Molecular structures of amino and nitro derivatives of 1,3-di(morpholin-4-yl)benzene

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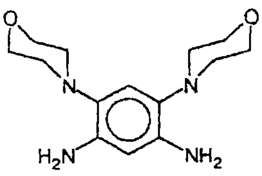
The 4,6-diamino-1,3-di(morpholin-4-yl)- and 5-amino-2,4-di(morpholin-4-yl)-1-nitro derivatives of benzene, which serve as model compounds in studies of spatial structures and reactivities of monomer units of many polymers of practical importance, have been studied by X-ray diffraction analysis. The morpholine rings are twisted so that they are virtually perpendicular to the benzene ring. According to the results of AM1 calculations, the hydrogen atoms of the methylene groups of these substituents carry noticeable positive charges. The introduction of different substituents into the benzene ring has no substantial effect on the charge distribution in the morpholine rings due to the absence of conjugation between the lone electron pairs of the nitrogen atoms of the ring and the π-system of the benzene ring.

Key words: molecular structure, 1,3-di(morpholin-4-yl)benzene, AM1 method, charge distribution.

Derivatives of 1,3-di(morpholin-4-yl)benzene that contain amino, amido, or nitro groups serve as starting compounds for preparing polymeric systems of practical importance such as polyamides, polyimides, *etc.*[1] The presence of substituents of different chemical nature in the *ortho* positions of the benzene rings of these polymers allows one to vary their chemical and physical properties (for example, the ability to undergo further intramolecular cyclization or intermolecular structurization, the appearance of different new modes of movements of the polymer chain, the optical properties, *etc.*[2]) within wide limits. A knowledge of the conformational characteristics and the electronic structures of monomer units, which form macromolecules, is of primary importance for explaining particular properties of polymers. With the aim of studying these characteristics, we studied the molecular structures and charge distribution in the molecules of model compounds **1** and **2**.



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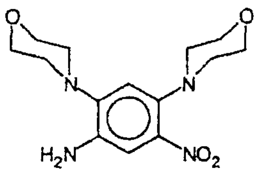

2

Experimental

Compounds **1** and **2** were prepared according to a procedure reported previously.[3]

X-ray diffraction analysis. Crystals of compound **1** ($C_{14}H_{22}N_4O_2$) are triclinic. At 20 °C, a = 7.794(4) Å, b = 9.093(3) Å, c = 11.046(5) Å, α = 77.27(2)°, β = 79.79(2)°, γ = 81.80(2)°, V = 747.1(8) Å^3, d_{calc} = 1.237 g cm^{-3}, μ = 0.080 mm^{-1}, space group $P\bar{1}$, Z = 2. The unit cell parameters and intensities of 4648 independent reflections were measured on an automated four-circle Siemens P3/PC diffractometer (graphite monochromator, Mo-$K\alpha$ radiation, $\theta/2\theta$ scanning technique, $2\theta_{max}$ = 60°).

The structure was solved by the direct method using the SHELXTL PLUS 4.2 program package.[4] The positions of the hydrogen atoms were calculated geometrically and refined using the riding model with fixed U_{iso} = 0.05 Å^2. The structure was refined based on F by the full-matrix least-squares method with anisotropic thermal parameters for nonhydrogen atoms using 2330 reflections with $F > 6\sigma(F)$. The final values of the R factors were as follows: R = 0.061, Rw = 0.059, S = 3.06. The atomic coordinates, bond lengths, and bond angles are given in Tables 1—3, respectively.

Crystals of compound **2** ($C_{14}H_{20}N_4O_4$) are orthorhombic. At 20 °C, a = 9.461(2) Å, b = 10.893(3) Å, c = 15.471(4) Å, V = 1594.5(7) Å^3, d_{calc} = 1.284 g cm^{-3}, μ = 0.096 mm^{-1}, space group $P2_12_12_1$, Z = 4. The unit cell parameters and intensities of 2656 independent reflections were measured on an automated four-circle Siemens P3/PC diffractometer (graphite monochromator, Mo-$K\alpha$ radiation, $\theta/2\theta$ scanning technique, $2\theta_{max}$ = 60°).

The X-ray intensity data set was processed according to a procedure reported in Ref. 5. The structure was solved by the direct method using the SHELXTL PLUS 5 program package.[6] The positions of the hydrogen atoms were located from the difference electron density synthesis and refined using the riding model with variable U_{iso}. The structure was refined based on F^2 by the full-matrix least-squares method with anisotropic thermal parameters for nonhydrogen atoms using 2074 reflections. The final values of the R factors were as

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Table 1. Coordinates $(\times 10^4)$ and equivalent isotropic thermal parameters $(\times 10^3/\text{Å})$ of nonhydrogen atoms in the structure of **1**

Atom	*x*	*y*	*z*	U_{eq}
N(1)	−2429(2)	2471(2)	8871(2)	51(1)
N(2)	470(2)	2241(2)	4515(1)	31(1)
N(3)	−2757(2)	3173(2)	3714(2)	40(1)
N(4)	−5596(3)	3402(3)	7948(2)	56(1)
O(1)	−1481(4)	1415(4)	11308(2)	113(1)
O(2)	3925(2)	2217(2)	3182(1)	49(1)
C(1)	−2462(2)	2616(2)	7549(2)	37(1)
C(2)	−970(2)	2322(2)	6699(2)	34(1)
C(3)	−1036(2)	2511(2)	5426(2)	29(1)
C(4)	−2655(2)	2966(2)	4990(2)	31(1)
C(5)	−4140(2)	3271(2)	5843(2)	35(1)
C(6)	−4064(2)	3111(2)	7111(2)	38(1)
C(7)	−836(4)	2831(5)	9193(3)	73(1)
C(8)	−1117(6)	2847(7)	10572(3)	113(2)
C(9)	−2967(6)	994(6)	10981(3)	115(2)
C(10)	−2801(4)	978(4)	9599(2)	73(1)
C(11)	1168(3)	3644(2)	3807(2)	40(1)
C(12)	2550(3)	3294(3)	2733(2)	47(1)
C(13)	3228(3)	849(3)	3867(2)	47(1)
C(14)	1891(2)	1146(3)	4977(2)	39(1)

Table 2. Bond lengths in molecule **1**

Bond	*d*/Å	Bond	*d*/Å
N(1)—C(1)	1.441(3)	N(1)—C(7)	1.449(4)
N(1)—C(10)	1.457(4)	N(2)—C(3)	1.434(2)
N(2)—C(11)	1.464(3)	N(2)—C(14)	1.463(2)
N(3)—C(4)	1.396(3)	N(4)—C(6)	1.406(3)
O(1)—C(8)	1.412(6)	O(1)—C(9)	1.397(6)
O(2)—C(12)	1.424(3)	O(2)—C(13)	1.430(3)
C(1)—C(2)	1.393(2)	C(1)—C(6)	1.397(3)
C(2)—C(3)	1.387(3)	C(3)—C(4)	1.405(2)
C(4)—C(5)	1.393(2)	C(5)—C(6)	1.387(3)
C(7)—C(8)	1.504(5)	C(9)—C(10)	1.512(4)
C(11)—C(12)	1.511(3)	C(13)—C(14)	1.509(3)

Table 3. Bond angles in molecule **1**

Angle	ω/deg	Angle	ω/deg
C(1)—N(1)—C(7)	115.7(2)	C(1)—N(1)—C(10)	112.9(2)
C(7)—N(1)—C(10)	108.2(2)	C(3)—N(2)—C(11)	112.6(1)
C(3)—N(2)—C(14)	116.2(1)	C(11)—N(2)—C(14)	110.0(1)
C(8)—O(1)—C(9)	109.3(3)	C(12)—O(2)—C(13)	109.9(2)
N(1)—C(1)—C(2)	122.9(2)	N(1)—C(1)—C(6)	117.8(2)
C(2)—C(1)—C(6)	119.3(2)	C(1)—C(2)—C(3)	121.6(2)
N(2)—C(3)—C(2)	123.5(1)	N(2)—C(3)—C(4)	117.3(1)
C(2)—C(3)—C(4)	119.2(1)	N(3)—C(4)—C(3)	120.4(1)
N(3)—C(4)—C(5)	120.6(2)	C(3)—C(4)—C(5)	118.9(2)
C(4)—C(5)—C(6)	121.7(2)	N(4)—C(6)—C(1)	120.6(2)
N(4)—C(6)—C(5)	120.1(2)	C(1)—C(6)—C(5)	119.2(2)
N(1)—C(7)—C(8)	108.7(3)	O(1)—C(8)—C(7)	111.5(4)
O(1)—C(9)—C(10)	113.3(3)	N(1)—C(10)—C(9)	109.1(3)
N(2)—C(11)—C(12)	109.5(2)	O(2)—C(12)—C(11)	110.9(2)
O(2)—C(13)—C(14)	111.0(2)	N(2)—C(14)—C(13)	108.4(2)

Table 4. Coordinates $(\times 10^4)$ and equivalent isotropic thermal parameters $(\times 10^3/\text{Å})$ of nonhydrogen atoms in the structure of **2**

Atom	*x*	*y*	*z*	U_{eq}
N(1)	2674(4)	5508(3)	903(2)	53(1)
O(1)	3512(4)	5825(4)	363(2)	95(1)
C(1)	2603(3)	6217(3)	1713(2)	40(1)
N(2)	2515(3)	4310(2)	2557(2)	44(1)
O(2)	1870(4)	4660(3)	800(2)	94(1)
C(2)	2487(3)	5621(2)	2499(2)	38(1)
N(3)	2273(3)	8441(2)	3903(1)	38(1)
O(3)	2221(3)	1900(2)	3202(2)	63(1)
C(3)	2411(3)	6383(2)	3227(2)	41(1)
N(4)	2676(3)	9477(2)	2291(2)	47(1)
O(4)	2421(3)	9467(2)	5570(2)	71(1)
C(4)	2437(3)	7656(2)	3171(2)	35(1)
C(5)	2609(3)	8230(2)	2357(2)	34(1)
C(6)	2682(3)	7483(3)	1632(2)	39(1)
C(7)	3489(4)	3827(3)	3206(3)	55(1)
C(8)	3576(4)	2455(3)	3097(3)	62(1)
C(9)	1270(4)	2374(3)	2583(4)	69(1)
C(10)	1106(4)	3755(3)	2681(3)	58(1)
C(11)	3575(4)	9007(3)	4212(2)	57(1)
C(12)	3210(5)	9981(4)	4873(3)	68(1)
C(13)	1138(5)	8956(4)	5258(3)	76(1)
C(14)	1462(6)	7938(4)	4621(2)	66(1)

Table 5. Bond lengths in molecule **2**

Bond	*d*/Å	Bond	*d*/Å
N(1)—O(1)	1.203(4)	O(3)—C(9)	1.412(5)
N(1)—O(2)	1.207(4)	O(3)—C(8)	1.427(4)
N(1)—C(1)	1.473(4)	C(3)—C(4)	1.389(4)
C(1)—C(2)	1.383(4)	N(4)—C(5)	1.363(4)
C(1)—C(6)	1.387(4)	O(4)—C(13)	1.419(5)
N(2)—C(2)	1.431(4)	O(4)—C(12)	1.426(5)
N(2)—C(7)	1.461(5)	C(4)—C(5)	1.416(4)
N(2)—C(10)	1.477(4)	C(5)—C(6)	1.387(4)
C(2)—C(3)	1.401(4)	C(7)—C(8)	1.505(5)
N(3)—C(4)	1.428(3)	C(9)—C(10)	1.519(5)
N(3)—C(14)	1.457(4)	C(11)—C(12)	1.513(5)
N(3)—C(11)	1.458(4)	C(13)—C(14)	1.515(5)

follows: $R_1 = 0.057$ (based on 1278 reflections with $F > 4\sigma(F)$), $wR_2 = 0.14$, $S = 1.04$. The atomic coordinates, bond lengths, and bond angles are given in Tables 4—6, respectively.

Quantum-chemical calculations. The spatial structures and the charge distributions in molecules **1**—**5** were calculated by the semiempirical quantum-chemical AM1 method[7] with full geometry optimization. The results of calculations are given in Scheme 1.

Results and Discussion

The saturated rings in molecule **1** (Fig. 1) adopt an almost ideal chair conformation (the endocyclic torsion angles are in the range of 57.0—61.6(4)°). The angles

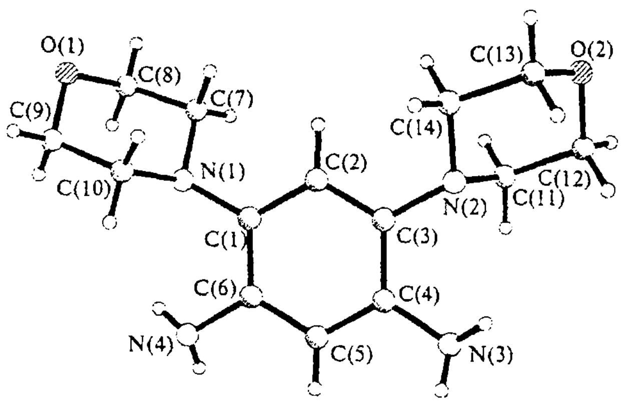


Fig. 1. Structure of compound **1**.

between the mean planes of the benzene ring and the central fragments of the morpholine groups, C(7)...C(10) and C(11)...C(14), are 62.2° and 71.3°, respectively. This arrangement of the saturated heterocycles is, apparently, dictated by steric interactions between the H(10) and H(11) protons of the methylene groups of the morpholine fragments and the amino substituents in the benzene ring, which result in the shortened intramolecular H(2)...H(7A) and H(2)...H(14B) contacts (2.27 Å and 2.23 Å, respectively; the sum of the van der Waals radii[8] is 2.32 Å). Owing to the twist of the morpholine rings, the lone electron pairs of the nitrogen atoms are not involved in conjugation with the π system of the benzene ring, which is confirmed by the elongation of the N(1)—C(1) and N(2)—C(3) bonds (1.441(3) Å and 1.434(2) Å, respectively) compared to the average value[9] of the C_{ar}—N bond (1.394 Å). The amino groups are conjugated with the benzene ring, which is confirmed by the values of the C_{ar}—N bonds and the H(4A)—N(4)—C(6)—C(1) and H(3A)—N(3)—C(4)—C(3) torsion angles (21.5° and 29°, respectively). The nitrogen atoms of the amino groups and the morpholine rings have a trigonal-pyramidal configuration (the sum of the bond angles at the N(1), N(2), N(3), and N(4) atoms are 336.8°, 338.8°, 327.4°, and 334.5°, respectively). This is favored by the shortened intramolecular N(2)...H(3A) and N(1)...H(4A) contacts (2.45 and 2.46 Å, respectively; the sum of the van der Waals radii is 2.66 Å).

The difference in the angles of rotation of the morpholine rings with respect to the benzene ring is worthy of note. The AM1 calculations of the geometry of isolated molecule **1** demonstrated that in the gaseous phase, the angles of rotation of both saturated heterocycles are equal (99°), and the molecule as a whole has a symmetry plane, which passes through the C(2) and C(5) atoms perpendicular to the benzene ring. The distortion of the molecular symmetry in the crystal is, apparently, associated with the effects of the crystal packing.

In the crystal, molecules **1** are packed in layers (Fig. 2). In the layer, molecules are linked through intermolecular hydrogen bonds H(2B)...O(2)′ (*x*−1, *y*, *z*) (the O...H distance is 2.18 Å, and the O...H—N angle is 176.0°). The second morpholine ring does not form shortened contacts with adjacent molecules. Therefore, the morpholine substituents occur in nonequivalent crystal environments, which, apparently, leads to a distortion of the symmetry of the molecule.

When one amino group in compound **1** is replaced by the nitro group (compound **2**, Fig. 3), the conformations of the morpholine rings and the angles of rotation of these rings with respect to the plane of the aromatic ring change only slightly. The angles between the mean planes of the benzene ring and the central fragments of the saturated C(7)...C(10) and C(11)...C(14) heterocycles are 75.9 and 54.3°, respectively. As in the case of compound **1**, the orientation of the substituents in compound **2** is dictated by the presence of the bulky substituents in the *ortho* positions, which is confirmed by the retention of the shortened intramolecular contacts: H(7A)...C(3), 2.64 Å (the sum of the van der Waals radii[8] is 2.87 Å); H(7A)...H(3), 2.16 Å (2.32 Å); H(11B)...H(4A), 2.24 Å; C(11)...H(4A), 2.59 Å; H(14A)...C(3), 2.77 Å; and H(14B)...C(3), 2.82 Å. Apparently, the difference in the number of shortened contacts with the participation of the atoms of the morpholine rings is responsible for the difference in the angles of rotation of these rings with respect to the benzene ring as well as for a more substantial deformation of the exocyclic bond angles at the C(4) atom compared to those at the C(5) atom (see Table 5). The calculations of the equilibrium geometry of molecule **2** demonstrated that, as in the case of compound **1**, the angles of rotation of the saturated heterocycles in the gaseous phase have equal values (100.5°).

The amino group is conjugated with the aromatic ring (the N(4)—C(5) bond is 1.363(4) Å, and the H(4A)—N(4)—C(5)—C(4) torsion angle is −5.2°). In

Table 6. Bond angles in molecule **2**

Angle	ω/deg	Angle	ω/deg
O(1)—N(1)—O(2)	122.9(3)	C(13)—O(4)—C(12)	110.2(3)
O(1)—N(1)—C(1)	118.1(3)	C(3)—C(4)—C(5)	119.9(3)
O(2)—N(1)—C(1)	119.0(3)	C(3)—C(4)—N(3)	123.2(3)
C(2)—C(1)—C(6)	123.4(3)	C(5)—C(4)—N(3)	116.9(2)
C(2)—C(1)—N(1)	120.3(2)	N(4)—C(5)—C(6)	121.4(2)
C(6)—C(1)—N(1)	116.3(3)	N(4)—C(5)—C(4)	120.8(3)
C(2)—N(2)—C(7)	114.5(2)	C(6)—C(5)—C(4)	117.7(2)
C(2)—N(2)—C(10)	113.6(2)	C(5)—C(6)—C(1)	120.6(3)
C(7)—N(2)—C(10)	109.4(3)	N(2)—C(7)—C(8)	108.4(3)
C(1)—C(2)—C(3)	115.7(2)	O(3)—C(8)—C(7)	111.1(3)
C(1)—C(2)—N(2)	121.5(3)	O(3)—C(9)—C(10)	111.1(4)
C(3)—C(2)—N(2)	122.8(3)	N(2)—C(10)—C(9)	107.5(3)
C(4)—N(3)—C(14)	115.9(2)	N(3)—C(11)—C(12)	109.0(3)
C(4)—N(3)—C(11)	114.9(3)	O(4)—C(12)—C(11)	110.8(3)
C(14)—N(3)—C(11)	110.7(3)	O(4)—C(13)—C(14)	109.6(4)
C(9)—O(3)—C(8)	109.8(3)	N(3)—C(14)—C(13)	109.1(3)
C(4)—C(3)—C(2)	122.7(3)		

