ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 7, pp. 980–987. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © O.V. Kulikov, L.Kh. Minacheva, A.V. Mazepa, 2008, published in Zhurnal Organicheskoi Khimii, 2008, Vol. 44, No. 7, pp. 991–998.

Investigation of the Reaction between Sodium Hydroxide and *syn*- and *anti*-Isomers of 5-Substituted 2-(4-Chlorobutyryl)-aminobenzophenones Oximes

O. V. Kulikov[a], L. Kh. Minacheva[b], and A. V. Mazepa[b]

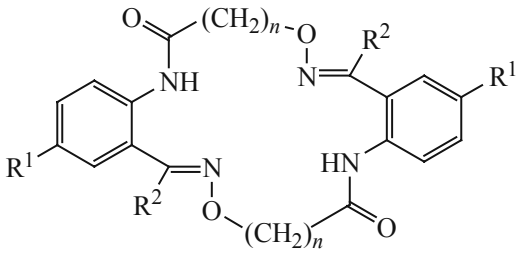
[a]*Bogatskii Physicochemical Institute, National Academy of Sciences of Ukraine, Odessa, 65080 Ukraine*
e-mail: viologen@rambler.ru
[b]*Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Moscow, Russia*

Received July 17, 2007

Abstract—By the reaction of *syn*-isomers of 5-substituted 2-(4-chlorobutyryl)aminobenzophenones oximes with NaOH *syn*-isomers of 5-substituted 2-(2-oxopyrrolidin-1-yl)benzophenones oximes were obtained. Similarly the *anti*-isomers of 5-substituted 2-(4-chlorobutyryl)aminobenzophenones oximes treated with NaOH underwent cyclization into *anti*-isomers of 5-substituted 2-(2-oxopyrrolidin-1-yl)benzophenones oximes. Crystal and molecular structures were investigated of the *syn*-isomer of 5-methyl-2-(2-oxopyrrolidin-1-yl)benzophenone oxime, the *anti*-isomer of 5-bromo-2-(2-oxopyrrolidin-1-yl)benzophenone oxime, and the *syn*-isomer of 5-methyl-2-(4-chlorobutyryl)aminobenzo-phenone oxime. The fragmentation features under the electron impact of *syn*- and *anti*-isomers of 5-substituted 2-(2-oxopyrrolidin-1-yl)benzophenones oximes are discussed.

DOI: 10.1134/S1070428008070075

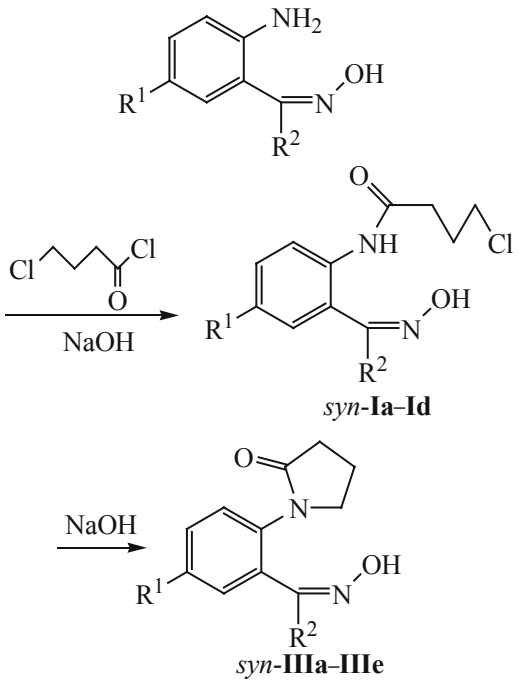
The chemistry of nitrogen dibenzodioxatetraaza-macroheterocycles is extensively developed nowadays [1]. We formerly demonstrated [2, 3] that cyclization of acyl derivatives of *syn*- and *anti*-isomers of 5-substituted 2-aminobenzophenones oximes led to the formation of the corresponding 16- and 18-membered dibenzo-dioxa-tetraazamacroheterocycles **A**.



A

R^1 = H, Me, Br, Cl, NO_2; R^2 = Ph, *o*-ClC_6H_4; *n* = 1, 2.

Aiming at the synthesis of 20-membered dibenzo-dioxatetraazamacroheterocycles we investigated the reaction of *syn*- (**Ia–Id**) and *anti*- (**IIa** and **IIb**) isomers of 5-substituted 2-(4-chlorobutyryl)aminobenzophenones oximes with NaOH. We established that under the conditions we had previously described [2, 3] both *syn*- (**Ia–Id**) and *anti*- (**IIa** and **IIb**) isomers underwent



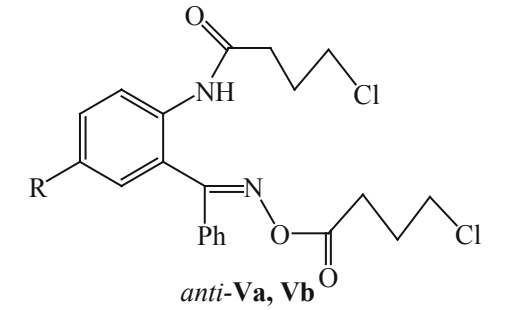
syn-**Ia–Id**

syn-**IIIa–IIIe**

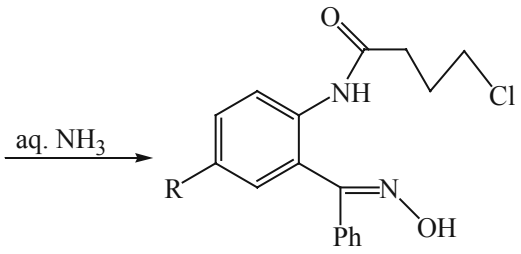
R^1 = H, Me, Br, Cl, NO_2; R^2 = Ph, *o*-ClC_6H_4; *n* = 1, 2.

intramolecular N-alkylation resulting in the formation of *syn*- (**IIIa–IIIe**) and *anti*- (**IVa** and **IVb**) isomers of 5-substituted 2-(2-oxopyrrolidin-1-yl)benzophenone oximes. We failed to detect in the reaction mixture products of intermolecular *o*-alkylation (20-membered dibenzodioxatetraazamacroheterocycles) presumably because the activation energy of the formation of the stable five-membered pyrrolidine ring was lower that that of the 20-membered macrocycle, and the reaction proceeded to give 2-(2-oxopyrrolidin-1-yl)benzophenones oximes.

