

On a New Unexpected Benzoxazino-Benzoxazine Derivative*

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The reaction between 2-amino-5-nitrophenol and 1,2-cyclohexanedione in ethanol leads to formation, in addition to corresponding propellane, of **3**. The X-ray diffraction, NMR and IR studies allowed to solve the structure of molecules. It has been shown that planar nitrobenzoxazine groups are oriented to each other perpendicularly with a chair conformation of the cyclohexyl unit. The possible mechanism of reaction leading to **3** is discussed.

Key words: benzoxazine-benzoxazines, X-ray structure, NMR and IR spectra

In searching for new materials showing non-linear optical properties heteropropellanes were synthesized in reaction between 1,2-cyclohexanedione and o-aminophenol derivatives [1]. In the case of 2-amino-5-nitrophenol 16,20-dinitroderivative of (3,4,8,9)-dibenzo-2,7-dioxa-5,10-diaza [4.4.4] propellane (**1**, Scheme 1) was obtained, which crystallizes in a non-centrosymmetric orthorhombic *Pcn*2 space group [2]. **1** is an analogue of 3,9-dinitro-5a,6,11a-tetrahydro[1,4]benzoxazino[3,2-b][1,4]benzoxazine (DNBB), which appeared to be highly efficient nonlinear crystal with largely expressed phase-matching characteristics and favourable for applications physical properties [3,4]. One should also notice that oxazino-oxazines and benzoxazino-benzoxazines evoke considerable interest as showing interesting chemical, structural and photophysical properties [5–11]. In this communication we report some details related to new and unexpected product of the reaction of 2-amino-5-nitrophenol with 1,2-cyclohexanedione. We present its main physico-chemical characteristics and possible formation mechanism.

RESULTS AND DISCUSSION

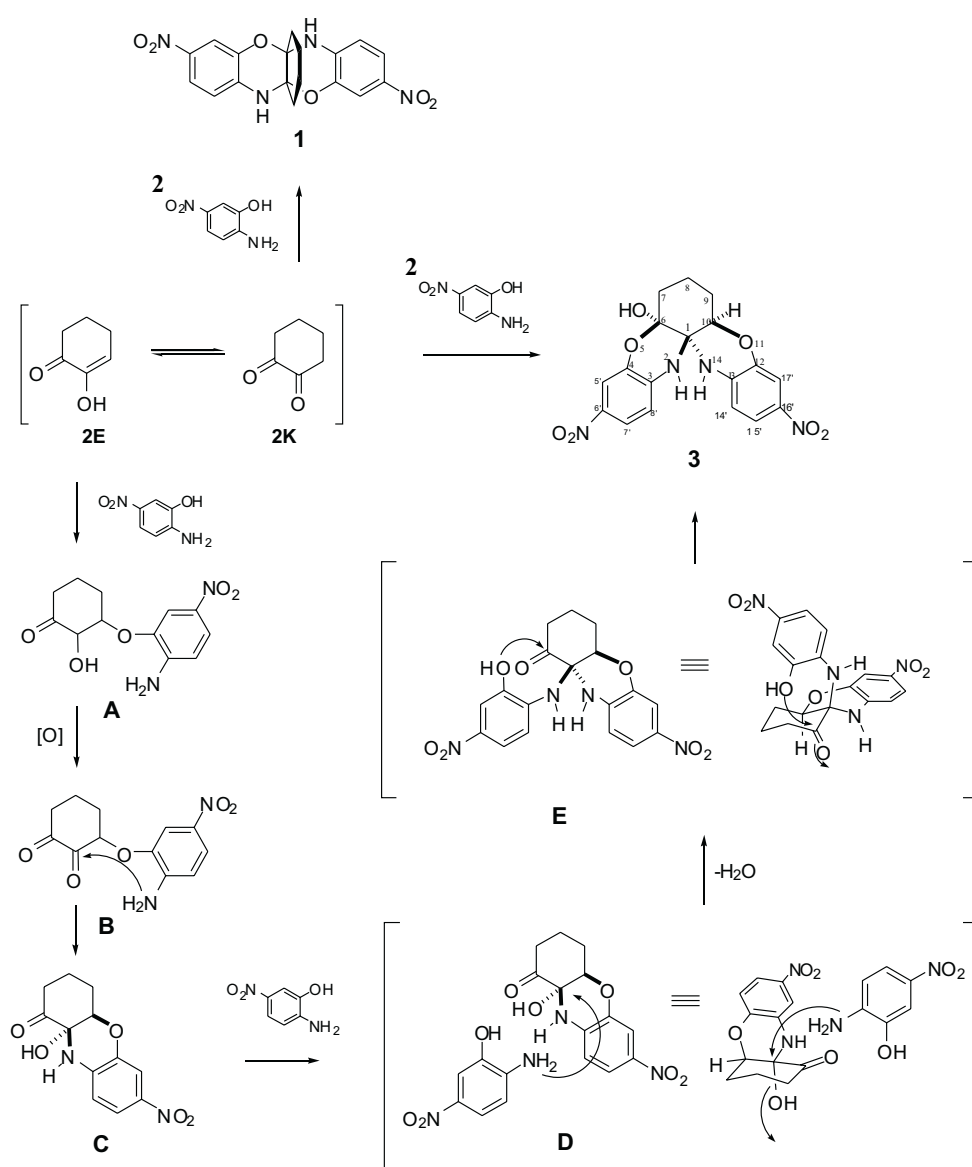
In the reaction of 1,2-cyclohexanedione with 2-amino-5-nitrophenol in refluxing ethanol carried after 2 hours product **1** was obtained in 60% yield (Scheme 1) [2].

