilines (BA's), *p*-chloro-N-(*p*-bromo-benzylidene) aniline (BrCl) and *p*-bromo-N-(*p*-chlorobenzylidene) aniline (ClBr) have been determined. The conformations of the two molecules are different from each other but are similar to those found in the crystal structures of the homodisubstituted derivatives with which they are isomorphous: *p*-bromo-N-(*p*-bromo-benzylidene) aniline (BrBr) and the orthorhombic form of *p*-chloro-N-(*p*-chloro-benzylidene)aniline (ClCl) respectively. Because of this isomorphous relationship it is concluded that the substituent on the benzylidene ring plays a crucial role in determining the packing mode of the structure.

The utilization of the organic solid state as a reactive medium or for specific physical properties depends upon our ability to predict or predesign the packing mode and molecular conformation of the component molecules of the solid. A great deal of progress has been made recently, especially by combining a number of experimental and computational techniques[1a]. One viable approach to the study of the relationship betweeen crystal forces and molecular conformation involves the investigation of conformational polymorphs[1b] of a particular substance. Since no chemical modifications are made in such systems the only variable on going from one polymorphic structure to another is the crystal environment. By thus limiting the number of experimental variables one is able to extract the maximum amount of information on the energetics of the different crystal environments and their influence on molecular conformation from computations of crystal energetics on the various polymorphs[2,3]. A natural extension of the study of the interplay betweeen crystal forces and molelcular conformation is to investigate the role of a substituent in determining simultaneously how a molecule packs in the crystal and its molecular conformation. This can be done by systematically varying the substituents on a molecule which has a limited number of conformational degrees of freedom and studying the resulting differences in crystal structure and molecular conformation. As part of our continuing study of the relationship between crystal forces and molecular conformation, we have been carrying out a systematic investigation of all the compounds of type (I), in which there are essentially two conformational degrees of freedom: the rotations about the N-phenyl and CH-phenyl bonds.



R,R' = Cl, Br, CH_3

Nine chemically distinct molecules may be obtained from all the possible combinations of R and R', some of which crystallize in polymorphic systems (e.g. R=R'=CH_3 [trimorphic], R=R'=Cl [dimorphic])[4], while several members exhibit isomorphous crystal structures (e.g., R=CH_3, R'=Cl, or Br; R=Cl or Br; R'=CH_3)[5]. No polymorphism has been found for the latter group of four compounds and there is no evidence of any isomorphism between these four cases and any of the homodisubstituted derivatives. Since the van der Waals radii of the substituents are similar, the polymorphism and isomorphism suggest that the polarizability of the substituents plays a dominating role here.

The two heterodisubstituted derivatives which do not contain methyl groups, R=Cl, R'=Br (ClBr) and R=Br, R'=Cl (BrCl), are not isomorphous; however, the former is isomorphous with the orthorhombic form[4b] of the dichloro analogue (R=R'=Cl) (ClCl), while the latter is isomorphous with the dibromo analogue (R=R'=Br) (BrBr)[5]. The relationship between these two heterodisubstituted derivatives shows that a simple change in the nature and mode of substitution can lead from one crystal structure to another, with accompanying conformational changes. The full crystal structures of the two compounds reported here reveal the details of the similarities and differences among these structures and those reported earlier.

Molecular Geometry. Atomic numbering for both molecules (Fig. 1) is consistent with the previously

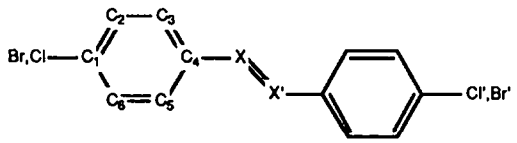


Figure 1. Atomic numbering for both compounds.

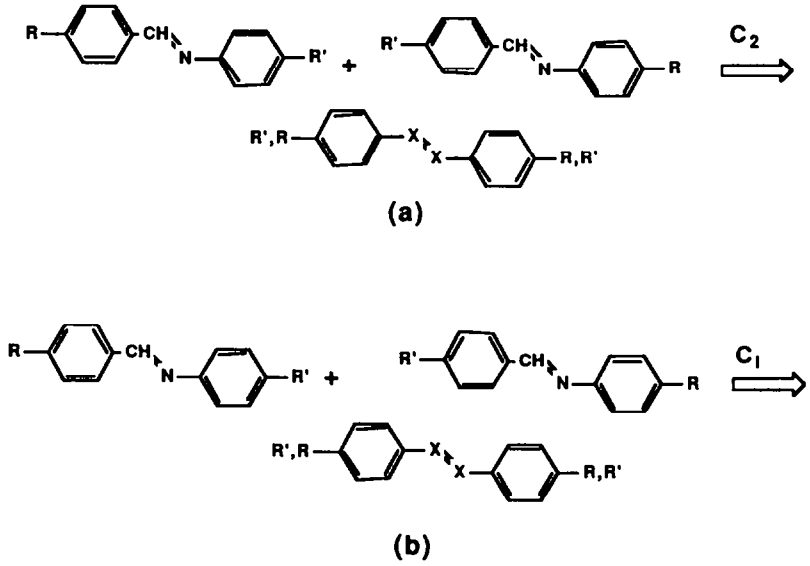
reported isomorphic structures of BrBr[5] and ClCl[4b]. Bond lengths and bond angles are compiled in Table 1. Molecular dimensions are compatible within experimental error with those obtained for the latter two compounds except

Table 1. Bond lengths (Å) and bond angles (°)

	BrCl	ClBr
C(1)-C(2)	1.395(5)	1.370(9)
C(2)-C(3)	1.369(6)	1.40 (1)
C(3)-C(4)	1.400(7)	1.39 (1)
C(4)-C(5)	1.388(5)	1.40 (1)
C(5)-C(6)	1.382(5)	1.40 (1)
C(6)-C(1)	1.379(4)	1.377 (9)
Br-C(1)	1.903(4)	1.880(8)
Cl-C(1)	1.713(8)	1.74(2)
C(4)-X	1.429(5)	1.44(1)
X-X'	1.268(4)	1.21(1)
C(1)-C(2)-C(3)	118.5(3)	117.3(6)
C(2)-C(3)-C(4)	121.8(3)	122.5(7)
C(3)-C(4)-C(5)	118.2(4)	117.9(7)
C(4)-C(5)-C(6)	120.8(3)	120.2(7)
C(5)-C(6)-C(1)	119.6(3)	119.2(6)
C(6)-C(1)-C(2)	121.0(3)	122.7(6)
Br-C(1)-C(2)	122.3(2)	118.2(5)
Br-C(1)-C(6)	116.7(3)	119.1(5)
Cl-C(1)-C(2)	113.2(3)	118.6(8)
Cl-C(1)-C(6)	125.7(3)	118.7(7)
C(4)-X-X'	122.4(3)	121.6(7)
C(3)-C(4)-X	118.2(3)	121.6(7)
C(5)-C(4)-X	123.6(4)	119.9(6)

for the geometric features about C(1) which are influenced by the substitutional disorder[6]. The bond lengths for theC(1) substituent are consistent with those for a benzene substituted with a chlorine atom[9] and for benzene substituted with a bromine atom[10]. The internal angles at C(1) are 120.0(3)° and 122.7(6)° for BrCl and ClBr respectively, which, in spite of the lowered precision due to the disorder, are compatible with those in BrBr (120.4°) and the average (121.3°) in the dimorphic ClCl system. The presence of the substitutional disorder and the model used in the refinement also lead to a deviation of the exocyclic angles from the nominal value slightly exceeding 120° due to the presence of electronegative substituents[9a]. Because the standard deviations for these angles are larger than for the rest of the atoms in the ring, it seems that the deviation is an artifact of the refinement.

The mode of substitutional disorder observed in BrCl was observed also in ClMe (I, R=Cl, R'=CH_3) and in its contrasubstitutional analogue MeCl (I, R=CH_3, R'=Cl)[11] in which molecules were also located on a center of symmetry (Scheme 1b) but not in the BrBr structure or is the triclinic polymorph of ClCl, which are homodisubstituted. The molecule of ClBr is the first among the *hetero*disubstituted group which is located on a two-fold axis and exhibits this kind of disorder (Scheme 1a), thus distinguishing it from the isomorphous ClCl structure.



Scheme 1. Orientational disorder is possible as a result of the presence of heteroatoms in the bridge and heterosubstitution in the *para* position. If statistical, it may be accompanied by a crystallographic element of symmetry: a twofold axis perpendicular to the plane of the paper as in (a) or by a center of symmetry as in (b).

Table 2 gives the best planes for the aromatic rings and the four central atoms of both molecules. The four bridge atoms comprise a planar group in BrCl (plane 2), while in ClBr they lie within 0.21Å of their best plane (plane 4). The rotations of the aromatic rings about the exocyclic single bonds are the essential features of the molecular conformation. The angles of rotation are 2.1° in BrCl and ±25.2° in ClBr[4b]. The essentially planar conformation of BrCl is similar to that found in the isomorphous structure BrBr, while the non-planar conformation of ClBr is similar to that found in the ClCl orthorhombic polymorph, but differs from the planar conformation in the triclinic ClCl.

Ab initio calculations on unsubstituted BA's[12] indicate that the conformation in which the twist angles about the exocyclic bonds are of equal magnitude but opposite sign is favored over the planar conformation by ~ 0.2 kcal/mole, which is the order of magnitude of the stabilization energy of ClBr over BrCl, but both molecules are unfavorable relative to the molecular conformation that approximates the lowest free molecular energy[13]. Hence in the present

Table 2. Best planes Equation of some best least-squares planes in the form Ax+By+Cz+D = 0, where x,y,z are fractional coordinates. Deviations (Å) of relevant atoms from the plane aregiven; e.s.d.'s of deviations in parentheses.

		A	B	C	D
BrCl	Plane 1 C(1)-C(6)	-0.031	-0.451	0.892	1.044
	Plane 2 C(4)-X-X'-C(4')	-0.041	-0.481	0.876	0.740
ClBr	Plane 3 C(1)-C(6)	-0.245	0.348	0.905	4.654
	Plane 4 C(4)-X-X'-C(4')	0.	0.	1.	4.823

	Plane 1	Plane 2	Plane 3	Plane 4
C(1)	0.001(4)	-0.037(4)	-0.005(5)	0.086(5)
C(2)	0.001(4)	0.013(4)	-0.006(7)	0.578(7)
C(3)	0.000(4)	0.031(4)	0.024(7)	0.550(7)
C(4)	-0.004(4)	0.0	-0.023(6)	-0.018(6)
C(5)	0.006(4)	-0.040(4)	0.012(7)	-0.478(7)
C(6)	-0.004(4)	-0.071(4)	0.005(6)	-0.438(6)
Br	-0.020(3)	-0.089(3)	-0.112(7)	0.050(7)
Cl	0.116(8)	0.058(8)	-0.07(2)	0.07(2)
X	-0.027(3)	0.0	0.073(7)	0.021(7)
C(1')	-0.032(4)	0.037(4)	-0.141(5)	0.086(5)
C(2')	-0.033(4)	-0.013(4)	0.749(7)	0.578(7)
C(3')	-0.031(4)	-0.031(4)	0.670(7)	0.550(7)
C(4')	-0.028(4)	0.0	-0.311(6)	-0.018(6)
C(5')	-0.037(4)	0.040(4)	-1.178(7)	-0.478(7)
C(6')	-0.028	-1.097(6)	-1.097(6)	-0.438(6)
Br'	-0.012(3)	0.089(3)	-0.100(7)	0.050(7)
Cl'	-0.147(8)	-0.058(8)	-0.09(2)	0.07(2)
X'	-0.004(3)	0.0	-0.337(7)	0.021(7)

structures the lattice must supply energy for the stabilization of the energetically unfavorable conformations observed[2,3,12,13].

The most intriguing point about this pair of structures is the fact that a simple reversal in the location of the chlorine and bromine substituents results in the significant change in the crystal structure accompanied by a change in the molecular conformation. The resulting isomorphism with the homodisubstituted derivatives indicates that it is the substituent on the benzylidene ring which plays the most important role in determining the crystal structure. Otherwise we might expect a reversal in the space groups for **BrCl** and **ClBr**, or in fact space groups different from those observed for **BrBr** and **ClCl**. (Although **ClCl** also crystallizes in a triclinic form, we have not detected crystals of **ClBr** which are isomorphous with it.) The substituent on the aniline ring must be more polar and/or smaller than a methyl group for this effect to be seen, since **BrMe** and **ClMe** do not crystallize (as far as we know) in the **BrBr** or **ClCl** structures, as might be expected from the pair of structures reported here.

The packing of the molecules gives some clue to the basis of the importance of the substituent on the benzylidene ring in these structures. The structures are shown in Figure 2 and intermolecular distances are presented in Table 3.

