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Reaction of 6-Chloropyrimidine-2,4(1*H*,3*H*)-dione with 2-(Chloromethoxy)ethyl Benzoate. Synthesis of New Acyclic Nucleosides

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Abstract—New acyclic pyrimidine nucleosides, analogs of the antiviral drug acyclovir, were synthesized starting from 6-chloropyrimidine-2,4(1*H*,3*H*)-dione. The addition of side carbohydrate chain to the N^1 or N^3 atoms of the heterocyclic base with formation of N^1- and N^3-substituted isomers, respectively, was confirmed by ^{1}H NMR and X-ray analysis. N^1- and N^3-Substituted 6-chloropyrimidine-2,4(1*H*,3*H*)-diones were subjected to amination with secondary amines, and cyclocondensation of 6-allylamino derivative afforded N^1-substituted pyrido[2,3-*d*]pyrimidine.

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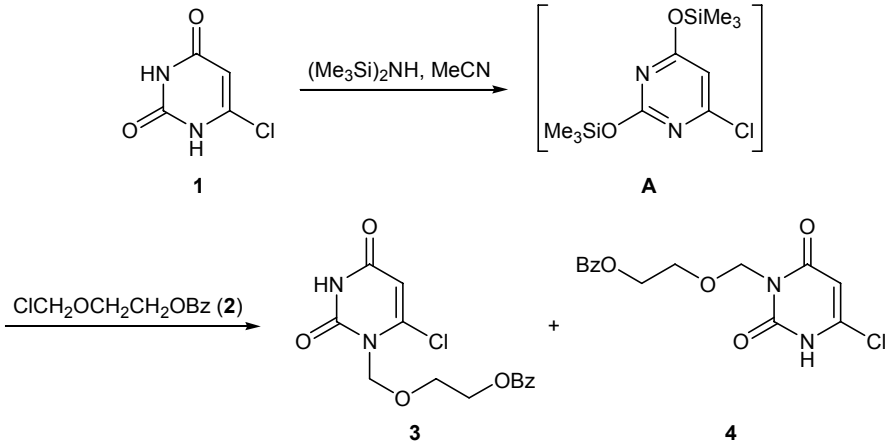
The discovery of potent antiviral properties of acyclic nucleosides such as acyclovir {9-[(2-hydroxyethoxy)methyl]-9*H*-guanine} [1, 2] and ganciclovir {9-[(1,3-dihydroxypropan-2-yloxy)methyl]guanine} [3, 4] has stimulated search for new acyclic nucleosides in the pyrimidine and fused pyrimidine series. However, compounds synthesized as a result of these studies did not exceed acyclovir in therapeutic efficiency. In the present article we describe the synthesis and X-ray diffraction study of some acyclic pyrimidine nucleosides.

As starting compound for the synthesis of targeted acyclic nucleosides we selected 6-chloropyrimidine-2,4(1*H*,3*H*)-dione (**1**) which was prepared according to the procedure reported in [5]. To append a side acyclic component we used 2-(chloromethoxy)ethyl benzoate

Scheme 1.



1 **A** **3** **4**

2. It was synthesized in two steps including the reaction of sodium benzoate with ethylene chlorohydrin to obtain 2-hydroxyethyl benzoate which was subjected to chloromethylation by treatment with paraformaldehyde in dichloroethane while passing dry gaseous hydrogen chloride [6, 7].

Freshly distilled chloride **2** was brought into reaction with intermediate bis(trimethylsilyl) derivative **A** in acetonitrile in the presence of $SnCl_4$ [8]. From the reaction mixture we isolated two isomeric N^1- and N^3-substituted compounds **3** and **4** melting at 123–124 and 169–170°C, respectively (51 and 10%; Scheme 1). The ^1H NMR spectra of **3** and **4** were almost identical, and it was difficult to distinguish them as N^1- or N^3-isomer. Unfortunately, we failed to obtain single crystals of **3** and **4** suitable for X-ray analysis.

On the other hand, by treatment of **3** and **4** with primary and secondary amines we synthesized the corresponding 6-amino derivatives **5a**–**5e** and **6** (Scheme 2) which gave high-quality single crystals. Major isomer **3** was reacted with methylamine, di-

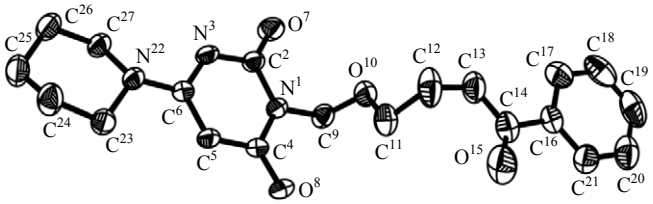


Fig. 1. Structure of the molecule of 2-{[6-(morpholin-4-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-3-yl]methoxy}ethyl benzoate (**6**) according to the X-ray diffraction data (arbitrary atom numbering); non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

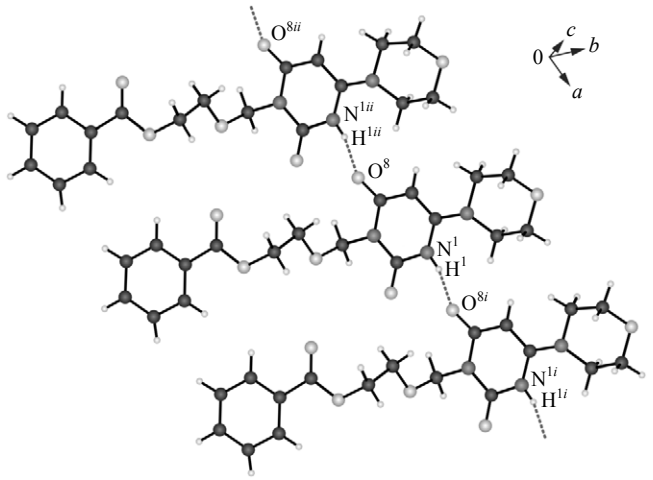
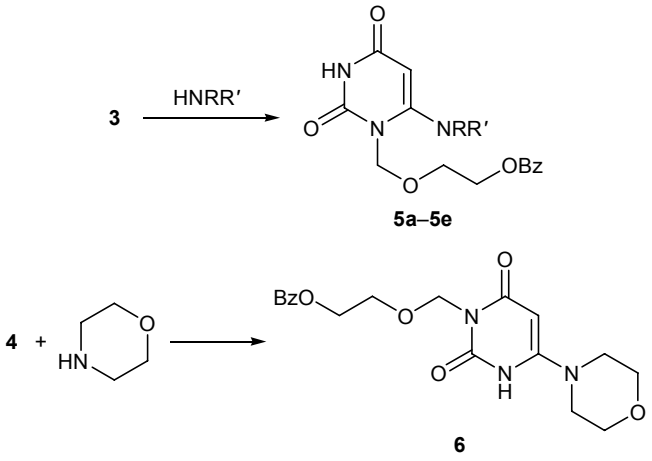


Fig. 2. One-dimensional infinite chain formed by molecules **6** in crystal along the [1 0 0] plane. Symmetry operations: *i* = 1 + *x*, *y*, *z*; *ii* = –1 + *x*, *y*, *z*.

Scheme 2.



R = H, R′ = Me (**a**); R = R′ = Et (**b**); RR′ = $(CH_2)_5$ (**c**), $(CH_2)_2O(CH_2)_2$ (**d**); R = H, R′ = CH_2=$CHCH_2$ (**e**).

ethylamine, piperidine, morpholine, and allylamine. The latter was used taking into account that 6-(allylamino)pyrimidines are convenient intermediate products for the preparation of pyrido[2,3-*d*]pyrimidines [9]. The reaction of isomer **4** (mp 169–170°C) with morpholine was carried out with the goal of comparing physical constants and fine structure of the isomeric amination products. The amination was performed in chloroform, and the reaction time depended on the amine nature.

The structure of 6-amino derivatives **5a**, **5d**, and **6** was unambiguously determined by X-ray analysis of their single crystals. The morpholine ring in molecule **6** (Fig. 1) adopts a *chair* conformation: deviations of the N^{22}, C^{23}, C^{24}, O^{25}, C^{26}, and C^{27} atoms from the mean-square plane were –0.1734(12), 0.1899(14), –0.2375(15), 0.2684(14), –0.2370(15), and 0.1896(14) Å, respectively. Molecules **6** in crystal are linked through intermolecular hydrogen bonds N^1–$H^1\cdots O^8$ [2.803(2) Å] to form infinite chains along the [1 0 0] axis (Fig. 2). In the three-dimensional crystal packing the chains are held together via van der Waals interactions. The structure of compound **6** was also confirmed by the 2D NOESY experiment which displayed coupling between the NH proton and NCH_2 protons of the morpholine ring.

Molecule **5d** (Fig. 3) is structurally related to **6**. In both molecules, the morpholine ring is attached to C^6. The difference is the position of the alkyl benzoate substituent which is linked to N^3 in **6** and to N^1 in **5d**. As in molecule **6**, the morpholine ring in **5d** has a *chair* conformation with the following deviations of atoms from the mean-square plane: 0.2440(15),

–0.2379(19), 0.2336(21), –0.2340(19), 0.2295(20), and –0.2352(19) Å for N^{22}, C^{23}, C^{24}, O^{25}, C^{26}, and C^{27}, respectively. Unlike compound **6**, molecules **5d** in crystal are linked to dimers by intermolecular hydrogen bond N^3–$H^3\cdots O^8$ 2.851(3) Å (Fig. 4).

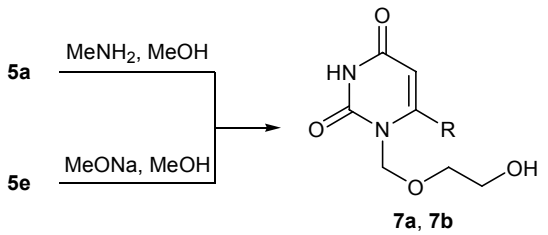
Molecule **5a** differs from **5d** and **6** by the presence of a methylamino group instead of morpholine ring on C^6. Its structure is closer to the structure of **5d** rather than **6** since the alkyl benzoate group in **5a** is linked to N^1 (Fig. 5). Molecule **5a** is characterized by intramolecular hydrogen bond N^{22}–$H^{22}\cdots O^{10}$ [2.999(2) Å]. Like compound **5d**, molecules **5a** in crystal form dimers via double hydrogen bonding N^3–$H^3\cdots O^8$ [2.809(2) Å]. However, the dimers are not isolated but are linked to infinite chains along the [1 1 –1] plane through double intermolecular hydrogen bonds N^{22}–$H^{22}\cdots O^{15}$ [3.008(2) Å] (Fig. 6).

According to the 2D NOESY data, the structures of **5b** and **5e** are similar to structure **5a**, i.e., the alkyl benzoate group is attached to N^1, and the amino group, to C^6. Compound **5b** displayed NOE between the N^1CH_2 and $C^6N(CH_2)_2$ protons, while correlation between the N^1CH_2 protons and 6-NH was observed for compound **5e**.

Thus, the X-ray diffraction study showed that the amination of 6-chloropyrimidine-2,4-dione **3** with lower melting point (123–124°C) yields exclusively N^1-substituted isomers **5a** and **5d** and that N^3-substituted analog **6** is formed from higher-melting isomer **4** (mp 169–170°C). These findings confirm the assignment of structures **3** and **4** (Scheme 1).

The benzoyl protection was removed from compounds **5a** and **5e** in two ways, by passing gaseous methylamine through a solution of **5a** in methanol or by heating compound **5e** in anhydrous methanol in the presence of sodium methoxide. We thus obtained 1-substituted 6-(methylamino)- and 6-(allylamino)-pyrimidine-2,4-diones **7a** and **7b**, respectively (Scheme 3). 6-Allylamino derivative **5e** was also subjected to intramolecular cyclization with formation

Scheme 3.



R = MeNH (**a**), CH_2=$CHCH_2NH$ (**b**).

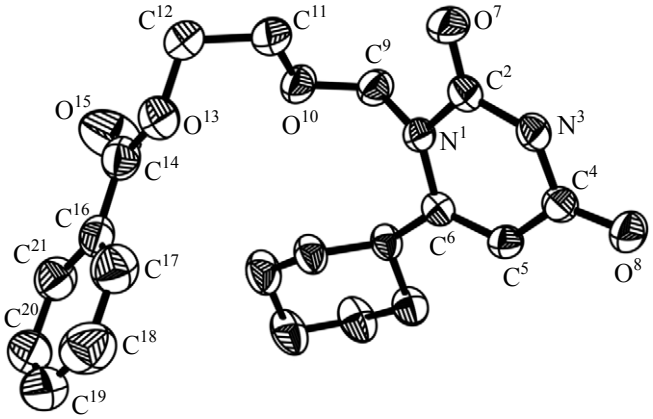


Fig. 3. Structure of the molecule of 2-{[6-(morpholin-4-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl]methoxy}ethyl benzoate (**5d**) according to the X-ray diffraction data (arbitrary atom numbering); non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

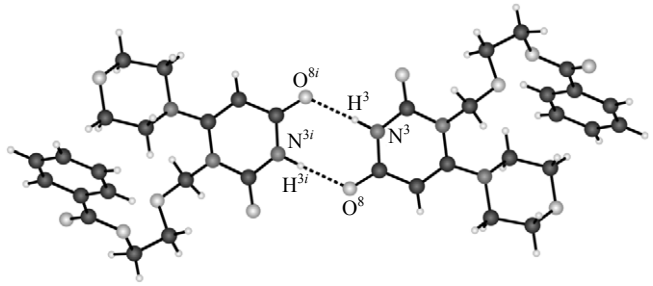


Fig. 4. Dimer formed by 2-{[6-(morpholin-4-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl]methoxy}ethyl benzoate (**5d**) in crystal; intermolecular hydrogen bonds are shown with dashed lines. Symmetry operation: $i = -x, -y, -z$.

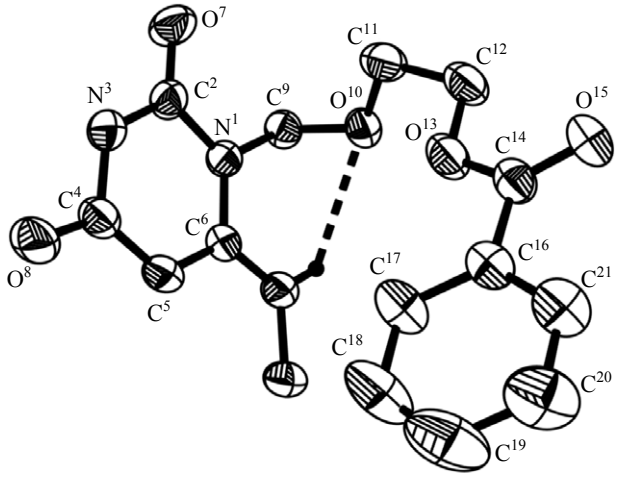


Fig. 5. Structure of the molecule of 2-{[6-(methylamino)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl]methoxy}ethyl benzoate (**5a**) according to the X-ray diffraction data (arbitrary atom numbering); non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%. Intramolecular hydrogen bond is shown with a dashed line.

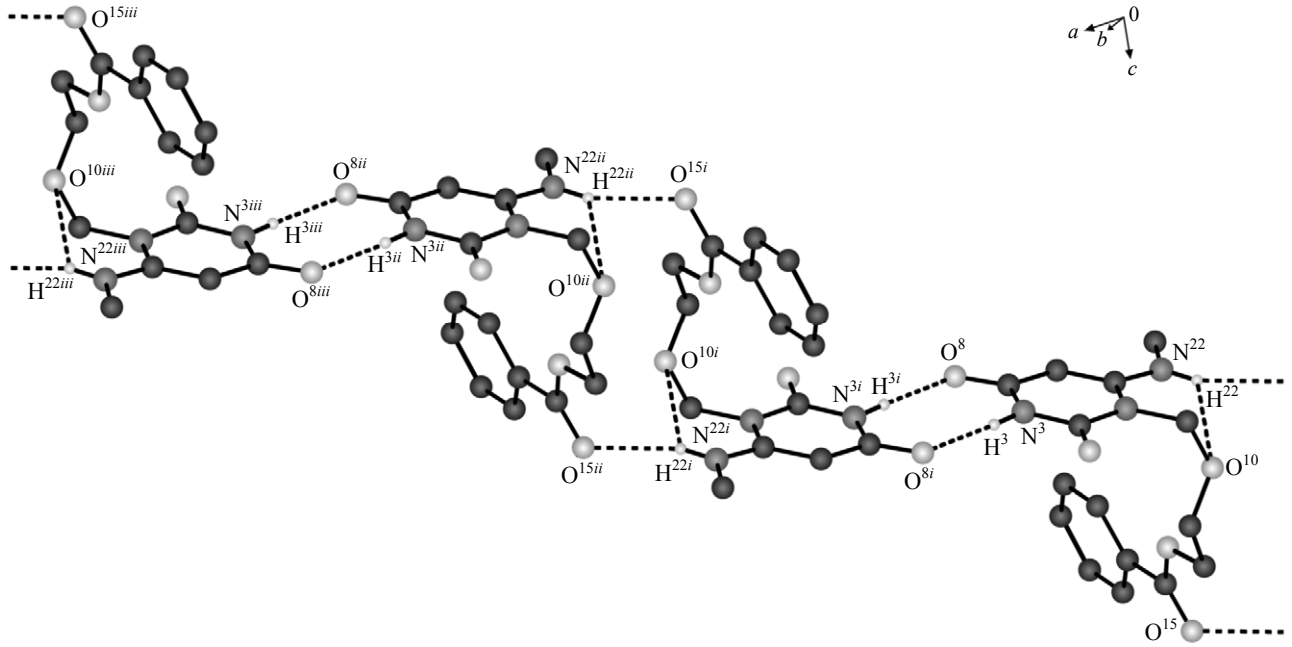
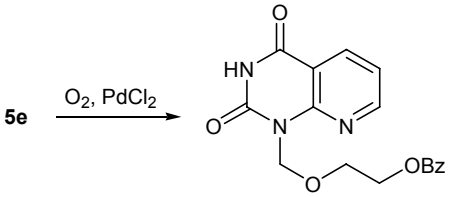


Fig. 6. Dimers of 2-{[6-(methylamino)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl]methoxy}ethyl benzoate (**5a**) molecules linked to an infinite chain along the [1 1 –1] plane. Hydrogen bonds are shown with dashed lines. Symmetry operations: $i = 1 - x, 1 - y, 1 - z$; $ii = 1 + x, 1 + y, -1 + z$; $iii = 2 - x, 2 - y, -z$.

of pyrido[2,3-*d*]pyrimidine **8** by heating in dioxane in a stream of oxygen in the presence of palladium(II) chloride (Scheme 4).

Scheme 4.



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In summary, we have developed procedures for the synthesis of new 1- and 3-substituted acyclic pyrimidine nucleosides on the basis of 6-chloropyrimidine-2,4(1*H*,3*H*)-dione. The synthesized compounds attract interest as both potential biologically active substances and substrates for further transformations into fused pyrido[2,3-*d*]pyrimidines.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian Mercury-300 spectrometer (300 MHz) from solutions in DMSO-d_6–CCl_4 (1:3) using tetramethylsilane as internal reference. The melting points were determined on a Boetius 72/2064 micro hot stage. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates; spots were visualized by UV irradiation.

The X-ray diffraction data for single crystals of **5a**, **5d**, and **6** were obtained at room temperature on an Enraf–Nonius CAD-4 automated diffractometer. All calculations were performed using SHELXTL software package [10]. The structures were solved by the direct method. The positions of hydrogen atoms were determined from the Fourier difference maps. The structures were refined by the full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms and isotropic approximation for hydrogen atoms. The sets of crystallographic data for compounds **5a**, **5d**, and **6** were deposited as CIF files to the Cambridge Crystallographic Data Centre (see table).

6-Chloropyrimidine-2,4(1*H*,3*H*)-diones 3 and 4. Hexamethyldisilazane, 15 mL, was added to a solution of 6 g (40 mmol) of chloropyrimidine **1** in 20 mL of anhydrous acetonitrile, and the mixture was heated under reflux until it became homogeneous (~1 h). The solution was evaporated to dryness, 100 mL of anhydrous acetonitrile and 8.6 g (40 mmol) of chloride **2** were added to the oily residue (bis-silyl derivative **A**), the resulting solution was cooled to –3 to –4°C, and a solution of 10.4 g (40 mmol) of tin(IV) chloride in 50 mL of anhydrous acetonitrile was added dropwise over a period of 1 h. The mixture was stirred for 2–3 h more at –3 to –4°C and left overnight. It was then

Crystallographic data and parameters of X-ray diffraction experiments for compounds **5a**, **5d**, and **6**[a]

Parameter	**5a**	**5d**	**6**
CCDC entry no.	945514	945511	945513
Formula	$C_{15}H_{17}N_3O_5$	$C_{18}H_{21}N_3O_6$	$C_{18}H_{21}N_3O_6$
Molecular weight	319.32	375.38	375.38
a, Å	9.1336(18)	5.9770(12)	6.6382(13)
b, Å	9.1637(18)	12.411(3)	11.344(2)
c, Å	9.891(2)	13.355(3)	12.512(3)
α, deg	81.39(3)	71.73(3)	74.44(3)
β, deg	74.57(3)	77.94(3)	81.86(3)
γ, deg	73.92(3)	77.27(3)	75.18(3)
V, Å^3	764.2(3)	907.1(4)	874.8(4)
d_{calc}, g/cm^3	1.388	1.374	1.425
μ(MoK_α), mm^{-1}	0.106	0.104	0.108
F(000)	336	396	396
Crystal dimensions, mm	0.35×0.40×0.42	0.25×0.32×0.38	0.32×0.38×0.40
$\theta_{min.}$, θ_{max}, deg	2.1, 30.0	1.6, 30.0	1.7, 30.0
Scan range	$0 \le h \le 12$ $-12 \le k \le 12$ $-13 \le l \le 13$	$0 \le h \le 8$ $-17 \le k \le 17$ $-18 \le l \le 18$	$0 \le h \le 9$ $-15 \le k \le 15$ $-17 \le l \le 17$
Total number of reflections	4703	5748	5501
Number of independent reflections	4442	5279	5091
Number of reflections with $I > 2\sigma(I)$	2758	2850	3211
Number of variables	276	328	328
R	0.0496	0.0557	0.0497
wR^2	0.1308	0.1452	0.1372
Goodness of fit *S*	1.02	1.00	1.02

[a] MoK_α radiation, λ 0.71073 Å; temperature 293 K; triclinic crystal system, space group *P*-1, *Z* = 2; weight scheme $w = 1/[\sigma^2(Fo^2) + (0.0620P)^2 + 0.1380P]$, where $P = (Fo^2 + 2Fc^2)/3$.

poured into 300 mL of water and extracted with chloroform (3×100 mL), the combined extracts were dried over sodium sulfate, the solvent was distilled off, the residue was treated with 50 mL of diethyl ether, and the crystalline product was filtered off, washed with 50 mL of diethyl ether, and dried. Recrystallization of the crude product from acetone gave crystals of N^3-isomer **3**, and N^1-isomer **4** was isolated from the mother liquor. Both isomers were purified by recrystallization from ethanol.

2-[(6-Chloro-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)methoxy]ethyl benzoate (3). Yield 6.6 g (51%), mp 123–124°C, R_f 0.74 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 3.90–3.94 m (2H, OCH_2), 4.38–4.42 m (2H, C**H**$_2$OCOPh), 5.44 s (2H, NCH_2O), 5.70 s (1H, 5-H), 7.38–7.45 m (2H, H_{arom}), 7.50–7.56 m (1H, H_{arom}), 7.94–7.99 m (2H, H_{arom}), 11.54 br.s (1H, NH). Found, %: C 58.35; H 4.24; N 9.37. $C_{14}H_{13}N_2O_5$. Calculated, %: C 58.13; H 4.53; N 9.68.

2-[(6-Chloro-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-3-yl)methoxy]ethyl benzoate (4). Yield 1.92 g (10%), mp 169–170°C, R_f 0.76 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 3.88–3.93 m (2H, OC**H**$_2$CH$_2$OCO), 4.35–4.40 m (2H, OCH$_2$C**H**$_2$OCO), 5.29 s (2H, NCH_2), 5.66 s (1H, =CH), 7.42–7.48 m (2H, H_{arom}), 7.53–7.60 m (1H, H_{arom}), 7.96–8.01 m (2H, H_{arom}), 12.34 br.s (1H, NH). Found, %: C 58.27; H 4.63; N 9.42. $C_{14}H_{13}N_2O_5$. Calculated, %: C 58.13; H 4.53; N 9.68.

2-[(6-Methylamino-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)methoxy]ethyl benzoate (5a). Gaseous methylamine was passed over a period of 2 h through a solution of 2.6 g (8 mmol) of compound **3** in 20 mL of chloroform. The solvent was distilled off to dryness, and the residue was recrystallized from

ethanol. