X-ray diffraction and quantum-chemical study of 3-(1,3-dioxolan-2-yl)-4,6-dinitrobenzo[*d*]isoxazole

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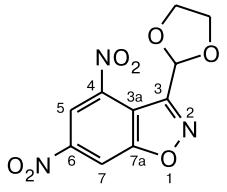
X-ray diffraction study of the molecular structure of 3-(1,3-dioxolan-2-yl)-4,6-dinitrobenzo[*d*]isoxazole in the crystal, and quantum-chemical calculations of the isolated molecule demonstrated that the differences in the reactivity of the nitro groups at positions 4 and 6 are not associated with the electronic structure of the molecule but are, apparently, attributed to the properties of the corresponding *ipso*-σ complexes.

Key words: X-ray diffraction analysis, quantum-chemical calculations, electron density distribution, nitro compounds, benzo[*d*]isoxazoles.

Earlier,[1] it has been demonstrated that the reactions of 4,6-dinitrobenzo[*d*]isoxazole-3-carbaldehyde acetal, O-substituted oxime, hydrazone, and *N*-phenylimine with anionic O-, S-, and N-nucleophiles led to the replacement of only the nitro group at position 4, *i.e.*, the group adjacent to the heterocyclic core, the reaction performed under more drastic conditions leaving the regiospecificity of substitution unchanged.

One of the possible reasons for this behavior of the above-mentioned benzo[*d*]isoxazole derivatives could be the distinguishing features of the electron density distribution in these aromatic systems characterized by a substantially lower π-electron density on the C(4) atom compared to the C(6) atom. However, this assumption is in contradiction with the ^{13}C NMR spectroscopic data for 3-(1,3-dioxolan-2-yl)-4,6-dinitrobenzo[*d*]isoxazole (**1**). Actually, it is known that the ^{13}C NMR chemical shifts depend predominantly on the π-electron density.[2,3] Hence, these shifts can be used as a test for the π charge[4] provided that the aromatic carbon atoms under comparison contain identical substituents.



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The ^{13}C NMR chemical shifts for positions 4 and 6 in benzo[*d*]isoxazole **1** are 141.9 and 148.3 ppm, respectively (in DMSO; with respect to Me_4Si)[1], *i.e.*, contrary to the expectations, the π-electron density on the C(4) atom is even somewhat higher than that on the C(6) atom because the signal for the C(4) atom is observed at higher field compared to that of the C(6) atom, although the differences in the electron density are, apparently, very small (*cf.* Ref. 4).

The fact that the 4-NO_2 group in compound **1** exhibits higher mobility in the nucleophilic substitution compared to that of 6-NO_2 can be alternatively accounted for by the structural differences between these nitro groups. It is known that the regioselectivity of the replacement of the *o*-NO_2 group in 2,4,6-trinitrotoluene (TNT) under the action of RS^- results from the nonequivalence of the nitro groups in TNT. Thus, the *para*-nitro group lies in the plane of the benzene ring, whereas the *ortho*-nitro groups are rotated (about the C—N axis) with respect to the benzene ring by a large angle.[5—7] It is believed that the rotation of the *o*-NO_2 group under the influence of the adjacent group substantially facilitates the formation of an *ipso*-σ complex upon the attack of the *ortho* position (generally, this is the rate-determining step of the S_NAr process) compared to an *ipso*-σ complex generated through the addition of a nucleophile at the *para* position. This is associated with the fact that the transition of the *ipso*-carbon atom from sp^2 to sp^3 hybridization is facilitated due to a decrease in the conjugation between the *o*-NO_2 group and the aromatic ring already in the starting compound as a result of rotation of this group.[7] Semiempirical quantum-chemical calculations of the corresponding activation energies (PM3 method with consideration for the effect of a polar solvent) demonstrated that the rate of formation of the *ipso*-σ complex of TNT with

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Table 1. Selected bond lengths (*d*) and bond angles (ω) in **1** in the crystal (I) and isolated molecule (II)