Both structures exhibit regions of halogen...halogen contacts alternating with regions of hydrocarbon contacts.These distances must be viewed with some caution, due to the presence of disorder, which is assumed to be totally random, but there is some information here nonetheless. Most of the noteworthy intermolecular distances are concentrated in the region of the halogen substituents which can be clearly seen in the stereo figures. The Br...Br distance (3.689(9) Å) in **ClBr** is significantly shorter than the corresponding distance in **BrCl** (3.840(3) Å) and both of them are slightly shorter than the sum of the van der Waals radii. In both compounds the Cl...Cl distance (3.81(3) Å) is longer than the sum of the van der Waals radii in both compounds, while the Br...Cl contact in **BrCl** (3.547(7) Å) is shorter than any of the corresponding intermolecular distances in **ClBr**. These trends reflect the directing power of the substituents in determining the crystal structure and the accompanying molecular conformation.

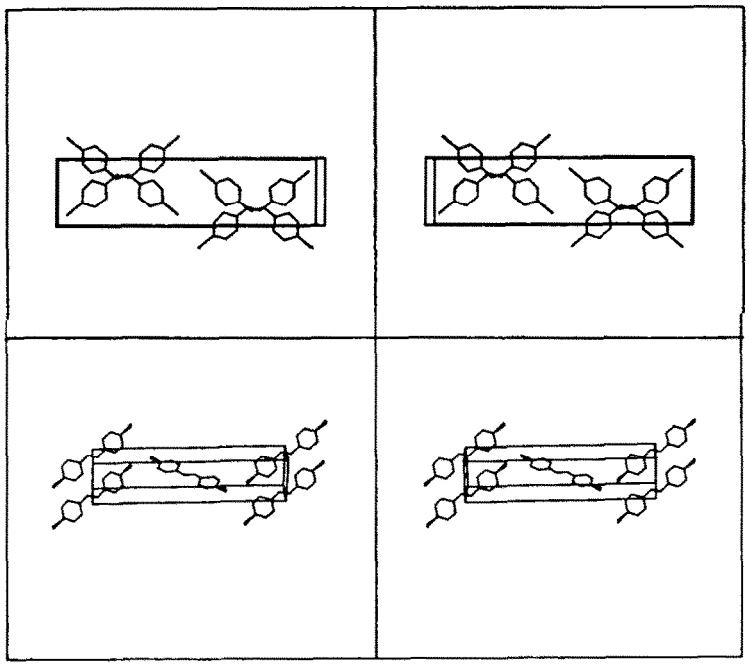


Figure 2. Stereo packing diagrams of ClBr (top) and BrCl (bottom). For ease in comparison, in both cases the is on the best plane of the four atoms C(4)-X-X'-C(4') comprising the bridge between the two rings.

Table 3. Intermolecular distances

Atom pair	Translation along *a*	*b*	*c*	Distance (Å)
BrCl				
Br...Br^{I}	2	1	2	3.840(3)
Cl...Cl^{I}	2	1	2	3.806(9)
Br...Cl^{I}	2	0	2	3.547(7)
Br...H(2)^{I}	2	0	2	3.14 (3)
Cl...H(2)^{I}	2	0	2	3.18 (3)
Symmetry: I 1/2-*x*, 1/2+*y*, -*z*				
ClBr				
Br...Br^{I}	0	0	1	3.689(9)
Br...Br^{III}	0	1	1	3.86 (1)
Br...Br^{II}	0	0	1	3.986(8)
Cl...Cl^{III}	0	1	1	3.81 (3)
Br...Cl^{II}	0	0	1	3.81 (2)
Br...Cl^{III}	0	1	0	3.81 (2)
Br...Cl^{III}	0	1	1	3.81 (2)
Br...Cl^{II}	0	-1	1	3.94 (2)
Br...C(6)^{II}	0	1	0	3.74 (9)
Br...C(6)^{II}	0	0	1	3.77 (9)
Br...H(6)^{I}	0	1	1	3.17 (7)
Br...H(6)^{I}	0	0	1	3.28 (7)
C(1)...H(2)^{III}	0	0	1	2.54 (6)
C(2)...H(2)^{III}	0	1	1	2.82 (6)
C(6)...H(2)^{III}	0	1	1	2.74 (6)
Symmetry: I -*x*,-*y*,-*z*; II -*x*, 1/2+*y*, 1/2-*z*; III *x*,1/2-*y*, 1/2+*z*				

Experimental. BrCl was prepared by condensation of *p*-bromobenzaldehyde and *p*-chloroaniline while ClBr was prepared by condensation of *p*-chlorobenzylidene and *p*-bromoaniline. Both compounds were crystallized from ethanol (m.p. 392°K, 390°K respectively). Cell dimensions for BrCl and ClBr are based on least squares refinement of fifteen reflections with $83°<2\theta<110°$ (Cu Kα) and $40°<2\theta<80°$ respectively. Crystal data are summarized in Table 5.