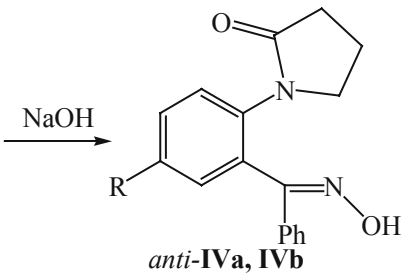
Compounds **Ia–Id** were obtained from the corresponding 5-substituted 2-aminobenzophenones oxines and 4-chlorobutyryl chloride in the presence of NaOH. Compounds **IIa** and **IIb** were prepared by hydrolysis of the corresponding *anti*-isomers of 5-substituted 2-(4-chlorobutyryl)aminobenzophenones *o*-(4-chlorobutyryl)-oximes (**Va** and **Vb**). Compound **Vb** can be synthesized by acylation of the *syn*-isomer of 5-bromo-2-aminobenzophenone oxime with 4-chlorobutyryl chloride in the absence of a base. In this reaction a mixture formed



anti-**Va, Vb**

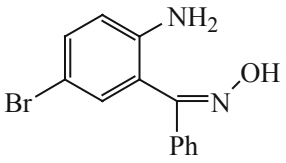


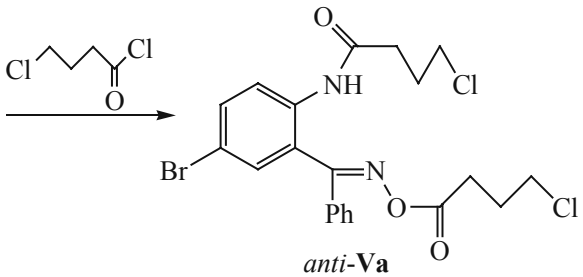
anti-**IIa, IIb**



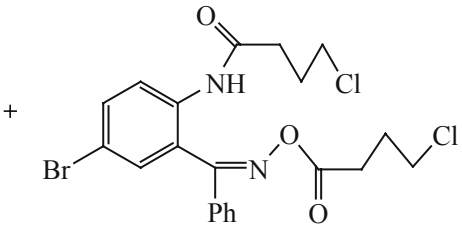
anti-**IVa, IVb**

R = Me (**a**), Br (**b**).





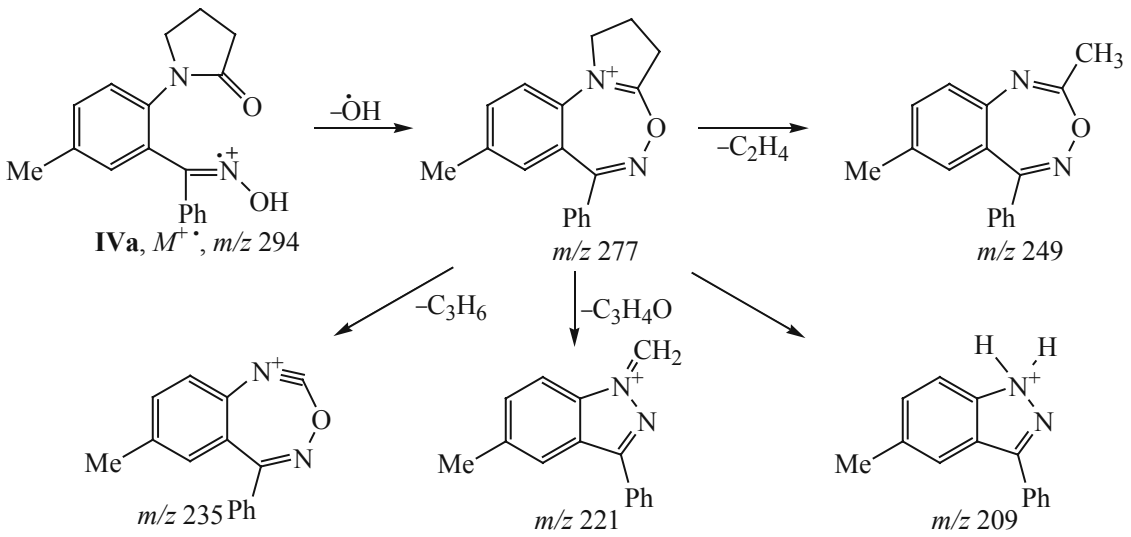
anti-**Va**



syn-**VI**

of isomeric oxime diacylderivatives, compounds **Vb** and **VI**. The synthesis of compound **Va** we reported previously [4]. All compounds synthesized were characterized by elemental analysis, IR, UV, ^{1}H NMR, and mass spectra (considering the presumable fragmentation paths), and compounds **Ia, IIIa**, and **IV** were also subjected to XRD analysis.

We formerly dicussed the fragmentation under the electron impact of 5-substituted 2-aminobenzophenones oximes (*syn*- and *anti*-isomers) [5]. The stability of molecular ions of compounds **IIIa–IIIe, IVa**, and **IVb** is considerably lower. The intensity of the corresponding peaks varied in the range from 0.5 (**IVb**) to 4.6% (**IIIb**). This fact is presumably due to the interaction between the lone electron pair of the carbonyl oxygen with the charged imide nitrogen facilitating the hydroxy group elimination and the stabilization of the arising fragments. This assumption is well consistent with the higher intensity of molecular ion peaks from *syn*-isomers **IIIa** and **IIIc** (2.8 and 2.6%) than those of *anti*-isomers **IVa**, and **IVb** (1.8 and 0.5% respectively). As an example we present the possible fragmentation scheme of oxime **IVa**. In the *syn*-isomers the hydroxy group sterically hampers the suggested interaction.



Further fragmentation of the formed ions involves the elimination of the fragments of the pyrrolidine ring. A small part of the molecular ions suffered decomposition by a successive elimination of two hydroxy radicals or by NOH ejection.

We showed formerly [3] that in the IR spectra of the *syn*-isomers of 2-aminobenzophenones oximes containing an amide moiety the characteristic band was that in the region 3390–3400 cm^{-1} corresponding to the absorption of a free NH group, whereas this band was lacking in the IR spectra of the corresponding *anti*-isomers. The presence of this band in the region 3385–3400 cm^{-1} in the spectra of compounds **Ia–Id** suggests that these compounds belong to the series of *syn*-isomers. This assumption was proved by the XRD analysis data of compound **Ia**.

