Chemistry of Heterocyclic Compounds, Vol. 42, No. 7, 2006

SYNTHESIS OF 2-[2-(5-PHENYL-1,2,4-OXADIAZOL-3-YL)-ETHYL]BENZIMIDAZOLE AND ITS X-RAY ANALYSIS

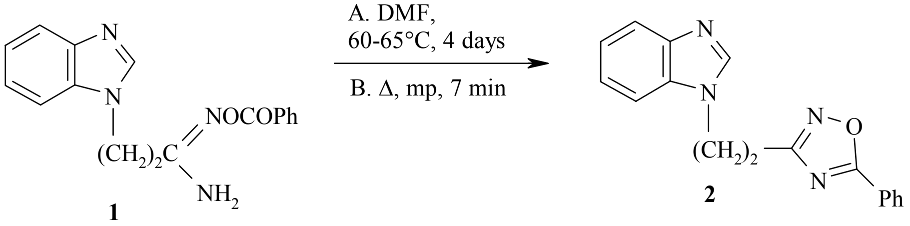
L. A. Kayukova, K. M. Beketov, A. L. Akhelova, and K. D. Praliev

Cyclization of O-benzoyl-2-(benzimidazol-1-yl)propioamidoxime under different temperature conditions gave 2-[2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl]benzimidazole whose structure has been determined by X-ray analysis.

Keywords: O-benzoyl-2-(benzimidazol-1-yl)propioamidoxime, 2-[2-(5-phenyl-1,2,4-oxadiazol-3-yl)-ethyl]benzimidazole, dehydration, X-ray analysis.

We have previously shown [1, 2] that heating O-aroyl-2-piperidino(morpholino)propioamidoximes in DMF solution at 60°C for 1-2.5 h (method A) causes cyclization to the corresponding oxadiazoles whereas heating in the solid phase for 30 seconds (method B) is sufficient to bring about the reaction.

Since the O-benzoyl-2-(benzimidazol-1-yl)propioamidoxime hydrochloride (**1**) prepared by us [3, 4] shows antitubercular and neuropharmacological activity we have carried out the dehydration of its base in order to study further the biological activity of the 2-[2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl]benzimidazole (**2**) formed. It was found that the cyclodehydration of base **1** using method A needs a much longer time (4 days) (yield 42%) than a simple melting of crystalline **1** (method B) when compound **2** was obtained in 58% yield after only 7 minutes. The structure of the compound obtained was confirmed from its ^{1}H NMR spectrum and elemental analysis and by X-ray analysis which showed it to be 2-[2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl]benzimidazole (**2**) (Figs. 1 and 2).



The values of the valence bonds of oxadiazole **2** (Fig. 1) are close to standard. As might be expected, the six-membered ring of the benzimidazole substituent in the molecule **2** is planar to within 0.001 and the five-membered ring to 0.002 Å respectively. The angle between the mean square planes of these rings is 0.8(3)°. The oxadiazole and phenyl rings (planar to within 0.004 and 0.002 Å respectively) lie in a single plane. The dihedral angle between them is 1.4(4)°.

A. B. Bekturov Institute of Chemical Sciences, Ministry of Education and Science, Almaty 010050, Kazakhstan Republic; e-mail: lkayukova@mail.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 1057-1061, July, 2006. Original article submitted November 16, 2004.

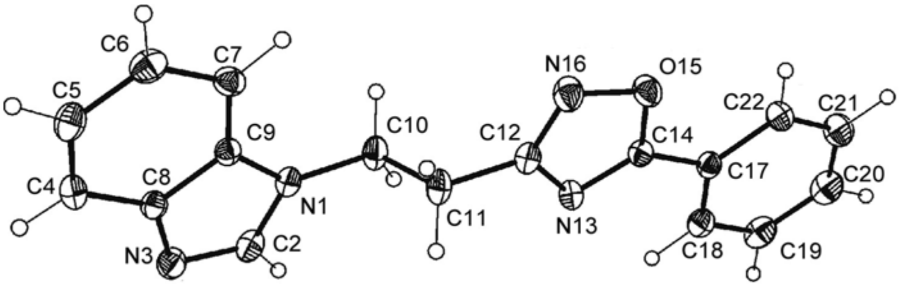


Fig. 1. Molecular structure and atomic numbering for compound **2**.