* Dedicated to Prof. M. Szafran on the occasion of his 70th birthday.

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When the same reaction mixture was stored for 4 weeks at room temperature, with the air access, the compound **3** was formed in ~20% yield. After separation of precipitate only the main product **1** and substrates were evidenced in the parent solution by means of the ^1H NMR spectra. The structure of product **3** was determined by using X-ray, ^1H , ^{13}C NMR and IR analysis.

Scheme 1



Perspective views of **3** molecule is shown in Fig. 1, while selected bond lengths and angles are compared in Table 1.

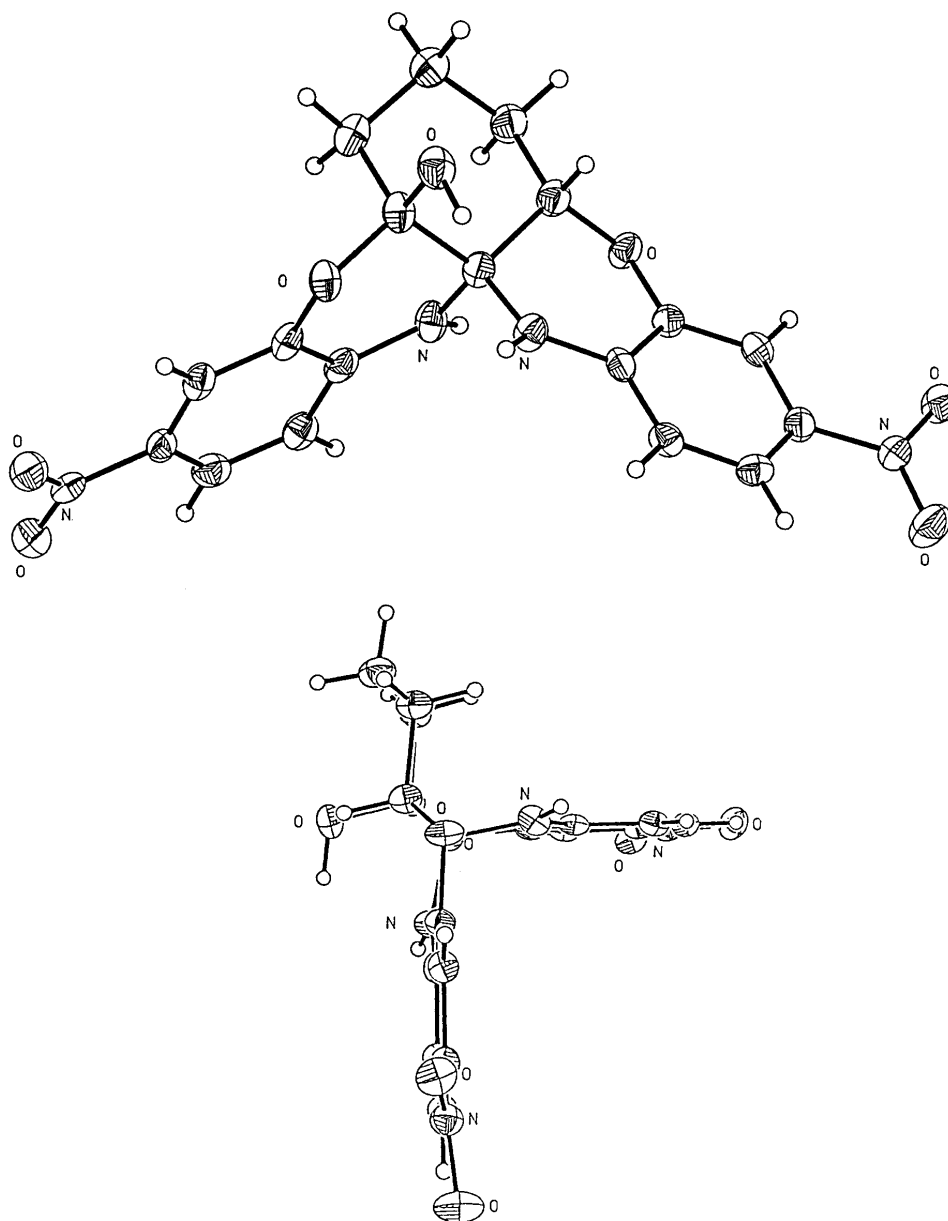


Figure 1. Perspective views of the **3** molecule with perpendicular arrangement of the benzoxazine fragments; oxygen and nitrogen atoms are indicated.

Non-hydrogen atomic coordinates with anisotropic displacement parameters, hydrogen atom coordinates with isotropic displacement parameters and all bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC No 197236). These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Table 1. Selected bond lengths (Å) and angles (°) for **3** molecule; numbering of atoms acc Scheme 1.

O(11)–C(12)	1.371(4)	C(11)–O(11)–C(10)	112.3(3)
O(11)–C(10)	1.446(4)	C(4)–O(5)–C(6)	115.3(3)
O(5)–C(4)	1.371(4)	C(13)–N(14)–C(1)	117.4(3)
O(5)–C(6)	1.454(4)	C(3)–N(2)–C(1)	120.8(3)
N(14)–C(13)	1.383(4)	O(11)–C(12)–C(13)	121.2(3)
N(14)–C(1)	1.452(5)	N(14)–C(13)–C(12)	120.3(3)
N(2)–C(3)	1.370(4)	O(5)–C(4)–C(3)	120.8(3)
N(2)–C(1)	1.438(5)	N(2)–C(3)–C(4)	118.1(3)
C(12)–C(13)	1.407(5)	N(2)–C(1)–N(14)	112.6(3)
C(17')–C(16')	1.376(5)	N(2)–C(1)–C(10)	110.8(3)