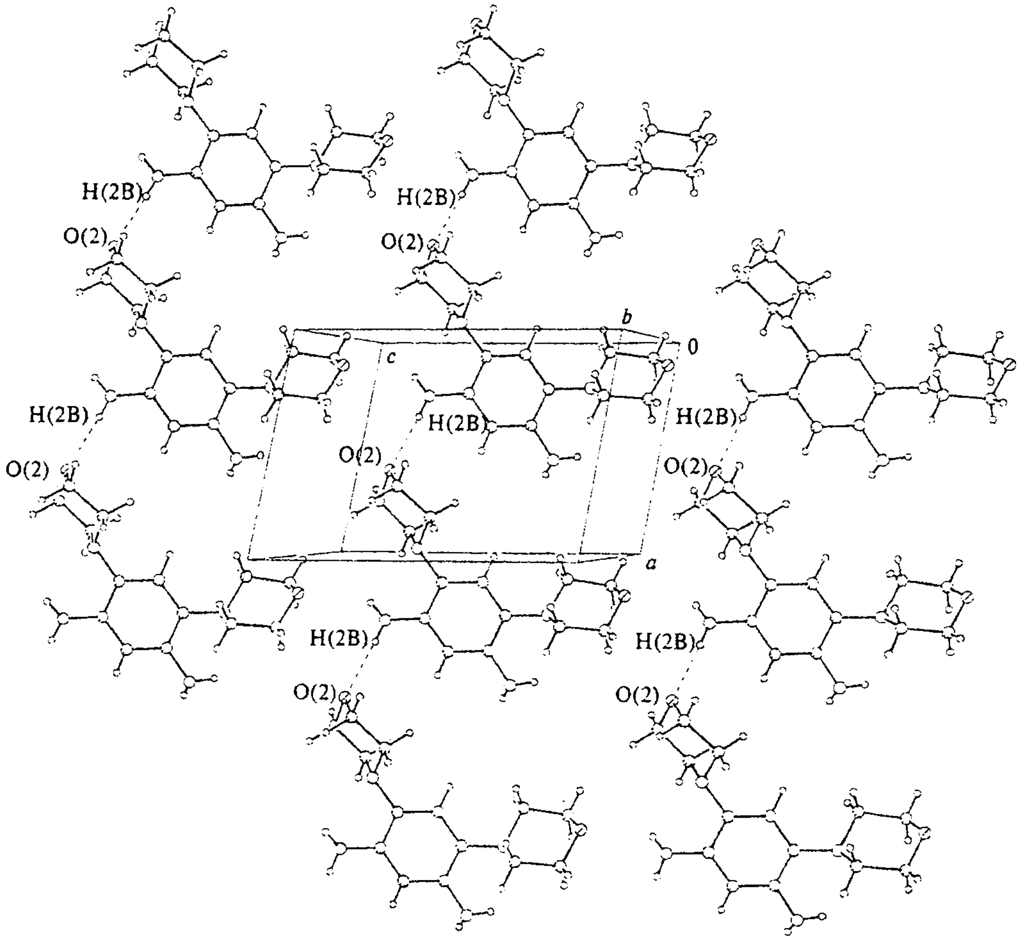


Fig. 2. Overall view of the layer in the crystal of **1**. Dashed lines indicate shortened O...N contacts, which correspond to hydrogen bonds.

molecule **2**, the nitrogen atom of the amino group has a more flattened pyramidal configuration (the sum of the van der Waals radii at the N(4) atom is 357°) than that in molecule **1** in spite of the shortened intramolecular contacts H(4A)...N(3) (2.32 Å; the sum of the van der Waals radii[8] is 2.66 Å) and H(4A)...H(11B) (2.24 Å). The degree of pyramidality of the nitrogen atoms of the morpholine rings is similar to that observed in molecule **1** (the sum of the bond angles at these atoms are 337.5° and 341.5°). The nitro group is twisted with respect to the aromatic ring (the C(2)—C(1)—N(1)—O(2) torsion angle is 44.6(5)°). The calculations of molecule **2** demonstrated that in the gaseous phase, the angle of rotation of the nitro group with respect to the benzene ring is larger than that in the crystal. According to calculations, the corresponding torsion angle is 54.6°. This difference in the angles of rotation of the nitro group is, apparently, attributable to the presence of the shortened intermolecular contacts H(12B)...O(1)′ (1−x, 0.5+y, 0.5−z) (2.41 Å, the sum of the van der Waals radii[8] is 2.45 Å).