Parameter	I	II
Bond	*d*/Å	
O(1)—C(7A)	1.349(2)	1.338
O(1)—N(2)	1.411(2)	1.379
N(2)—C(3)	1.296(2)	1.300
C(3)—C(3A)	1.449(2)	1.440
C(3)—C(10)	1.522(2)	1.521
C(3A)—C(4)	1.406(2)	1.401
C(3A)—C(7A)	1.391(2)	1.396
C(4)—C(5)	1.374(2)	1.376
C(5)—C(6)	1.391(2)	1.395
C(6)—C(7)	1.370(2)	1.379
C(7)—C(7A)	1.383(2)	1.387
C(4)—N(3)	1.466(2)	1.475
C(6)—N(4)	1.467(2)	1.467
N(3)—O(2)	1.217(2)	1.212
N(3)—O(3)	1.224(2)	1.210
N(4)—O(4)	1.220(2)	1.211
N(4)—O(5)	1.227(2)	1.212
Angle	ω/deg	
N(3)—C(4)—C(3A)	122.1(1)	120.5
N(3)—C(4)—C(5)	117.1(1)	117.3
C(5)—C(6)—N(4)	117.7(1)	118.3
N(4)—C(6)—C(7)	118.4(1)	123.4
C(10)—C(3)—C(3A)	131.5(1)	129.8
C(10)—C(3)—N(2)	117.7(1)	119.6

PhS^- at position 2 is approximately two orders of magnitude higher than the rate of formation of the analogous complex at position 4 (in the temperature range of 20—50 °C).[7] Consequently, the replacement of *o*-NO_2 is accelerated to the same extent, because the formation of the *ipso*-σ complexes is the rate-determining step.[7,8] The rotation of the *ortho*-nitro group in TNT is associated with the steric effect of the methyl group. It cannot be excluded that the substituent in the *peri* position (the dioxolanyl fragment at position 3) in benzo[*d*]isoxazole **1** has an analogous effect on the 4-NO_2 group, which is responsible for high mobility of the 4-NO_2 group in the nucleophilic substitution. To examine these assumptions, we carried out X-ray diffraction study of crystal **1**.

X-ray diffraction study (Table 1) demonstrated that the nitro group at position 4 lies in the plane of the benzo[*d*]isoxazole system, whereas the nitro group at position 6 is rotated with respect to this plane by 18.3°. The C(4)—N(3) and C(6)—N(4) bond lengths are equal (1.466(2) and 1.467(2) Å, respectively). In the crystal, the nitro group at position 4, which is subjected to the nucleophilic substitution, lies in the plane of the ring, and, hence, this group should to a greater extent be conjugated with the aromatic system than the nitro group at position 6 that remains nonsubstituted. Therefore, the orientations of the nitro groups with respect to the plane of the ring are inconsistent with the data on their reactivities.

However, it cannot be stated that the geometry of **1** in the crystal (Fig. 1 and Table 1) is identical with that in the solvated state (in solution). Analysis of the crystal packing of molecules **1** demonstrates that the N(3) atom forms directed intermolecular contacts with the O(11) and O(5) atoms (Fig. 2); the N...O interatomic distances are ~2.94 Å; the angles between the N...O lines and the plane of the aromatic system are, on the average, 83°. Therefore, the observed arrangement of the nitro groups with respect to the plane of the conjugated benzo[*d*]isoxazole system in the crystals of **1** is apparently determined by the

