Reaction of 3(*Z*)-benzoylmethylidene-6-nitro-3,4-dihydro-2*H*-1,4-benzooxazin-2-one with oxalyl chloride

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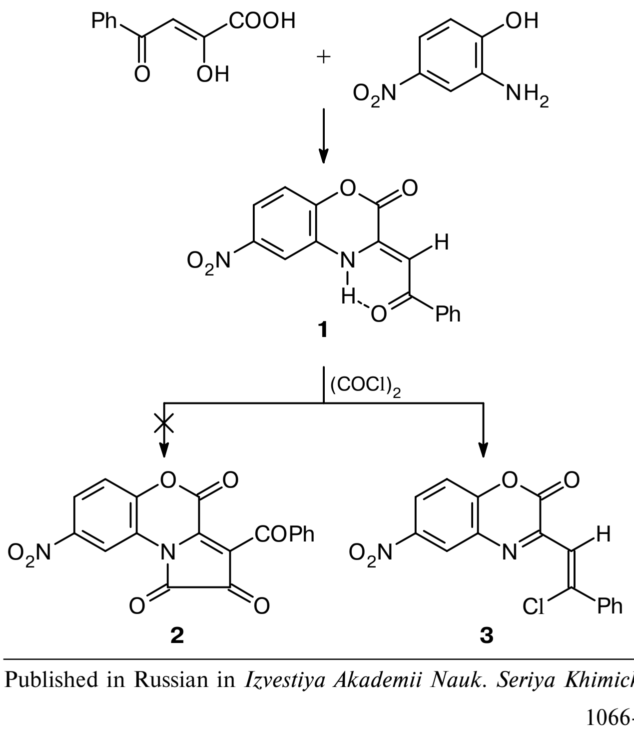
3(*Z*)-Benzoylmethylidene-6-nitro-3,4-dihydro-2*H*-1,4-benzooxazin-2-one reacts with $(COCl)_2$ as imino enol rather than enamino ketone. The reaction is accompanied by replacement of the hydroxy group by chlorine. The molecular and crystal structures of the starting 1,4-benzooxazin-2-one and its chlorinated derivative were studied by X-ray diffraction analysis.

Key words: benzoylmethylidene-1,4-benzooxazin-2-one, tautomers, β-chlorovinyl-1,4-benzooxazin-2-one, crystal and molecular structures.

4-Acyl-2,3-dihydropyrrole-2,3-diones are most often obtained by the reactions of oxalyl chloride with enaminoketones.[1] Substituted 3(*Z*)-benzoylmethylidene-3,4-dihydro-2*H*-1,4-benzooxazin-2-ones react with oxalyl chloride as typical enamines to give 3-aroyl-2,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzooxazine-1,2,4-triones in virtually quantitative yields.[2] The reaction of benzoylpyruvic acid with 2-amino-4-nitrophenol resulted in 3(*Z*)-benzoylmethylidene-6-nitro-3,4-dihydro-2*H*-1,4-benzooxazin-2-one (**1**) as a possible precursor for the preparation of the corresponding pyrrolobenzooxazinetrione. However, the reaction of benzooxazinone **1** with oxalyl chloride (Scheme 1) yields, instead of the expected compound **2**, 6-nitro-3(*Z*)-(2-chloro-2-phenylvinyl)-2*H*-1,4-benzooxazin-2-one (**3**), whose structure was established by X-ray diffraction analysis.

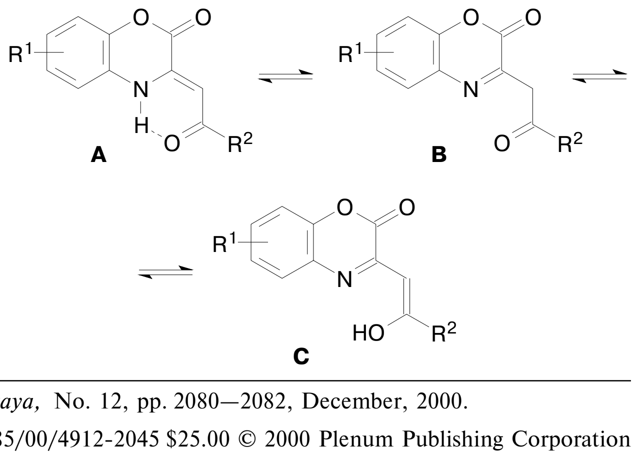
Scheme 1



In some reactions, oxalyl chloride is employed as a chlorinating agent;[3] however, in this case, the formation of compound **3** was rather unexpected. Theoretically, one can assume that substituted 3-benzoylmethylidene-3,4-dihydro-2*H*-1,4-benzooxazin-2-ones exist not only as enamino ketone (**A**), but also as imino ketone (**B**) and imino enol tautomers (**C**) (Scheme 2).

The presence of the tautomer **C** might explain the course of the reaction of compound **1** with oxalyl chlo-

Scheme 2



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ride as an ordinary replacement of the enolic OH group by a chlorine atom. However, neither form **B** nor **C** were detected by spectroscopic methods in the crystals and solutions of compound **1** and of its analogs devoid of the nitro group at the C(6) atom, which react with oxalyl chloride to give pyrrolobenzooxazinetriones of the type **2**.[2] The structure of benzooxazinone **1** was studied by X-ray diffraction analysis in order to reveal peculiarities that can be responsible for the change in the regioselectivity of its reaction with oxalyl chloride.

The general views of structurally similar molecules of **1** and **3** are shown in Fig. 1. Both are strongly flattened. The benzooxazine fragment of the starting enaminoketone **1** is planar with an accuracy of 0.01 Å, while the dihedral angle with the O(3)...C(8) line as an edge in the analogous fragment of chloride **3** is equal to 6.8°. The angles between mean planes of the benzooxazine system and the phenyl group are 8.2° and 12.1° in compounds **1** and **3**, respectively. The orientation of the benzoylmethylidene substituent with respect to the oxazine is determined by the torsion angles O(1)—C(17)—C(18)—C(23) (−5.4°), N(6)—C(8)—C(16)—C(17) (−1.2°), and C(8)—C(16)—C(17)—O(1) (2.8°). Analogous angles for the chlorovinyl substituent in compound **3** are equal to −20.5°, 10.4°, and −4.4°. The nitro group in compound **3** is coplanar to benzooxazine, while that in compound **1** makes an angle of 10°.

Compound **1** exists in the form of enamino ketone with an H-chelate intramolecular hydrogen bond, which is characteristic of compounds of this series.[2,4] The O(1)...H(6) distance is equal to 1.92 Å, while the angle at the H atom is 133.6°. The presence of intramolecular hydrogen bonding is also evidenced by a somewhat longer C(17)=O(1) bond of the carbonyl group (1.249 Å).

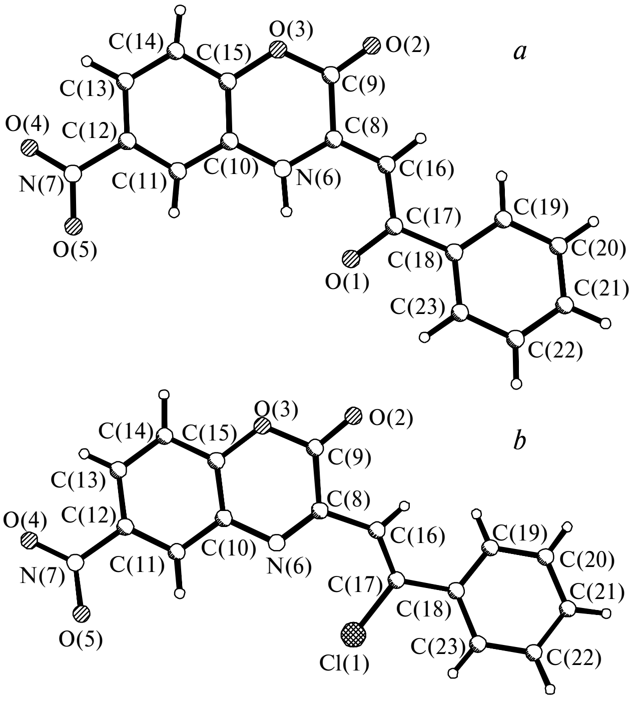

Fig. 1. Structures of compounds (*a*) **1** and (*b*) **3**.

The main bond lengths in molecules **1** and **3** are presented in Table 1. Comparison shows that the characteristic structural feature of compounds **1** and **3** is a pronounced localization of the C(8)=C(16) double bond in **1** and that of the N(6)=C(8) and C(16)=C(17) double bonds in **3**. Thus, taking into account that the other interatomic distances have standard values, one can conclude that the overall π-conjugation in these molecules is absent or rather weak. Another structural feature of the benzooxazine derivatives is that the single bonds between the heteroatoms and the benzene C atoms are longer than the bonds linking the heteroatoms with two other C atoms of the oxazine ring. Thus the two endocyclic C—O bonds in compound **1** measure 1.359(4) and 1.376(4) Å, while the two C—N bond lengths are 1.358(4) and 1.383(4) Å. The difference in the bond lengths is substantially larger than the corresponding measurement error. A similar pattern is observed in some of the 3,4-dihydro-2*H*-1,4-benzooxazine-2-one derivatives previously studied by us.[5,6]

In crystals of **1** and **3**, there are no intermolecular hydrogen bonds or other shortened contacts.

Thus, X-ray analysis of compound **1** provided no data that would allow one to convincingly explain the unexpected regioselectivity of the reaction of substituted 3(*Z*)-benzoylmethylidene-3,4-dihydro-2*H*-1,4-benzooxazin-2-ones with oxalyl chloride. Apparently, the decisive factor is a considerable decrease in the basicity of the N atom as a result of the strong electron-withdrawing effect of the *meta*-NO_2 group. Moreover, although the imino enol form **C** was not detected in the starting benzooxazinone **1**, the formation of this tautomer or its synthetic equivalent in the reaction is quite possible. As a result, oxalyl chloride does not attack the deactivated enamine fragment to give a diacylated product; instead, the OH group in the imino enol form **C** of the starting benzooxazinone **1** is replaced by the chlorine atom.

The reaction mechanism and the factors influencing its stereoselectivity are currently under investigation.

Table 1. Selected bond lengths (*d*) in structures **1** and **3**

Bond	*d*/Å	
	1	**3**
O(1)—C(17)	1.249(4)	—
Cl(1)—C(17)	—	1.727(2)
O(2)—C(9)	1.188(4)	1.192(3)
O(3)—C(9)	1.359(4)	1.370(2)
O(3)—C(15)	1.376(4)	1.373(2)
N(6)—C(8)	1.358(4)	1.292(2)
N(6)—C(10)	1.383(4)	1.390(2)
C(8)—C(9)	1.487(4)	1.500(3)
C(8)—C(16)	1.355(4)	1.455(2)
C(10)—C(15)	1.381(5)	1.391(2)
C(16)—C(17)	1.438(5)	1.338(3)
C(17)—C(18)	1.492(4)	1.488(2)

Table 2. Crystallographic data and a summary of data collection for crystals **1** and **3**

Parameter	**1**	**3**
Molecular mass	310.26	328.70
Space group	$P2_1/n$	$P\bar{1}$
a/Å	10.193(2)	10.548(2)
b/Å	12.834(3)	8.911(1)
c/Å	10.589(2)	7.560(3)
α/deg	90	87.75(2)
β/deg	96.71(3)	100.43(3)
γ/deg	90	94.65(3)
V/Å^3	1375.7(5)	696.3(3)
d_{calc}/g cm^{-3}	1.498	1.568
Z	4	2
μ/mm^{-1}	0.963	2.656
Radiation	Cu	Cu
Number of measured reflections	2388	2872
Number of reflections used in the least-squares method with $I > 2\sigma(I)$	1148	2401
R	0.045	0.046

Experimental

IR spectra were recorded on a UR-20 spectrometer (Nujol mulls). ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer. UV spectra were obtained with a Specord M-40 spectrophotometer. Mass spectrum was recorded on an MKh-1320 instrument (ionzing voltage 70 eV). The purity of the compounds synthesized was checked by TLC on Silufol UV-254 plates.

3(*Z*)-Benzoylmethylidene-6-nitro-3,4-dihydro-2*H*-1,4-benzooxazin-2-one (1). A mixture of benzoylpyruvic acid (10.0 g, 0.05 mol) and 2-amino-4-nitrophenol (8.02 g, 0.05 mol) was dissolved in 200 mL of propan-2-ol, refluxed for 2.5 h, and cooled. The precipitate that formed was filtered off. Yield 15.1 g (94%), m.p. 253—255 °C (decomp., from toluene). Found (%): C, 62.20; H, 3.02; N, 9.26. $C_{16}H_{10}N_2O_5$. Calculated (%): C, 61.94; H, 3.25; N, 9.03. IR, ν/cm^{-1}: 3090, 3050 (C—H); 1750 (C(2)=O); 1615 (PhCO); 1530, 1355 (NO_2). ^{1}H NMR (DMSO-d_6), δ: 6.97 (s, 1 H, =CH); 7.40 (d, 1 H, H(7), J = 9 Hz); 7.68 (m, 3 H, H(3′), H(4′), H(5′)); 7.91 (d, 1 H, H(8), J = 9 Hz); 8.02 (m, 2 H, H(2′), H(6′)); 8.69 (s, 1 H, H(5)); 12.60 (s, 1 H, NH). UV (MeCN), λ_{max}/nm (logε): 266 (4.62), 405 (4.46).

6-Nitro-3(*Z*)-(2-chloro-2-phenylvinyl)-2*H*-1,4-benzooxazin-2-one (3). Oxalyl chloride (3.81 g, 0.03 mol) was added dropwise to a solution of compound **1** (6.0 g, 0.02 mol) in 170 mL of anhydrous chloroform. The reaction mixture was refluxed for 3.5 h and cooled. The precipitate that formed was filtered off. Yield 3.55 g (56%), m.p. 215—216 °C (from dioxane). Found (%): C, 58.81; H, 2.95; Cl, 11.20; N, 8.95. $C_{16}H_9ClN_2O_4$. Calculated (%): C, 58.46; H, 2.76; Cl, 10.79; N, 8.52. IR, ν/cm^{-1}: 3110 (C—H); 1735 (C(2)=O); 1590 (C=C, C=N); 1525, 1348 (NO_2). ^{1}H NMR (DMSO-d_6), δ: 7.53 (m, 3 H, H(3′), H(4′), H(5′)); 7.60 (s, 1 H, =CH); 7.64 (d, 1 H, H(7), J = 9 Hz); 7.95 (m, 2 H, H(2′), H(6′)); 8.40 (d, 1 H, H(8), J = 9 Hz); 8.54 (s, 1 H, H(5)). UV (MeCN), λ_{max}/nm (logε): 271 (4.50), 354 (4.57). MS, m/z (I_{rel} (%)): 330/328 $[M]^+$ (38/100), 329/327 $[M - H]^+$ (52/99), 302/300 $[M - CO]^+$ (6/17), 301/299 $[M - H - CO]^+$ (32/85), 293 $[M - Cl]^+$ (26), 265 $[M - CO - Cl]^+$ (9), 256/254 $[M - CO - NO_2]^+$ (5/17), 255/253 $[M - CO - H - NO_2]$ (29/86), 190 (14), 128 $[PhCCHCN]^+$ (10), 102 $[PhCCH]^+$ (17).

X-Ray diffraction analysis of compounds 1 and 3. Sets of experimental reflections from crystals **1** and **3** were collected on a KM-4 automated four-circle diffractometer (KUMA DIFFRACTION) with χ geometry (θ—2θ scan mode, monochromated Cu-Kα radiation, 4° < θ < 80°). Corrections for absorption were not applied. Crystallographic data and a summary of data collection are presented in Table 2. The coordinates of atoms are deposited in the Cambridge Structural Database.

The structures were solved by the direct statistical method with subsequent electron-density mapping. Hydrogen atoms in both structures were objectively located from difference syntheses calculated after the refinement of nonhydrogen atoms in the isotropic approximation. The structures were refined in the full-matrix anisotropic (isotropic for H atoms) approximation. All computer-assisted calculations were performed with the SHELX-86 and SHELXL-93 programs.[8]

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References

1. Yu. S. Andreichikov, V. L. Gein, V. V. Zalesov, A. P. Kozlov, G. Kollenz, A. N. Maslivets, E. V. Pimenova, and S. N. Shurov, *Khimiya pyatichlennykh 2,3-dioksogeterotsiklov* [*The Chemistry of Five-Membered 2,3-Dioxoheterocycles*], Izd. Perm Univ., Perm, 1994, 211 pp. (in Russian).
2. A. N. Maslivets, I. V. Mashevskaya, O. P. Krasnykh, S. N. Shurov, and Yu. S. Andreichikov, *Zh. Org. Khim.*, 1992, **28**, 2445 [*Russ. J. Org. Chem.*, 1992, **28** (Engl. Transl.)].
3. L. Fieser and M. Fieser, *Reagents for Organic Synthesis*, J. Wiley, New York, 1968.
4. Y. Iwanami, T. Seki, and T. Iganaki, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 1316.
5. Z. G. Aliev, A. N. Maslivets, I. V. Mashevskaya, Yu. S. Andreichikov, and L. O. Atovmyan, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 566 [*Russ. Chem. Bull.*, 1997, **46**, 546 (Engl. Transl.)].
6. Z. G. Aliev, O. P. Krasnykh, A. N. Maslivets, Yu. S. Andreichikov, and L. O. Atovmyan, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 2154 [*Russ. Chem. Bull.*, 1999, **48**, 2131 (Engl. Transl.)].
7. G. M. Sheldrick, *SHELX-86*, *Programme for Crystal Structure Determination*, University of Cambridge, UK, 1986.
8. G. M. Sheldrick, *J. Appl. Cryst.*, 1993, **26**, 593.

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