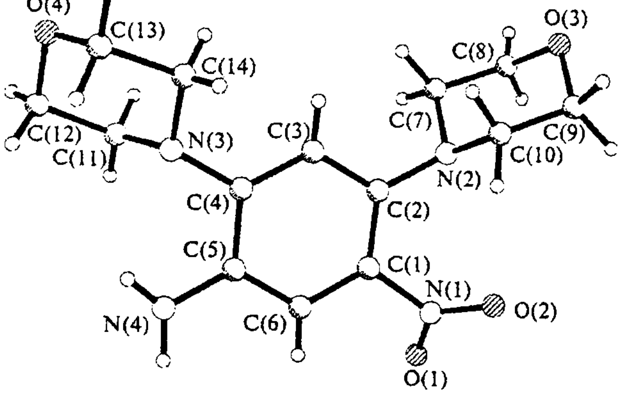


Fig. 3. Structure of compound **2**.

In the crystal, molecules **2** are linked in chains (Fig. 4) through the intermolecular hydrogen bonds H(4B)...O(4)′ (0.5−x, 2−y, z−0.5) (the O...H distance is 2.01 Å, and the O...H—N angle is 173.4°). As a result, the morpholine rings in the crystal of **2**, as in the

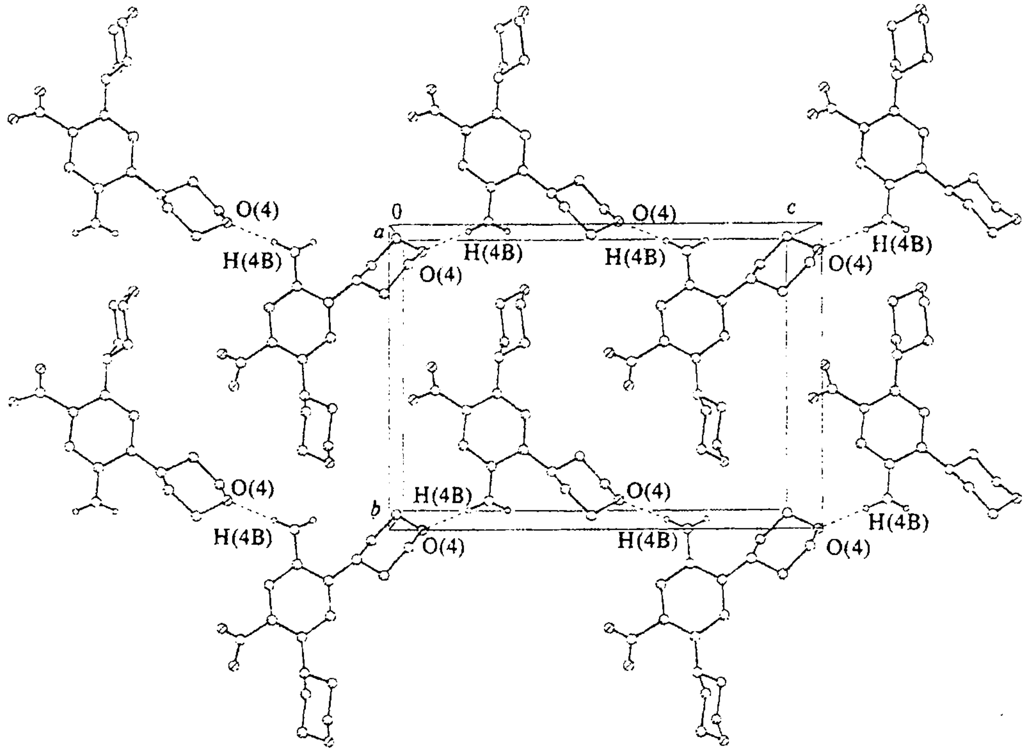
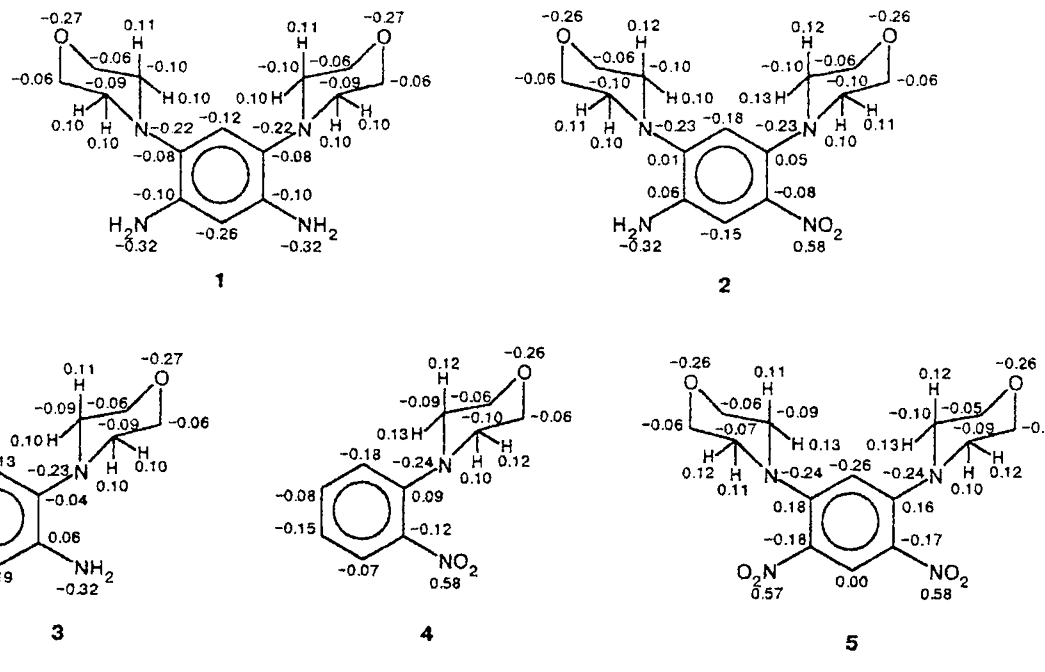


Fig. 4. Overall view of the layer in the crystal of 2. Dashed lines indicate shortened O...N contacts, which correspond to hydrogen bonds.

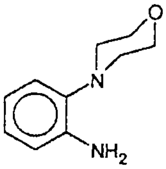
case of compound 1, are in different environments, which, apparently, has an additional effect on their arrangement with respect to the aromatic ring.

Traditionally, aromatic amines that contain various functional groups (NH_2, OH, COOH, $COCH_3$, *etc.*) in the *ortho* positions have attracted the interest of chem-

Scheme 1



ists involved in synthesis of polymers because these compounds allow one to perform polymer-analogous conversions (intramolecular condensation) to form condensed heterocyclic systems.[1] A knowledge of the charge distribution on the atoms of the substituents is of importance for searching for these intramolecular condensations. In our case, the morpholine rings are such substituents. They contain methylene groups in the *ortho* positions with respect to the nitrogen atom. The methylene groups can be involved in intramolecular cyclization. With the aim of evaluating this possibility, we analyzed the charge distributions in compounds **1**—**5**.



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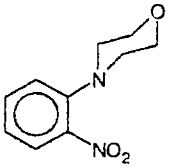

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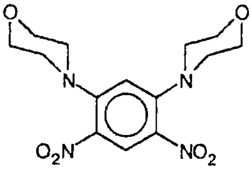

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The semiempirical quantum-chemical AM1 calculations demonstrated that the hydrogen atoms of the *ortho*-methylene groups of the morpholine rings carry noticeable positive charges and, therefore, they are acidic (see Scheme 1). In going from the disubstituted (**3** and **4**) to the tetrasubstituted derivatives (**1**, **2**, and **5**) as well as when the amino group is replaced by the nitro group, the charge distribution over the atoms of the benzene ring changes substantially. However, the charges on the atoms of the morpholine rings remain virtually unchanged, which is due to the absence of conjugation between the lone electron pairs of the nitrogen atoms of the ring and the π system of the benzene ring owing to the virtually perpendicular arrangement of the heterocyclic substituents with respect to the plane of the aromatic ring.

To summarize, in this work we demonstrated that in the model compounds under study, the methylene hydrogen atoms of the morpholine substituents are acidic. Therefore, these compounds can be used in reactions of intramolecular condensation with the aim of preparing new classes of heterocyclic polymers.

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