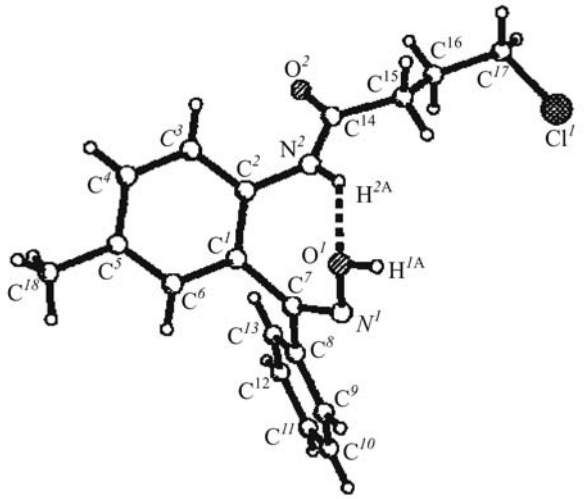


Fig. 1. General view of molecule **Ia**, and numeration of the atoms.

The general view of molecules **Ia, IIIa**, and **IVb** is shown on Figs. 1, 2, and 3 respectively. All bond distances have values common for the corresponding atoms, the double bonds are localized. Compounds **Ia** and **IIIa** are *syn*-isomers, compound **IVb** is *anti*-isomer. The isomer

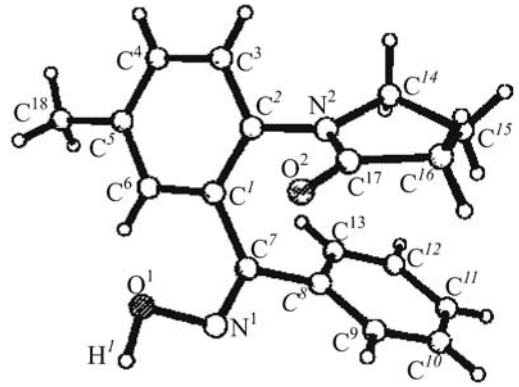


Fig. 2. General view of molecule **IIIa**, and numeration of the atoms.

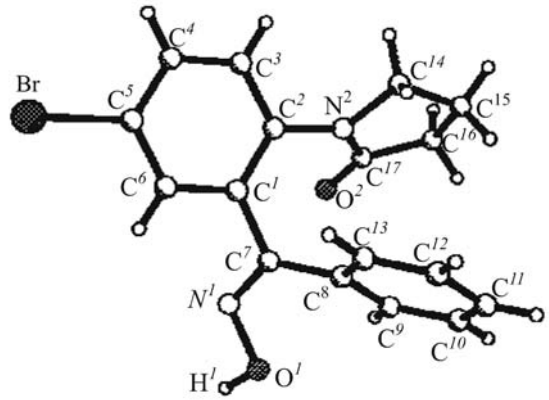


Fig. 3. General view of molecule **IVb**, and numeration of the atoms.

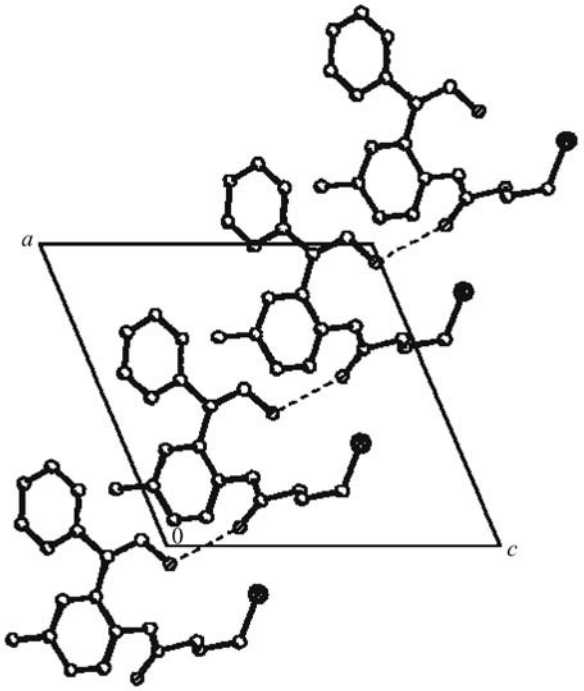


Fig. 4. A fragment of packing of molecules **Ia** in the crystal.

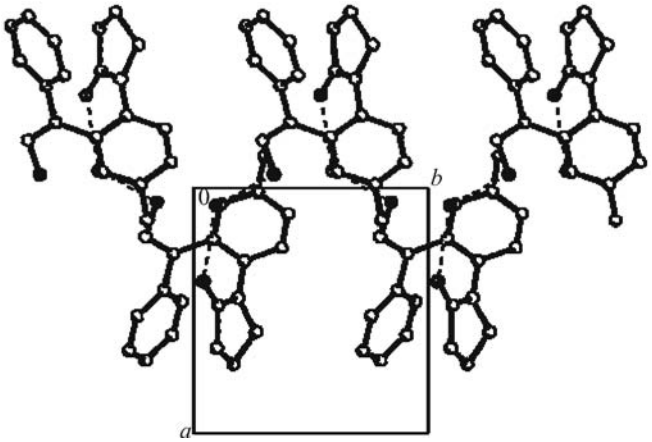


Fig. 5. A fragment of packing of molecules **IIIa** in the crystal.

type can be characterized by the torsion angle $C^1C^7N^1O^1$ that is equal in compounds **Ia, IIIa**, and **IVb** to 1.2, 2.5, and 173.4 deg respectively. The amide group in compound **Ia** is of *E*-configuration.