C(12)–C(17')	1.374(5)	N(14)–C(1)–C(10)	106.7(3)
C(16')–C(15')	1.384(5)	N(2)–C(1)–C(6)	107.9(3)
		N(14)–C(1)–C(6)	110.2(3)

The main structural parameters of **3** are as follows. Both benzoxazine groups are almost planar with some deviation, which can be ascribed most probably to the packing effects. These groups are oriented to each other perpendicularly (the angle equals to 91°) as shown in Fig. 1. The cyclohexyl fragment possesses a chair conformation. The O(11)–C(12) and O(5)–C(4) bonds show to a large extent a double character (corresponding bond length is 1.371(4) Å). Similarly, a double character is also expressed in N(14)–C(13) (1.383(4) Å) and N(2)–C(3) (1.370(4) Å) bonds. For comparison O(11)–C(10) and O(5)–C(6) bond lengths are equal 1.446(4) and 1.454(4) Å, respectively, while N(14)–C(13) and N(2)–C(3) 1.452(5) and 1.438(5) Å, respectively. The phenyl rings are only a little deformed. One should only mention about noticeable elongation of C(12)–C(13) and C(3)–C(4) bonds that reflects a coupling of lone electron-pairs of oxygen and nitrogen atoms with phenyl π -electron system. The nitro groups are somewhat inclined towards the phenyl ring: the angles are equal to 9.06(2) and 6.02(2)°. In the crystalline lattice one finds hydrogen bonds between OH and NH groups and oxygen atoms of nitro groups of neighbouring molecules. The hydrogen bond lengths for two different NH...O bridges equal to 2.994(4) and 2.950(4) Å, while for the OH...O bridge it is equal to 2.870(4) Å. As shown in Table 2, all hydrogen bonds are highly deformed with respect to the most stable geometry.

Table 2. Hydrogen bonds in the crystal of **3** (Å and °).