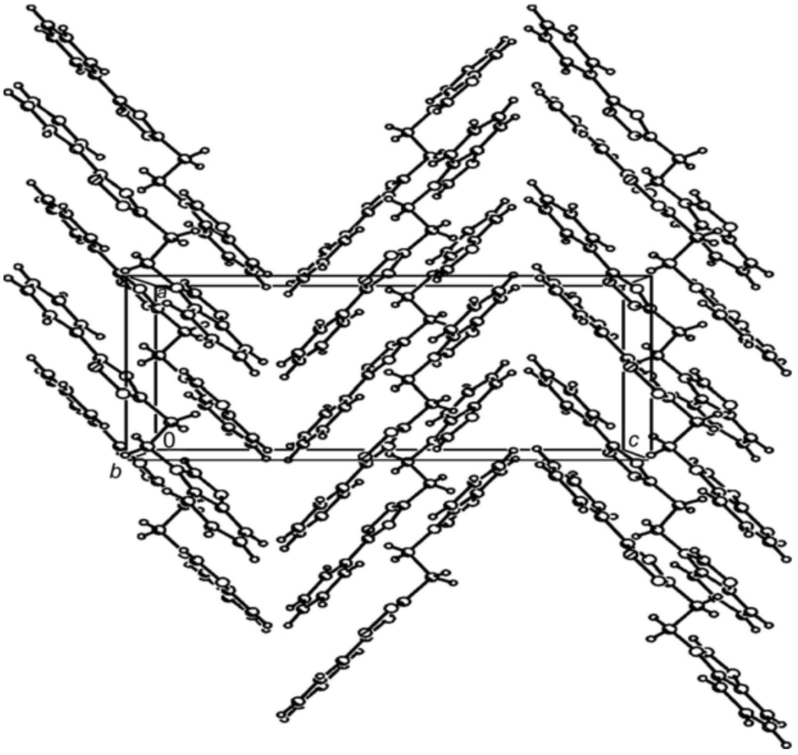


Fig. 2. Crystalline structure of compound **2**.

Van der Waal interactions are basically observed in the crystals of molecule **2** (Fig. 2). In addition, there are weak C–H···N bonds with the geometric parameters $C_{(7)}$–H···$N_{(16)}$ [-0.5 + *x*, 2.5 - *y*, *z*], C···N 3.419(3), H···N 2.50(3), and C–H 1.00(3) Å and the molecules of **2** are joined into a stack parallel to the *a* axis *via* these bonds (Fig. 2).

TABLE 1. Crystallographic Parameters and Experimental Data for Compound **2**

Empirical formula	$C_{17}H_{14}N_4O$
Unit parameters	
a, Å	8.2131(4)
b, Å	11.1885(5)
c, Å	16.0551(7)
α, deg	90
β, deg	90
γ, deg	90
Space group	*Pna*(2)1
V, Å^3	1475.34(12)
Z	4
$\rho_{calc,}$ g/cm^3	1.307
$\rho_{calc,}$ g/cm^3	0.085
F(000)	608
Total number of reflections	16 640
Number of reflections used in calculation	1563
GOOF	1.033
Final *R*-factor [$I > 2\sigma(I)$]	$R_1 = 0.0306$, $wR_2 = 0.0803$
Residual electron density, e·Å^{-3}	0.123 and -0.111

TABLE 2. Bond Lengths (*d*) in Compound **2**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
N(1)–C(2)	1.356(3)	C(7)–C(9)	1.378(3)	O(15)–N(16)	1.422(2)
N(1)–C(9)	1.385(2)	C(8)–C(9)	1.394 (3)	C(17)–C(18)	1.383(3)
N(1)–C(10)	1.452(3)	C(10)–C(11)	1.517(3)	C(17)–C(22)	1.395(3)
C(2)–N(3)	1.310(3)	C(11)–C(12)	1.495(3)	C(18)–C(19)	1.390(3)
N(3)–C(8)	1.390(2)	C(12)–N(16)	1.296(3)	C(19)–C(20)	1.370(4)
C(4)–C(5)	1.368(3)	C(12)–N(13)	1.375(3)	C(20)–C(21)	1.372(4)
C(4)–C(8)	1.396(3)	N(13)–C(14)	1.297(2)	C(21)–C(22)	1.390(3)
C(5)–C(6)	1.393(4)	C(14)–O(15)	1.337(2)		
C(6)–C(7)	1.386(3)	C(14)–C(17)	1.464(3)		

TABLE 3. Valence Angles (ω) in Compound **2**

Angle	ω, deg	Angle	ω, deg
C(2)–N(1)–C(9)	106.24 (17)	N(16)–C(12)–N(13)	114.79 (18)
C(2)–N(1)–C(10)	126.24 (19)	N(16)–C(12)–C(11)	122.56 (19)
C(9)–N(1)–C(10)	127.44 (18)	N(13)–C(12)–C(11)	122.63 (19)
N(3)–C(2)–N(1)	114.37 (18)	C(14)–N(13)–C(12)	102.44 (15)
C(2)–N(3)–C(8)	103.86 (16)	N(13)–C(14)–O(15)	113.70 (16)
C(5)–C(4)–C(8)	117.6 (2)	N(13)–C(14)–C(17)	127.89 (17)
C(4)–C(5)–C(6)	121.4 (2)	O(15)–C(14)–C(17)	118.41 (17)
C(7)–C(6)–C(5)	122.0 (2)	C(14)–O(15)–N(16)	105.70 (15)
C(9)–C(7)–C(6)	116.1 (2)	C(12)–N(16)–O(15)	103.35 (16)
N(3)–C(8)–C(9)	110.52 (17)	C(18)–C(17)–C(22)	120.4 (2)
N(3)–C(8)–C(4)	129.29 (19)	C(18)–C(17)–C(14)	118.78 (18)
C(9)–C(8)–C(4)	120.18 (17)	C(22)–C(17)–C(14)	120.80 (19)
C(7)–C(9)–N(1)	132.33 (19)	C(17)–C(18)–C(19)	119.7 (2)
C(7)–C(9)–C(8)	122.65 (19)	C(20)–C(19)–C(18)	120.0 (3)
N(1)–C(9)–C(8)	105.01 (16)	C(19)–C(20)–C(21)	120.4 (2)
N(1)–C(10)–C(11)	111.96 (17)	C(20)–C(21)–C(22)	120.8 (3)
C(12)–C(11)–C(10)	110.98 (18)	C(21)–C(22)–C(17)	118.6 (3)