In oximes **Ia, IIIa**, and **IVb** the dihedral angel between the benzene rings equals 104.7, 102.0, and 105.4 deg respectively. In compound **IIIa** the five-memebered ring formed with the six-membered rings C^1–C^6 and C^8–C^{13} angles 117.4 and 24.6° respectively. The corresponding angles in compound **IVb** are 123.4

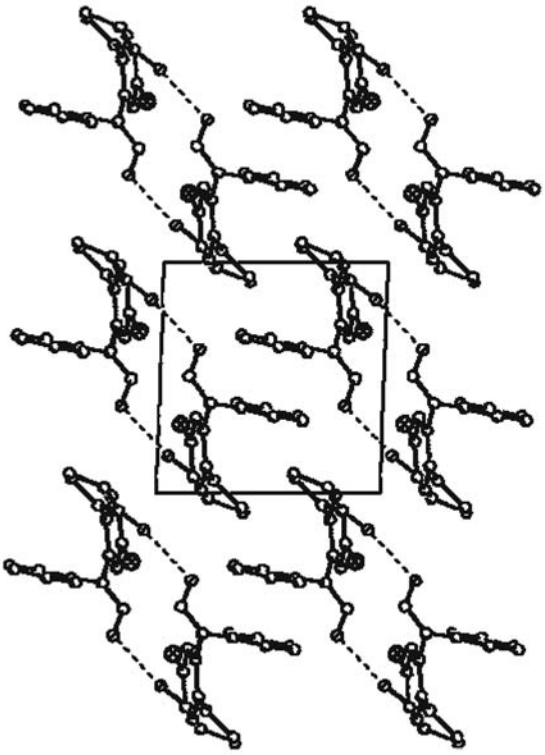


Fig. 6. A fragment of packing of molecules **IVb** in the crystal.

and 30.0°. In both compounds **IIIa**, and **IVb** the 2-oxo-pyrrolidine ring exists in the *envelope* conformation with the apical C^{15} atom. The latter deviated from the plane of the other four atoms by 0.337 and 0.309 Å respectively.

Compounds **Ia, IIIa**, and **IVb** differ in the packing of molecules in the crystal. The oxime hydroxy group of compound **Ia** is involved in hydrogen bonds of two kinds: an intramolecular bond with the hydrogen of the amide group [forming a 7-membered pseudoring, N^2–$H^{2A}\cdots O^1$ (N^2–H^{2A} 0.86, $H^{2A}\cdots O^1$ 2.05, $N^2\cdots O^1$ 2.735(5) Å, angle $N^2H^{2A}O^1$ 136°], and an intermolecular bond with the carbonyl oxygen of the neighboring molecule [O^1–$H^{1A}\cdots O^2$ (x + 0.5, –y + 1.5, z + 0.5) (O^1–H^{1A} 0.82, $H^{1A}\cdots O^2$ 1.85, $O^1\cdots O^2$ 2.671(4) Å, angle $O^1H^{1A}O^2$ 178°], joining the molecules in the crystal into chains in the *a*0*c* plane (Fig. 4).

Compound **IIIa** like oxime **Ia** has a chain structure (Fig. 5). But in this substance in contrast to compound **Ia** the molecules in the chain do not interact directly but through a solvate water molecule involved into the crystal packing of compound **IIIa**. In the hydrogen bond with the hydroxy oxygen O^1 of the oxime fragment O^1–$H^1\cdots O_w$ (–x + 1, y – 0.5, –z + 1) the water molecule is a proton acceptor [O^1–H^1 1.02, $H^1\cdots O_w$ 1.72, $O^1\cdots O_w$ 2.712(4) Å, angle $O^1H^1O_w$ 163°]. In the hydrogen bond with the

Crystallographic data and parameters of the experiment for compounds **Ia, IIIa**, and **IVb**

Parameter	**Ia**	**IIIa**	**IVb**
Empirical formula	$C_{18}H_{19}ClN_2O_2$	$C_{18}H_{20}N_2O_3$	$C_{17}H_{15}BrN_2O_2$
M	330.80	312.36	359.22
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	*Cc*	$P2_1$	$P\bar{1}$
Unit cell parameters:			
a, Å	11.0400(18)	8.5869(13)	8.808(3)
b, Å	15.0349(15)	8.1642(2)	9.485(3)
c, Å	11.2140(13)	11.525(3)	10.551(3)
α, deg	90	90	63.61(3)
β, deg	112.836 (9)	93.070(16)	82.46(3)
γ, deg	90	90	88.40(3)
V, Å	1715.5(4)	806.8(2)	782.3(4)4
Z	4	2	2
ρ_{calc}, g/cm^3	1.281	1.286	1.525
μ_{Cu}, mm^{-1}	2.058	0.716	3.654
F(000)	696	332	364
Crystal size, mm	0.46×0.32×0.91	0.25×0.31×0.81	0.13×0.09×0.35
Range of angles θ, deg	5.61–69.88	3.84–69.91	4.72–69.91
Indices range	–2 = *h* = 13, –1 = *k* = 18, –13 = *l* = 13	–2 = *h* = 10, –1 = *k* = 9, –14 = *l* = 14	–1 = *h* = 10, –11 = *k* = 11, –12 = *l* = 12
Overall number of reflexions	2218	2397	3392
Number of independent reflexions	2063 (R_{int} 0.0178)	1835 (R_{int} 0.0318)	2781 (R_{int} 0.0820)
Number of reflexions with $I > 2\sigma$	1835	1778	2343
(*I*)	209	204	204
Number of refined parameters	1.030	1.045	1.053
GOOF by F^2	0.0533, 0.1555	0.0553, 0.1500	0.0595, 0.1684
R_1, wR_2 [$I > 2\sigma(I)$]	0.0588, 0.1625	0.0567, 0.1520	0.0690, 0.1803
R_1, wR_2 (for all reflexions)	.02(4)	–0.2(5)	–
Absolute structural parameter	0.0072(7)	0.025(4)	0.0016(10)
Extinction factor	0.516/–0.355	0.645/–0.462	0.909/–1.173
$\Delta\rho_{max}/\Delta\rho_{min}$, *e* Å^{-3}			

carbonyl oxygen of 2-oxo-pyrrolidine O_w–$H^1{}_w\cdots O^2$ (*x* – 1, *y*, *z*) water is a proton donor [O_w–$H^1{}_w$ 1.15, $H^1{}_w\cdots O^2$ 1.66, $O_w\cdots O^2$ 2.77(5) Å, angle $O_wH^1{}_wO^2$ 161°].