D–H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
N(14)–H···O* ⁱ	0.86	2.51	2.994(4)	116.8
N(2)–H···O* ⁱⁱ	0.86	2.16	2.950(4)	152.7
O**–H···O* ⁱⁱⁱ	0.98	2.06	2.870(4)	138.7

Symmetry code: (i) $-x + 1, -y + 1, -z + 1$; (ii) $-x + 1, -y, -z + 1$; (iii) $-x + 3/2, y + 1/2, z$

*oxygen atoms of nitro groups

**oxygen atom of the OH group attached to C(6)

In the IR spectra of solid compound the $\nu(\text{NH})$ and $\nu(\text{OH})$ bands overlap, so that one observes fairly broad asymmetric band with rather sharp peak at 3365 cm^{-1} . Asymmetry of this band is due to a broad low frequency wing that can be interpreted in terms of the stochastic theory of IR spectra of hydrogen bonded systems [12]. In the region of C–H stretching vibrations three peaks: at 3083 (weak) assigned to $\nu(\text{C}_{\text{Ar}}\text{--H})$ and at 2938 (w) and 2868 (w) cm^{-1} corresponding to $\nu_{\text{as}}(\text{CH}_2)$ and $\nu_{\text{s}}(\text{CH}_2)$ were observed. The $-\text{NO}_2$ vibrations are manifested in the two characteristic peaks at 1516 (strong) and 1332 (s) cm^{-1} ascribed to $\nu_{\text{as}}(\text{NO}_2)$ and $\nu_{\text{s}}(\text{NO}_2)$. The modes corresponding to the benzene ring vibrations (in-plane stretching and bending and out-of-plane bending) are ascribed to peaks at 1606 (s), 1500 (w), 1140 (medium), 1072 (s), 881 (w), 825 (m) and 790 (w) cm^{-1} . As known [13] to these modes contribute, to a changeable extent, the $\delta(\text{C}_{\text{Ar}}\text{--H})$ vibrations. The cyclohexane unit is characterized, in addition to the $\nu(\text{CH}_2)$ peaks, by CH_2 deformation bands at 1463 (w) and 981 (w) cm^{-1} . It seems that most characteristic peaks assigned to the benzoxazine unit are localized at 1287 (m) cm^{-1} ($\nu(\text{C}_{\text{Ar}}\text{--N})$) and 1200 (m) cm^{-1} ($\nu(\text{C}_{\text{Ar}}\text{--O})$) and 1236 (w) cm^{-1} of more complex nature. The $\delta(\text{OH})$ vibrations are manifested by a band at 1376 (m) cm^{-1} , while $\nu(\text{C--O})$ vibrations by a peak at 1118 (m) cm^{-1} . The $\delta(\text{NH})$ vibrations are visible as a shoulder at 1610 cm^{-1} . Finally, one can mention that $\gamma(\text{C}_{\text{Ar}}\text{--H})$ vibrations are manifested in the three bands at 744 (s), 732 (w) and 724 (w) cm^{-1} .

The ^{13}C NMR data correlate well with the X-ray structure. In the ^1H NMR spectrum the assignment of signals at 7.14 ppm (singlet), 7.88 ppm (doublet), and 8.18 ppm (singlet), which belong to one OH and two NH groups is ambiguous. However, it seems that two last ones should be assigned to the NH groups which, activated by the nitrophenyl rings, form relatively strong hydrogen bonds with solvent molecules. One of them, as can be deduced from the review articles [14], namely N(14)–H, couples with the axial C(10)–H group (coupling constant about 4.0 Hz). The chemical shift of the OH group proton is 7.14 ppm, *i.e.* less than those ascribed to the NH groups protons.

The possible mechanism of unexpected reaction leading to **3** is presented in Scheme 1. Because in the product three substituents at three neighbouring carbon atoms of the cyclohexane ring exist, one can assume that in this case the reactive form of 1,2-cyclohexanedione is its enol form **2E**. This form can be considered at the same time as Michael acceptor which, with a nucleophilic reagent, can lead to an adduct **A** (substituted α -hydroxyketone). According to the literature data [15,16], α -hydroxy-

ketones can easily be oxidized in air to 1,2-diketones. If it would be possible the further step of reaction consists in formation of diketone **B**. In this diketone an intramolecular addition of amino group to the carbonyl group is possible with formation of *cis*-substituted rings (**C**). The subsequent stage of the reaction consists in nucleophilic substitution of the OH group by NH₂ group of the second molecule of 2-amino-5-nitrophenol (**D**) with formation of the product **E**. This substitution takes place with inversion on the carbon atom C(1) changing the configuration of bound previously rings from *cis* to *trans*. The final stage of the process is the *cis*-anelation consisting in intramolecular attachment of OH group to the carbonyl group (**E**).

EXPERIMENTAL

The X-ray diffraction studies were performed on a Kuma KM4CCD κ -axis four circle diffractometer equipped with an Oxford Cryosystem Cooler using graphite monochromated MoK α radiation. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with Kuma Diffraction programs. The details related to the crystal data and refinement procedure are summarized in Table 1. The structure was solved and refined by the full-matrix least-squares methods on F^2 data using the SHELXS and SHELXL programs [17]. Non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included at calculated positions and refined as rigid groups. Figure was drawn by using the XP program [18]. Crystal for X-ray analysis was grown by slow evaporation from ethyl acetate.