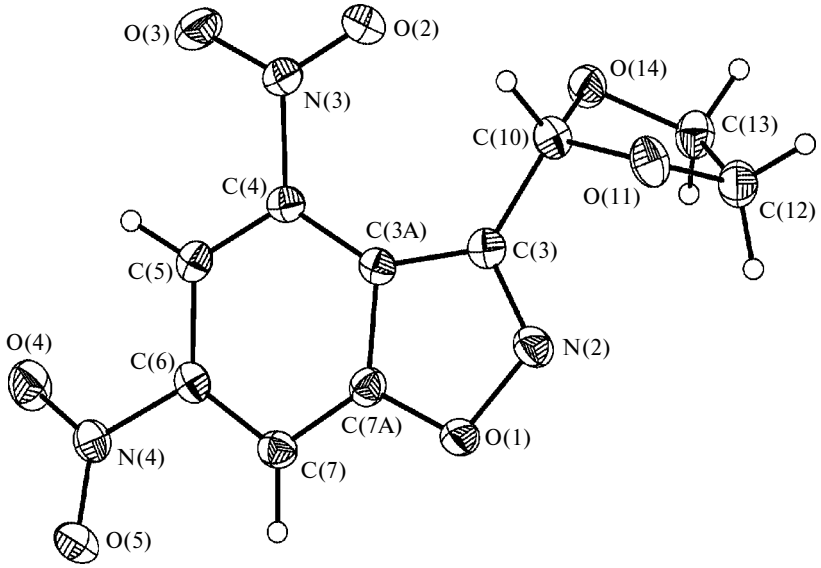

Fig. 1. Molecule **1** represented by thermal ellipsoids at the 50% probability level.

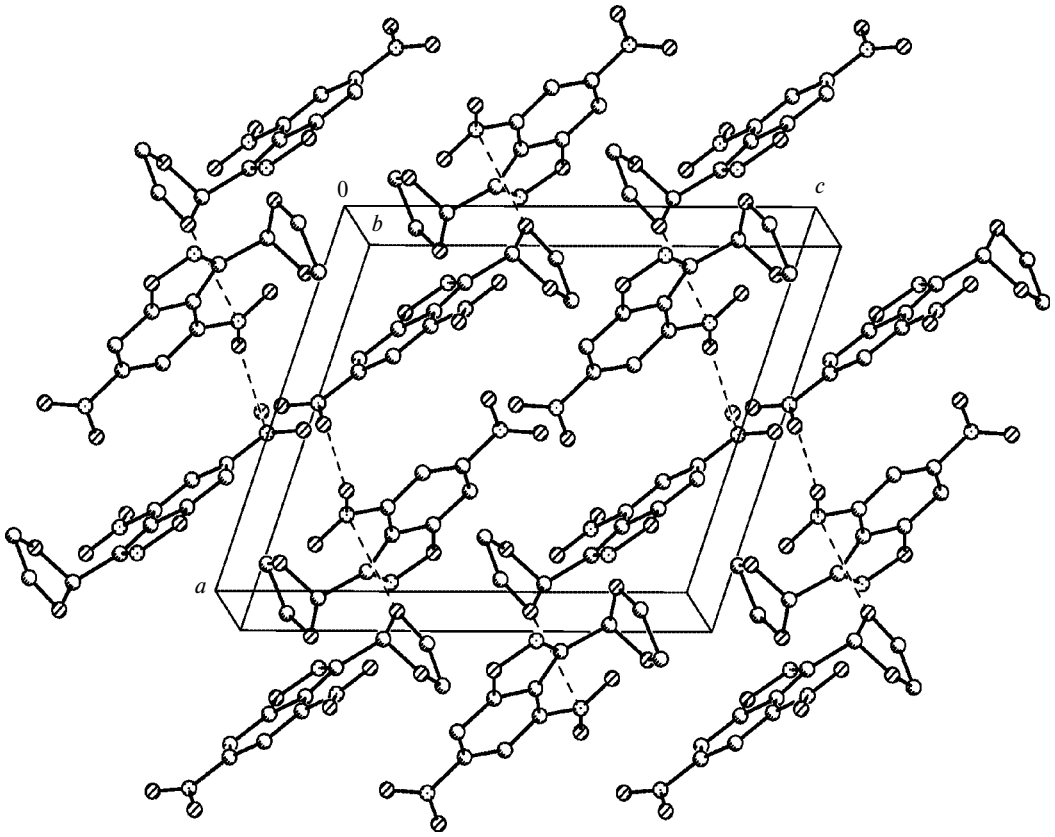

Fig. 2. Crystal packing of molecules **1**.