Table 5. Crystal Data

	BrCl	ClBr
	$C_{13}H_9BrClN$	
a (Å)	24.692(2)	24.880(10)
b	5.912(1)	6.379(2)
c	4.022	7.436(2)
β(°)	92.10(1)	---
V(Å^3)	586.73	1180.16
D_x (Mg m^{-3})	1.67	1.66
Space group	$P2_1/a$	$Pccn$
Z	2	4
μ (CuKα) (cm^{-1})	62.72	62.40
M_r	294.59	294.59
F(000)	292	584
Total number of intensities measured	1213	2269
Total intensities with I>2.0σ(I)	984	906
R	0.062	0.079
R_w	0.070	0.091

Intensities for both compounds were collected on a Syntex automated diffractometer with a θ:2θ scan and scan rate varying from 2° to 24° min^{-1} as determined by a rapid prescan of the peak intensities. Data were corrected for Lorentz and polarization factors, but not for absorption due to the nearly equal dimensions of the data crystals.

Comparison of the cell parameters and structure factors for **BrCl** with those of earlier determined structures suggested isomorphism with **BrBr**[5] and trans-*p,p'*-dibromo- azobenzene[6]. The molecule thus occupies site symmetry 1, which requires orientational disorder[6]; hence the scattering factor of the two atoms at the bridge was taken to be the average of carbon and nitrogen by located one atom per block with "tied" positional and temperature factors[7] and occupancy of 0.5 for each atom.

Because of the substitutional disorder[6], the bromine atom was assigned occupancy of 0.5 also was assigned an occupancy of 0.5. A trial structure based on the coordinates of **BrBr** and the above considerations yielded R=0.25 for relfections with $\sin\theta/\lambda<0.4$. The difference map revealed a new peak in the vicinity of Br, suggesting that this is the chlorine (1/2 Cl). the refinement was continued, first with isotropic temperature factors to an R of 0.098 for all data. Expected hydrogen atom positions were calculated from geometric considerations and included in the final cycles of refinement with fixed isotropic temperature factors for all heavy atoms with bond length constraints for the disordered substituent atoms. The refinement converged at R=0.062 (0.064 including unobserveds) R_w=0.070, exlcuding five refelctions which showed signs of extinction. The hydrogen atom of half occupancy on the bridge was not located.

Cell dimensions of ClBr are very similar to those of the orthorhombic form of ClCl[4b]. The structure factors of the two structures also show consistent corrrespondence, suggesting that they are isomorphic. The presence of four molecules in the unit cell and the isomorphism with ClCl implies disorder about the two-fold axis; therefore the scattering factor of the X atoms was taken as for BrCl.

A difference map based on the coordinates of the atoms from the ClCl structure revealed an additional peak in the vicinity of the chlorine atom, which is the bromine with 0.5 occupancy. The final strucutre based on these considerations and anisotropic temperature factors for all heavy atoms yielded R=0.089 for all data. Expected hydrogen atom positions on the ring were calculated from geometric considerations and included in the refinement with a fixed isotropic temperature factor. At this stage a difference electron density map showed a peak of 0.29 eÅ^{-3} at the chemically expected position of the disordered hydrogen on the bridge. The final stage of the refinement, in which the hydrogen was included with half occupancy and bond constraints were applied for the substituent atoms resulted in R=0.079 (0.083 including unobserveds), R_w=0.091.

Final positional parameters for both compounds are given in Table 6. Temperature factors and structure factors have been deposited. Scattering factors were taken from the International Tables for Crystallography[8].