EXPERIMENTAL

^{1}H NMR spectra were measured on a Mercury-300 (300 MHz) instrument using DMSO-d$_6$ and with HMDS as internal standard (δ 0.05 ppm). Monitoring of the course of the reaction was carried out by TLC on Silicagel (Fluka) plates and with ethanol–benzene as eluent (3:1).

O-Benzoyl-2-(benzimidazol-1-yl)propioamidoxime (1). K_2CO_3 (0.40 g, 2.9 mmol) was added to a solution of compound **1** hydrochloride [5] (1.0 g, 2.9 mmol) in distilled water (10 ml). The precipitate formed was filtered off and recrystallized from ethanol. Yield 0.67 g (75%), R_f 0.40; mp 118°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.74 (2H, t, J = 7.0, α-CH_2); 4.63 (2H, t, J = 7.0, β-CH_2); 6.82 (2H, s, NH_2); 8.62 (1H, s, $C_{(2)sp2}$-H); 7.62-8.12 (9H, m, CH_{Ar}). Found, %: C 66.55; H 5.39. $C_{17}H_{16}N_4O_2$. Calculated %: C 66.22; H 5.23.

2-[2-(5-Phenyl-1,2,4-oxadiazol-3-yl)ethyl]benzimidazole (2). A. A mixture of compound **1** (0.67 g, 2.2 mmol), molecular sieve (0.3 g), and DMF (15 ml) was heated on a water bath at 60-65°C for 4 days. The molecular sieves were filtered off and the filtrate was evaporated using an oil pump. The obtained residue was recrystallized from ethanol. Yield 0.27 g (42%); R_f 0.63, mp 86°C.

B. Compound **1** (0.4 g, 1.3 mmol) was heated to melting (118°C) and after 7 minutes the obtained melt was recrystallized from ethanol. Yield 0.22 g (58%); R_f 0.63, mp 86°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.38 (2H, t, J = 7.0, α-CH_2); 4.72 (2H, t, J = 7.0, β-CH_2); 8.22 (1H, s, $C_{(2)sp2}$); 7.16-8.07 (9H, m, CH_{Ar}). Found, %: C 70.21; H 5.16. $C_{17}H_{14}N_4O$. Calculated, %: C 70.33; H 4.86.

X-ray Structural Investigation was carried out on a KUMA/OXFORD KM4 diffractometer at room temperature (θ/2θ scanning with use of a graphite monochromator for MoKα radiation, θ_{max} = 26.37, λ = 0.71073 Å). Crystals of compound **2** had an orthorhombic space group. The structure was solved by a direct method and refined in the anisotropic (isotropic for hydrogen atoms) approximation for atomic thermal vibrations using the least squares method and the SHELX-97 program package [6]. The positions of hydrogen atoms were determined by difference syntheses. The final factor was 0.0306 for 1563 reflections with $I > 2\sigma(I)$. Unit cell parameters and experimental details are given in Table 1 and bond lengths and valence angles in Tables 2 and 3.

X-ray data has been deposited in the Cambridge data bank (CCDC 254116),

REFERENCES

1. L. A. Kayukova, K. D. Praliev, and I. S. Zhumadil'daeva, *Izv. Akad. Nauk, Ser. Khim.*, 1945 (2002).
2. L. A. Kayukova, *Khim. Geterotsikl. Soedin.*, 253 (2003) [*Chem. Heterocycl. Comp.*, **39**, 223 (2003)].
3. L. A. Kayukova, K. D. Praliev, A. L. Kotova, and A. E. Krivtsova, Prov. Pat. KR No. 8391; *Industrial Resources* [in Russian], Almaty (2000), No. 1, p. 46.
4. L. A. Kayukova, K. D. Praliev, G. M. Pichkhadze, D. M. Kadyrova, E. E. Braun, and K. U. Esetova, Prov. Pat. KR No.10512; *Industrial Resources* [in Russian], Almaty (2001), No. 8, p. 104.
5. L. A. Kayukova, K. D. Praliev, and A. L. Akhelova, *Izv. Min. Ed. Sci. KR, Nat. Acad. Sci. KR, Ser. Khim.*, No. 5, 75 (2003).
6. G. M. Sheldrick, *SHELXS97 and SHELXL97.* Göttingen University (1997), Germany.