Molecules of compound **IVb** form centrosymmetrical pseudodimers through an intermolecular hydrogen bond O^1–$H^1\cdots O^2$ between the H^1 atom of the hydroxy group in the fragment C=N–OH and the O^2 atom of the contiguous 2-oxopyrrolidine molecule [O^1–H^1 1.01(8), $H^1\cdots O^2$ 1.72(8), $O^1\cdots O^2$ 2.659(4) Å , angle $O^1H^1O^2$ 153(7)°]. These pseudodimers are bound with each other in the crystal only by the van der Waals forces (Fig. 6). Thus the replacement of a methyl substituent in the position *5* of compound **IIIa** by a bromine atom in compound **IVb** resulted in the change in the packing of molecules in the crystal.

The study of the applicability of the given synthetic approach to the synthesis of 20-membered dibenzodioxatetraazamacroheterocycles (cyclization of monoacyl derivatives of 2-aminobenzophenone oximes effected by bases) requires further investigation (variation of the base power, dilution, etc.). This problem will be discussed in later publications.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Specord 75IR from solutions in $CHCl_3$. UV spectra were taken on a spectrophotometer SF-56 from ethanol solutions of concentration 3×10^{-5} mol l^{-1} , layer thickness 10 mm. Mass spectra were registered on a mass

spectrometer MKh-1321 (direct sample admission into the ion source, ionizing electrons energy 70 eV, ionization chamber temperature 150°C). ^{1}H NMR spectra were measured on a spectrometer Varian VXR-300 at operating frequency 300 MHz, solvent DMSO-d_6, internal reference TMS.

X-ray diffraction study. Main crystallographic data on the crystals of compounds **Ia, IIIa**, and **IVb** are compiled in the table. The set of experimental reflexions was obtained at room temperature on a four-circle automatic diffractometer Enraf-Nonius CAD-4 (Cu-radiation, λ 1.54178 Å, graphite monochromator, ω-scanning). In the processing of experimental data Lorentz factors and polarization were taken into account. The correction for extinction for compound **Ia** was introduced by method [6]. Structures of molecules **Ia, IIIa**, and **IVb** were solved by the direct method (SHELXS-97 [7]) and refined by the least-squares procedure by F^2 (SHELXL-97 [8]) in the full-matrix anisotropic approximation for all non-hydrogen atoms. For structures **Ia, IIIa**, and **IVb** the positions of hydrogen atoms were calculated from the geometrical considerations and were refined along the *rider* model. In compound **IIIa** the positions of hydrogen atoms of water molecule and hydroxy group were found experimentally and were not refined. In compoundя **IVb** The position of the hydrogen of the hydroxy group was found experimentally and refined isotropically. The complete set of experimental data is deposited into the Cambrige Structural Database [registered nos. CCDC 643878 (**Ia**), CCDC 643879 (**IIIa**), CCDC 643880 (**IVb**)].

***syn*-5-Methyl-2-(4-chlorobutyryl)aminobenzophenone oxime (Ia).** To a solution of 8.6 g (38.1 mmol) of *syn*-5-methyl-2-aminobenzophenone oxime in 50 ml of dioxane was added dropwise at stirring a solution of 4.5 ml (39.8 mmol) of 4-chlorobutyryl chloride and a solution of 1.59 g (39.8 mmol) of NaOH in 20 ml of water. After stirring for 4 h the reaction mixture was poured into water, the separated precipitate was filtered off, washed with water on the filter, dried, and recrystallized from benzene. Yield 8.7 g (69%), mp 68–70°C. IR spectrum, ν, cm^{-1}: 1585 (C=N), 1675 (C=O), 3395 (N–H), 3545 (O–H). UV spectrum, λ_{max}, nm (log ε): 240 (4.38). ^{1}H NMR spectrum, δ, ppm: 11.49 s (1H, OH), 8.87 s (1H, NH), 7.52–6.92 m (8H$_{Ar}$), 3.46 t (2H, CH_2Cl, *J* 6.7 Hz), 2.28 s (3H, CH_3), 2.20 t (2H, CH_2CO, *J* 7.2 Hz), 1.76 q (2H, $CH_2CH_2CH_2$, *J* 6.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 330 (19.6) $[M]^+$, 277 (25.9), 247 (10.6), 246 (36.5), 245 (31.2), 235 (8.2), 234 (10.2), 232 (8.3), 231 (43.6), 226 (21.3), 210 (59.6), 208 (100.0), 207 (47.9), 206 (9.6), 106 (9.5). Found, %: C 65.25; H 5.83; N 8.24. $C_{18}H_{19}ClN_2O_2$. Calculated, %: C 65.35; H 5.79; N 8.47.

Compounds **Ib–Id** were similarly obtained.

***syn*-5-Chloro-2-(4-chlorobutyryl)aminobenzophenone oxime (Ib)** was obtained from *syn*-5-chloro-2-aminobenzophenone oxime and 4-chlorobutyryl chloride. Yield 64%, mp 60–65°C. IR spectrum, ν, cm^{-1}: 1590 (C=N), 1680 (C=O), 3395 (N–H), 3540 (O–H). UV spectrum, λ_{max}, nm (log ε): 239 (4.43). ^{1}H NMR spectrum, δ, ppm: 11.61 s (1H, OH), 8.97 s (1H, NH), 7.76–7.12 m (8H$_{Ar}$), 3.42 t (2H, CH_2Cl, *J* 6.7 Hz), 2.20 t (2H, CH_2CO, *J* 7.2 Hz), 1.76 q (2H, $CH_2CH_2CH_2$, *J* 7.0 Hz). Mass spectrum, *m/z* (I_{rel}, %): 352 (9.2) $[M]^+$, 350 (15.0), 297 (18.6), 254 (8.50), 246 (14.0), 231 (20.7), 230 (42.1), 229 (48.7), 228 (100.0), 227 (9.4). Found, %: C 58.33; H 4.64; N 7.82. $C_{17}H_{16}Cl_2N_2O_2$. Calculated, %: C 58.13; H 4.59; N 7.98.