effect of the crystal packing, all the more that the aromatic nitro group is readily rotated about the C—N bond (barrier to rotation is ~3 kcal mol^{-1}).[9]

To test this assumption, we carried out quantum-chemical calculations (the MPW1PW91 functional and the 6-311G* basis set) using the GAUSSIAN 98W program.[10] In isolated molecule **1**, the arrangement of the nitro groups with respect to the plane of the conjugated benzo[*d*]isoxazole system is opposite to that observed in the crystal. The nitro group at position 6 is in the plane of the benzo[*d*]isoxazole ring, whereas the nitro group at position 4 is rotated with respect to this plane by 29.1°. It should be noted that the C(4)—N(3) bond is essentially longer than the C(6)—N(4) bond (1.475 and 1.467 Å, respectively), which is indicative of the difference in the conjugation between the nitro groups and the aromatic system. The rotation of the nitro group at position 4 is, apparently, associated with the presence of the C(10)—H(10)...O(2) contact. According to the results of calculations, the interatomic O...H distance is 2.31 Å and the C(10)—H(10)—O(2) angle is 111.5°. In the crystal, these parameters are 2.36 Å and 105°, respectively. It should be noted that the mutual arrangement of the dioxolane ring and the aromatic system in the crystal is identical with that in the isolated molecule.

To reveal the extent to which positions 4 and 6 are sensitive to the nucleophilic attack, we studied the electronic structure of molecule **1** in the context of the Bader topological theory known as "Atoms in Molecules"[11] with the use of the AIMPAC program.[12]

The critical points (CT) (3, −1) were located not only in the regions of all expected bonds in **1** but also in the region of the C(10)—H(10)...O(2) contact. The semi-quantitative estimate[13] of the energy of this cotact is 3.3 kcal mol^{-1}, which is comparable to the barrier to rotation of the nitro group about the C—N bond.

The topological parameters of the bonds in the benzo[*d*]isoxazole ring correspond to shared interactions[11] (covalent bonds, Fig. 3) and are close to the values observed in aromatic organic compounds. The ellipticities of the C(4)—N(3) and C (6)—N(4) bonds have virtually equal values (0.11 and 0.12, respectively). The charges on the C(4) and C(6) atoms, which were calculated by integrating the electron density function in the corresponding atomic pools, are 0.23 and 0.26 e, respectively. This provides evidence that positions 4 and 6 are virtually equally accessible for the nucleophilic attack if only factors determined by the electronic structure are taken into account. Consequently, the difference in the reactivity of positions 4 and 6 is, apparently, associated with the factors

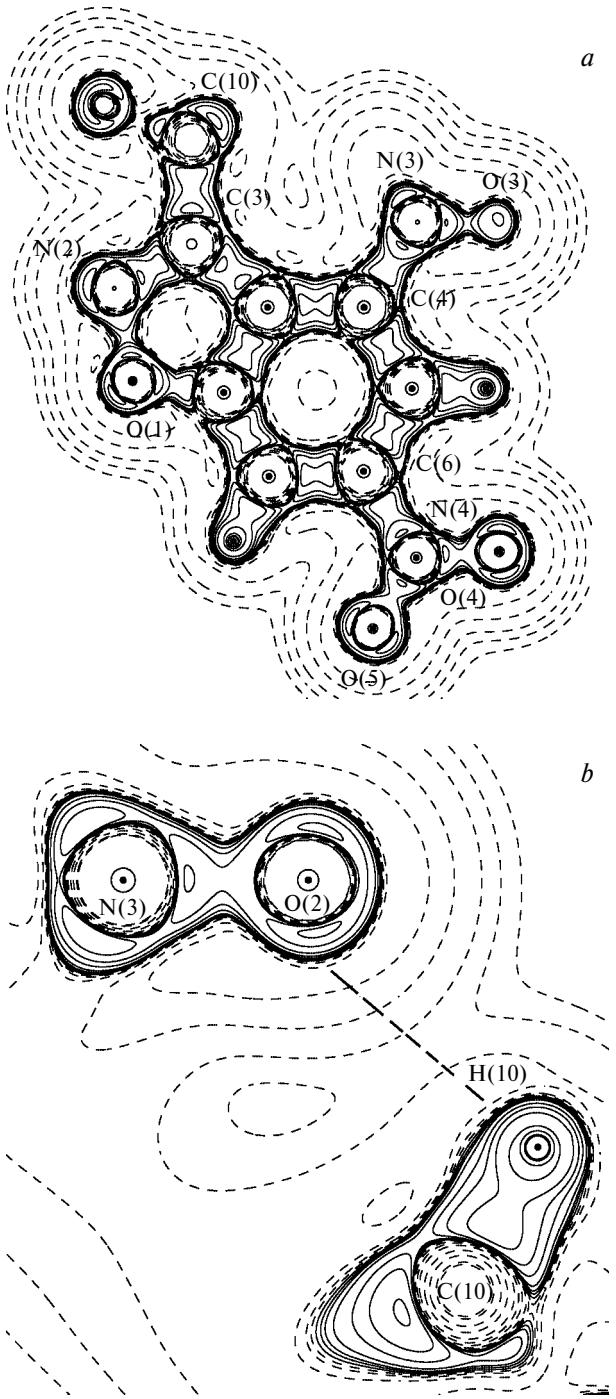

Fig. 3. Map of the Laplacian of the electron density ($-\nabla^2\rho(r)$) in the plane of the benzo[*d*]isoxazole ring (*a*) and in the region of the C(10)—H(10)...O(2) contact (*b*) on the base 2 logarithmic scale; the regions of charge accumulation ($-\nabla^2\rho(r) > 0$) and charge depletion are contoured by solid and dashed lines, respectively.

responsible for thermodynamic stability of *ipso*-σ complexes.

In addition to the C(10)—H(10)...O(2) contact, the conjugation between the C(4)—N(3) bond and the aromatic system can be weakened due to coordination of the K^+ cations present in solution (Nu^-K^+ were used as anionic nucleophiles) by the oxygen atoms of the nitro groups and the dioxolane ring.[14] The problem of stability of *ipso*-σ complexes at positions 4 and 6 can be solved by performing quantum-chemical calculations at a high level of theory with consideration for the electron correlation, which is a very time-consuming and laborious process due to a large number of atoms and low symmetry of possible *ipso*-σ complexes. The results of these calculations will be published elsewhere.

Therefore, the difference in the reactivity of the nitro groups at positions 4 and 6 is attributed not to their electronic characteristics but, apparently, to the properties of the corresponding *ipso*-σ complexes, whose formation is facilitated by rotation of the NO_2 group with respect to the plane of the aromatic ring.[7]

Experimental

X-ray diffraction study. Yellow crystals of compound **1** with composition $C_{10}H_7N_3O_7$ were prepared by crystallization from chloroform. The unit cell parameters: a = 10.838(2) Å, b = 8.081(2) Å, c = 13.025(3) Å, β = 105.915(4)°, V = 1082.5(4) Å^3. The space group $P2_1/c$, Z = 4, d_{calc} = 1.725 g cm^{-3}, M = 281.19. The unit cell parameters and the intensities of 2017 independent reflections were measured on an automated Syntex $P2_1$ diffractometer at 150 K (graphite monochromator, λ(Mo-Kα) 0.71072 Å, θ/2θ scan technique, $3 \le 2\theta \le 50°$); 1910 independent reflections were used in subsequent calculations. The structure was solved by direct methods. The nonhydrogen atoms were refined anisotropically by the full-matrix least-squares method based on F^2. The hydrogen atoms were revealed from difference Fourier electron density syntheses and refined isotropically. The final reliability factors are as follows: R_1 = 0.0291 (based on 1662 reflections with $I > 2\sigma$), wR_2 = 0.0815 (based on all reflections), GOOF = 1.022. All calculations were carried out using the SHELXTL PLUS program package[15] (version 5.10).

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