Table 6. Atomic coordinates ($x10^4$ for non-hydrogen atoms and $x10^3$ for hydrogen atoms)

	x	y	z
BrCl			
Br*	7979(1)	6205(4)	9161(9)
Cl*	7956(3)	5587(8)	9076(23)
X	9749(1)	-0195(6)	4770(8)
C(1)	8513(1)	4143(5)	7803(9)
C(2)	8384(1)	2092(7)	6255(10)
C(3)	8798(2)	0719(6)	5320(11)
C(4)	9342(2)	1321(5)	5874(9)
C(5)	9457(1)	3366(7)	7442(11)
C(6)	9045(1)	4785(7)	8380(10)
H(2)	798(1)	163(6)	593(11)
H(3)	879(2)	-064(5)	377(8)
H(5)	985(1)	371(5)	755(11)
H(6)	910(1)	628(4)	936(10)
ClBr			
Br*	0388(2)	1672(9)	6552(10)
Cl*	0424(6)	1841(27)	6585(32)
X	2268(3)	7785(12)	6513(9)
C(1)	0963(2)	3584(10)	6601(7)
C(2)	1447(3)	2910(11)	7262(9)
C(3)	1876(3)	4333(11)	7225(10)
C(4)	1832(3)	6312(11)	6461(8)
C(5)	1325(3)	6949(12)	5843(9)
C(6)	0980(3)	5560(11)	5896(8)
H(2)	134(3)	218(11)	848(8)
H(3)	220(3)	378(11)	784(9)
H(5)	128(3)	851(9)	576(9)
H(6)	058(3)	618(11)	549(9)
HX*	225(6)	927(15)	680(17)

* Occupancy of 0.5; X=(C+N)/2

Acknowledgement. This work was supported in part by a grant from the U.S.-Israel Binational Science Foundation, Jerusalem. We are grateful to Hai Cohen and Rami Peles for technical assistance.

References

1. a) Kearsley, S.K.; Desiraju, G.R. *Proc. Roy Soc. (London) A* **1985**, *397*, 157; Nakanishi, H.; Jones, W.; Thomas, J.M.; Hursthouse, M.B.; Mollevalli, M. *J. Phys. Chem.* **1981**, *85*, 3636.
b) Corradini, *P.Chim. Ind. (Milan)* **1971**, *55* 122; Panagiotopoulis, N.C.; Jeffrey, G.A.; LaPlaca, S.J.; Hamilton, W.C. *Acta Crystallogr., Sect. B*, **1974**, *30*, 1421.

2. Bernstein, J. ; Hagler, A.T. *J. Am. Chem. Soc.* **1978**, ***100***, 673; Hagler, A.T.; Bernstein, J. *J. Am. Chem. Soc.* **1978**, ***100***, 5346.

3. Bar, I ; Bernstein, J. *J. Phys. Chem.* **1982**, *86*, 3223.

4. a) Bernstein, J.; Bar, I.; Christensen, A., *Acta Crystallogr. Sect. B* **1976**, *32*, 1609; Bar, I.; Bernstein, J. *Acta Crystallogr. Sect. B* **1977**, *33*, 1738; Bar, I.; Bernstein, J. *Acta Crystallogr. Sect. B* **1982**, *38*, 121.
b)Bernstein, J.; Schmidt, G.M.J. *J. Chem. Soc. Perkin II*, **1972**, 951; Bernstein, J. ; Izak, I. *J. Chem. Soc. Perkin II*, **1976**, 423.

5. Bernstein, J.; Izak, I.*J. Cryst. Molec. Struct.* **1975**, *5*, 257.

6. Bar, I.; Bernstein, J., *J. Phys. Chem* . **1983**, *88*, 243.

7. Sheldrick, G.M.; "The SHELX Program System; University Chemical Laboratory, Cambridge, U.K., 1976.

8. "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1968; Vol. IV, pp. 201-20

9. a) Domenicano, A.; Vaciago, A.; Coulson, C.A. *Acta Crystallogr. Sect. B.*, **1975**, *31*, 221; Domenicano, A.; Vaciago, A.; Coulson, C.A. *Acta Crystallogr. Sect. B.*, **1975**, *31*, 1631.
b) Domenicano, A.; Mazzeo, P.; Vaciago, A. *Tetrahedron Lett.* **1976**, 1029.

10. James, M.N.G.; Williams, G.J.B., *Acta Crystallogr. Sect. B.* **1973** *29*, 1172.

11. Bar, I. and Bernstein, J. *Acta Crystallogr. Sect. B* . **1983**, *39*, 266.

12. Bernstein, J.; Hagler, A.T.; Engel, M. *J. Chem. Phys.* **1981**, *75*, 2346.

13. Burgi, H.-B.; Dunitz, J.D. *Helv. Chim. Acta* **1971**, *54*, 1255.