***syn*-5-Bromo-2-(4-chlorobutyryl)aminobenzophenone oxime (Ic)** was obtained from *syn*-5-bromo-2-aminobenzophenone oxime and 4-chlorobutyryl chloride. Yield 59%, mp 63–67°C. IR spectrum, ν, cm^{-1}: 1595 (C=N), 1680 (C=O), 3400 (N–H), 3550 (O–H). UV spectrum, λ_{max}, nm (log ε): 245 (4.41). ^{1}H NMR spectrum, δ, ppm: 11.67 s (1H, OH), 9.14 s (1H, NH), 7.65–7.31 m (8H$_{Ar}$), 3.45 t (2H, CH_2Cl, *J* 6.5 Hz), 2.20 t (2H, CH_2CO, *J* 7.3 Hz), 1.74 q (2H, $CH_2CH_2CH_2$, *J* 6.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 396 (8.8) $[M]^+$, 344 (21.4), 343 (100.0), 342 (13.8), 341 (99.8), 329 (6.6), 327 (11.2). Found, %: C 51.54; H 4.12; N 7.16. $C_{17}H_{16}BrClN_2O_2$. Calculated, %: C 51.60; H 4.08; N 7.08.

***syn*-5-Bromo-2'-chloro-2-(4-chlorobutyryl)aminobenzophenoneoxime (Id)** was obtained from *syn*-5-bromo-2'-chloro-2-aminobenzophenone oxime and 4-chlorobutyryl chloride. Yield 65%, mp 133–135°C. IR spectrum, ν, cm^{-1}: 1600 (C=N), 1690 (C=O), 3385 (N–H), 3550 (O–H). UV spectrum, λ_{max}, nm (log ε): 248 (4.29). ^{1}H NMR spectrum, δ, ppm: 12.24 s (1H, OH), 8.71 s (1H, NH), 7.67–7.16 m (7H$_{Ar}$), 3.59 t (2H, CH_2Cl, *J* 6.5 Hz), 2.34 t (2H, CH_2CO, *J* 7.3 Hz), 1.94 q (2H, $CH_2CH_2CH_2$, *J* 6.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 430 (30.72) $[M]^+$, 428 (14.1), 377 (21.9), 375 (16.5), 359 (7.4), 351 (8.3), 335 (8.9), 334 (21.9), 332 (17.9), 326 (19.4), 324 (17.9). Found, %: C 47.54; H 3.44; N 6.50. $C_{17}H_{15}BrCl_2N_2O_2$. Calculated, %: C 47.47; H 3.52; N 6.51.

***N*-{2-[(*E*)-(Hydroxyimino)(phenyl)methyl]-4-methylphenyl}-4-chlorobutanamide (IIa).** To a solution of 5 g (11.5 mmol) of *anti*-O-(4-chlorobutyryl)-5-

methyl-2-(4-chlorobutyryl)aminobenzophenone oxime (**Va**) in 50 ml of dioxane was added dropwise at room temperature while stirring 5 ml of aqueous ammonia. After stirring for 1 h the reaction mixture was poured into water, the separated precipitate was filtered off, washed with water on the filter, dried, and recrystallized from benzene. Yield 3.49 g (92%), mp 110–112°C. IR spectrum, ν, cm^{-1}: 1590 (C=N), 1675 (C=O), 3265 (N–H), 3545 (O–H). UV spectrum, λ_{max}, nm (log ε): 247 (4.38), 315 (3.50). ^{1}H NMR spectrum, δ, ppm: 11.51 s (1H, OH), 9.87 s (1H, NH), 7.60–6.96 m (8H$_{Ar}$), 3.56 t (2H, CH_2Cl, *J* 6.5 Hz), 2.37 s (3H, CH_3), 2.22 t (2H, CH_2CO, *J* 7.2 Hz), 1.85 q (2H, $CH_2CH_2CH_2$, *J* 6.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 330 (23.6) [*M*]$^+$, 277 (40.3), 235 (7.4), 226 (11.9), 209 (80.8), 208 (100), 207 (40.6). Found, %: C 65.27; H 5.84; N 8.34. $C_{18}H_{19}ClN_2O_2$. Calculated, %: C 65.35; H 5.79; N 8.47.

***N*-{4-Bromo-2-[(*E*)-(hydroxyimino)(phenyl)-methyl]phenyl}-4-chlorobutanamide (IIb)** was obtained from *anti-o*-(4-chlorobutyryl)-5-bromo-2-(4-chlorobutyryl)aminobenzophenone oxime (**Vb**) similarly to compound **IIa**. Yield 1.25 g (98%), mp 115–117°C. IR spectrum, ν, cm^{-1}: 1600 (C=N), 1675 (C=O), 3255 (N–H), 3540 (O–H). UV spectrum, λ_{max}, nm (log ε): 245 (4.36), 313 (3.54). ^{1}H NMR spectrum, δ, ppm: 11.74 s (1H, OH), 10.19 s (1H, NH), 7.87–7.23 m (8H$_{Ar}$), 3.56 t (2H, CH_2Cl, *J* 6.5 Hz), 2.21 t (2H, CH_2CO, *J* 7.2 Hz), 1.83 q (2H, $CH_2CH_2CH_2$, *J* 7.0 Hz). Mass spectrum, *m/z* (I_{rel}, %): 396 (19.6) [*M*]$^+$, 394 (14.2), 343 (9.3), 341 (8.9), 292 (13.8), 290 (13.7), 275 (49.4), 274 (100), 273 (54.6). Found, %: C 51.45; H 4.12; N 7.09. $C_{17}H_{16}BrClN_2O_2$. Calculated, %: C 51.60; H 4.08; N 7.08.

1-{2-[(*Z*)-(Hydroxyimino)(phenyl)methyl]-4-methylphenyl}pyrrolidin-2-one (IIIa). To a solution of 7 g (21.2 mmol) of compound **Ia** in 50 ml of dioxane was added dropwise while stirring a solution of 0.93 g (23.3 mmol) of NaOH in 20 ml of water. After stirring for 8 h the reaction mixture was poured into water, the separated precipitate was filtered off, washed with water on the filter, dried, and recrystallized from benzene. Yield 2.81 g (45%), mp 165–170°C. IR spectrum, ν, cm^{-1}: 1600 (C=N), 1685 (C=O), 3550 (O–H). UV spectrum, λ_{max}, nm (log ε): 227 (4.28). ^{1}H NMR spectrum, δ, ppm: 11.36 s (1H, OH), 7.40–7.03 m (8H$_{Ar}$), 3.50 t (2H, CH_2N, *J* 6.9 Hz), 2.32 s (3H, CH_3), 2.06 t (2H, CH_2CO, *J* 7.9 Hz), 1.73 q (2H, $CH_2CH_2CH_2$, *J* 7.3 Hz). Mass spectrum, *m/z* (I_{rel}, %): 294 (2.8) [*M*]$^+$, 277 (100), 276 (10.0), 263 (17.8), 260 (19.2), 235 (16.5). Found, %: C 73.40; H 6.24; N 9.48. $C_{18}H_{18}N_2O_2$. Calculated, %: C 73.45; H 6.16; N 9.52.

Compounds **IIIb–IIId, IVa**, and **IVb** were obtained in the same way.

1-{2-[(*Z*)-(Hydroxyimino)(phenyl)methyl]-4-chlorophenyl}pyrrolidin-2-one (IIIb) was obtained by treating with NaOH compound **Ib**. Yield 65%, mp 162–165°C. IR spectrum, ν, cm^{-1}: 1580 (C=N), 1680 (C=O), 3540 (O–H). UV spectrum, λ_{max}, nm (log ε): 247 (4.32). ^{1}H NMR spectrum, δ, ppm: 11.48 s (1H, OH), 7.51–7.24 m (8H$_{Ar}$), 3.50 t (2H, CH_2N, *J* 6.7 Hz), 2.06 t (2H, CH_2CO, *J* 7.8 Hz), 1.74 q (2H, $CH_2CH_2CH_2$, *J* 7.3 Hz). Mass spectrum, *m/z* (I_{rel}, %): 314 (4.6) [*M*]$^+$, 300 (19.8), 299 (100.0), 298 (62.8), 285 (9.1), 283 (30.8), 282 (9.7). Found, %: C 64.78; H 4.83; N 8.91. $C_{17}H_{15}ClN_2O_2$. Calculated, %: C 64.87; H 4.80; N 8.90.

1-{4-Bromo-2-[(*Z*)-(hydroxyimino)(phenyl)-methyl]phenyl}pyrrolidin-2-one (IIIc) was obtained by treating with NaOH compound **Ic**. Yield 68%, mp 189–191°C. IR spectrum, ν, cm^{-1}: 1585 (C=N), 1680 (C=O), 3545 (O–H). UV spectrum, λ_{max}, nm (log ε): 225 (4.44). ^{1}H NMR spectrum, δ, ppm: 11.58 s (1H, OH), 7.70–7.33 m (8H$_{Ar}$), 3.49 t (2H, CH_2N, *J* 6.9 Hz), 2.06 t (2H, CH_2CO, *J* 7.9 Hz), 1.71 q (2H, $CH_2CH_2CH_2$, *J* 7.3 Hz). Mass spectrum, *m/z* (I_{rel}, %): 360 (2.6) [*M*]$^+$, 344 (17.5), 343 (85.0), 342 (21.9), 341 (100), 327 (7.5). Found, %: C 56.83; H 4.18; N 7.85. $C_{17}H_{15}BrN_2O_2$. Calculated, %: C 56.84; H 4.21; N 7.80.

1-{4-Bromo-2-[(*E*)-(hydroxyimino)(2-chlorophenyl)methyl]phenyl}pyrrolidin-2-one (IIId) was obtained by treating with NaOH compound **Id**. Yield 70%, mp 210–214°C. IR spectrum, ν, cm^{-1}: 1600 (C=N), 1690 (C=O), 3555 (O–H). UV spectrum, λ_{max}, nm (log ε): 230 (4.41). ^{1}H NMR spectrum, δ, ppm: 11.79 s (1H, OH), 7.73–7.20 m (7H$_{Ar}$), 3.33 t (2H, CH_2N, *J* 6.9 Hz), 2.06 t (2H, CH_2CO, *J* 7.9 Hz), 1.58 q (2H, $CH_2CH_2CH_2$, *J* 7.5 Hz). Mass spectrum, *m/z* (I_{rel}, %): 394 (3.8) [*M*]$^+$, 379 (27.8), 378 (21.7), 377 (100), 376 (19.3), 375 (93.7). Found, %: C 51.83; H 3.62; N 7.08. $C_{17}H_{14}BrClN_2O_2$. Calculated, %: C 51.87; H 3.58; N 7.12.

1-{2-[(*Z*)-(Hydroxyimino)(phenyl)methyl]-phenyl}pyrrolidin-2-one (IIIe) was obtained by treating with 4-chlorobutyryl chloride *syn*-2-aminobenzophenone oxime in the presence of excess NaOH (2.5 equiv) by the procedure analogous to the preparation of compound **Ia**. In this case the synthesis of pyrrolidine oxime **IIIe** was carried out directly from 2-aminobenzophenone oxime without isolation of its unstable monoacyl derivative. Yield 32%, mp 165–167°C. IR spectrum, ν, cm^{-1}: 1595 (C=N), 1680 (C=O), 3555 (O–H). UV spectrum, λ_{max}, nm, (log ε): 247 (4.21). ^{1}H NMR spectrum,

δ, ppm: 11.26 s (1H, OH), 7.47–7.21 m ($9H_{Ar}$), 3.54 t (2H, CH_2N, *J* 6.9 Hz), 2.07 t (2H, CH_2CO, *J* 7.9 Hz), 1.77 q (2H, $CH_2CH_2CH_2$, *J* 7.5 Hz). Mass spectrum, *m/z* (I_{rel}, %): 280 (3.5) $[M]^+$, 264 (18.9), 263 (100), 249 (8.7), 246 (6.1), 235 (5.6). Found, %: C 72.80; H 5.63; N 9.89. $C_{17}H_{16}N_2O_2$. Calculated, %: C 72.84; H 5.75; N 9.99.

1-{2-[(*E*)-(Hydroxyimino)(phenyl)methyl]-4-methylphenyl}pyrrolidin-2-one (IVa) was obtained by treating with NaOH compound **IIa**. Yield 57%, mp 230–235°C. IR spectrum, ν, cm^{-1}: 1600 (C=N), 1680 (C=O), 3550 (O–H). UV spectrum, λ_{max}, nm (log ε): 223 (4.25). ^1H NMR spectrum, δ, ppm: 11.17 s (1H, OH), 7.33–7.06 m ($8H_{Ar}$), 3.27 t (2H, CH_2N, *J* 6.9 Hz), 2.35 s (3H, CH_3), 1.95 t (2H, CH_2CO, *J* 7.9 Hz), 1.51 q (2H, $CH_2CH_2CH_2$, *J* 7.4 Hz). Mass spectrum, *m/z* (I_{rel}, %): 294 (1.8) $[M]^+$, 278 (19.6), 277 (100.0), 249 (5.6), 235 (6.3), 221 (7.8), 209 (3.5). Found, %: C 73.43; H 6.10; N 9.48. $C_{18}H_{18}N_2O_2$. Calculated, %: C 73.45; H 6.16; N 9.52.

1-{4-Bromo-2-[(*E*)-(hydroxyimino)(phenyl)-methyl]phenyl}pyrrolidin-2-one (IVb) was obtained by treating with NaOH compound **IIb**. Yield 70%, mp 216–220°C. IR spectrum, ν, cm^{-1}: 1575 (C=N), 1685 (C=O), 3545 (O–H). UV spectrum, $\lambda_{max.}$, nm (log ε): 240 (4.24). ^1H NMR spectrum, δ, ppm: 11.54 s (1H, OH), 7.68–7.23 m ($8H_{Ar}$), 3.25 t (2H, CH_2N, *J* 6.5 Hz), 1.94 t (2H, CH_2CO, *J* 7.9 Hz), 1.41 q (2H, $CH_2CH_2CH_2$, *J* 7.3 Hz). Mass spectrum, *m/z* (I_{rel}, %): 360 (0.5) $[M]^+$, 344 (15.2), 343 (99.6), 342 (15.6), 341 (100), 275 (11.3), 273 (11.8). Found, %: C 56.79; H 4.19; N 7.82. $C_{17}H_{15}BrN_2O_2$. Calculated, %: C 56.84; H 4.21; N 7.80.

(*E*)- and (*Z*)-*N*-{4-Bromo-2-[(phenyl)(4-chlorobutyryloxyimino)methyl]phenyl}-4-chlorobutanamides (Vb, VI). To a solution of 5 g (17.2 mmol) of *syn*-5-bromo-2-aminobenzophenone oxime in 30 ml of dioxane was added dropwise at stirring a solution of 4.1 ml (36.1 mmol) 4-chlorobutyryl chloride. After stirring for 3 h the reaction mixture was poured into water, the separated precipitate was filtered off, washed with water on the filter, dried, and recrystallized from benzene. Yield of compound **VI** 1.93 g (45%), mp 125–126°C. IR spectrum, ν, cm^{-1}: 1585 (C=N), 1675 ($C=O_{amide}$), 1745 ($C=O_{ester}$), 3400 (N–H). UV spectrum, λ_{max}, nm (log e): 249 (4.44). ^1H NMR spectrum, δ, ppm: 10.34 s (1H, NH), 8.09–8.41 m ($8H_{Ar}$), 4.31 t (2H, CH_2, *J* 6.7 Hz), 4.18 t (2H, CH_2, *J* 6.7 Hz), 3.22 t (2H, CH_2, *J* 2.8 Hz), 2.89 t (2H, CH_2, *J* 6.4 Hz), 2.64 q (2H, CH_2, *J* 6.9 Hz), 2.46 q (2H, CH_2, *J* 6.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 500 (7.4) $[M]^+$, 396 (22.1), 394 (15.8), 343 (8.8), 341 (8.6), 301 (6.6), 275 (41.3), 274 (88.2), 273 (47.4), 272 (78.8), 105 (75.7). Found, %: C 50.35; H 4.32; N 5.35. $C_{21}H_{21}BrCl_2N_2O_3$. Calculated, %: C 50.42; H 4.23; N 5.60.

The mother liquor was passed through a column packed with silica gel using benzene as eluent. Yield of compound **Vb** 1.33 g (31%), mp 85–90°C. IR spectrum, ν, cm^{-1}: 1595 (C=N), 1680 ($C=O_{amide}$), 1755 ($C=O_{ester}$), 3245 (N–H). UV spectrum, λ_{max}, nm (log ε): 243 (4.56), 325 (3.75). ^1H NMR spectrum, δ, ppm: 10.80 s (1H, NH), 8.05–8.46 m ($8H_{Ar}$), 4.33 t (2H, CH_2, *J* 5.6 Hz), 4.24 t (2H, CH_2, *J* 6.5 Hz), 3.27 t (2H, CH_2, *J* 7.3 Hz), 2.90 t (2H, CH_2, *J* 7.2 Hz), 2.67 q (2H, CH_2, *J* 6.2 Hz), 2.52 q (2H, CH_2, *J* 5.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 500 (10.9) $[M]^+$, 396 (25.4), 394 (18.9), 343 (4.6), 341 (6.2), 301 (4.1), 275 (41.4), 274 (96.5), 273 (52.0), 272 (85.6), 105 (77.6). Found, %: C 50.25; H 4.40; N 5.45. $C_{21}H_{21}BrClN_2O_{32}$. Calculated, %: C 50.42; H 4.23; N 5.60.

Oximes of 5-substituted 2-aminobenzophenones were obtained previously [5].

REFERENCES

1. Kulikov, O.V., Pavlovskii, V.I., and Andronati, S.A., *Khim. Geterotsikl. Soedin.,* 2005, p. 1763.
2. Kulikov, O.V., Andronati, S.A., Pavlovskii, V.I., Mazepa, O.V., and Kabanova, T.A., *Vestn. ONU, Ser. Khim*., 2000, vol. 5, p. 68.
3. Andronati, S.A., Simonov, Yu.A., Pavlovskii, V.I., Kulikov, O.V., Gdanets, M., and Mazepa, A.V., *Zh. Obshch. Khim.,* 2005, vol. 75, p. 969.
4. Kulikov, O.V. and Mazepa, A.V., *Khim. Geterotsikl. Soedin*., 2007, p. 1043.
5. Pavlovskii, V.I., Kulikov, O.V., Karaseva, T.L., Kabanova, T.A., Mazepa, A.V., and Andronati, S.A., *Ukr. Khim. Zh.,* 1998, vol. 64, p. 123.
6. *SHELXTL*, ver.1, Madison: Bruker AXS Inc., 1998.
7. Sheldrick, G.M., *SHELXS-97. Program for the Solution of Crystal Structures*, Univ. Göttingen, Germany, 1997.
8. Sheldrick, G.M., *SHELXL-97. Program for the Refinement of Crystal Structures,* Univ. Göttingen, Germany, 1997.