Table 3. Crystal data and structure refinement for (1SR,6RS,10SR)-6-hydroxy-6',16'-dinitro-3,4,12,13-dibenzo-5,11-dioxa-14-diaza-tricyclo[8.4.0.0^{1,6}]tetradecane (**3**).

Identification code	P7-S (3)	CCDC deposit No 197236
Empirical formula	C ₁₈ H ₁₆ N ₄ O ₇	
Formula weight	400.35	
Temperature	100 (1) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	<i>Pbca</i>	
Unit cell dimensions	$a = 12.233(2)$ Å	
	$b = 16.347(3)$ Å	
	$c = 16.762(3)$ Å	
Volume	3351.9(10) Å ³	
<i>Z</i>	8	
Density (calculated)	1.587 Mg/m ³	
Absorption coefficient	0.125 mm ⁻¹	
$F(000)$	1664	
Crystal size	0.20×0.20×0.25 mm	
Θ range for data collection	3.20 to 25.00°	
Index ranges	-14 to 12, -19 to 19, -19 to 19	
Reflections collected/unique	7950/2943 [R(int) = 0.0631]	

Table 3 (continuation)

Refinement method	Full-matrix least-squares on F^2
Data [$I > 2\sigma(I)$]/parameters	2369/263
Goodness-of-fit on F^2	1.224
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0751, wR2 = 0.1537
R indices (all data)	R1 = 0.0993, wR2 = 0.1643
Extinction coefficient	0.0022(6)
Largest diff. peak and hole	0.610 and $-0.391 \text{ e}\text{\AA}^{-3}$

IR spectra were recorded for the samples in Nujol suspensions (KBr windows) using a FTIR Bruker IFS 113V spectrophotometer.

^1H , ^{13}C NMR spectra were collected by using a Bruker DPX 400 spectrometer equipped with a 5 mm $^1\text{H}/\text{BB}$ – inverse probehead, operating at 400.13 and 10.62 MHz, respectively. Two-dimensional spectra (^{13}C , ^1H , COSY) were acquired using standard Bruker Software. The multiplicities of the carbon resonances were recognized by the DEPT editing technique. DMSO- d_6 was used as a solvent with TMS as an internal reference.

Preparation of **3** ((1SR,6RS,10SR)-6-hydroxy-6',16'-dinitro-3,4,12,13-dibenzo-5,11-dioxo-2,14-diazatricyclo[8.4.0.0^{1,6}]tetradecane). The mixture of 2-amino-5-nitrophenol (17.8 mmol) and 1,2-cyclohexanedione (8.9 mmol) was dissolved in 30 cm³ ethanol and was kept at room temperature by 4 weeks in an open flask equipped with condenser. After this time the orange solid product was filtered off and washed with ethyl acetate; $R_f = 0.125$ (TLC silicagel with 1:1 ethyl acetate – hexane); M.p. = 257–260°C. Elemental analysis (calculated in brackets): C – 53.60 (53.97); H – 4.24 (4.03); N – 13.52 (13.98)%. ^{13}C NMR: 18.31 (t, CH₂-8), 28.71 (t, CH₂-9), 30.20 (t, CH₂-7), 49.80 (d, CH-10), 79.40 (s, C-1), 93.71 (s, C-6), 111.78, 112.32 (each d, C-5', C-17'), 112.56, 113.33 (each d, C-8', C-14'), 118.06, 119.07 (each d, C-7', C-15'), 136.08, 137.52, 137.58, 138.47, 139.30, 140.00 (each s, C-3, C4, C-6', C12, C-13, C-16'). ^1H NMR: 1.25–1.38 (m, 1H, CHH-9), 1.59–1.70 (br s, 2H, CH₂-8), 1.70–1.79 (br d, J = ca. 10.0 Hz, 1H, CHH-9), 2.00–2.06 (br s, 2H, CH₂-7), 3.64 (dt, J = 11.2 and ca. 4.0 Hz, 1H, Hax-10), 6.77 (dd, J = 1.0 and 8.9 Hz, 1H, H-8' or H-14'), 6.87 (dd, J = 0.9 and 8.9 Hz, 1H, H-8' or H-14'), 7.14 (s, 1H, NH or OH), 7.33 (d, J = 1.5 Hz, 1H, H-5' or H-14'), 7.63 (d, J = 1.5 Hz, 1H, H-5' and H-17'), 7.66–7.77 (m, 2H, H-7' and H-15'), 7.88 (d, J = 3.8 Hz, 1H, OH or NH), 8.18 (s, 1H, NH or OH).

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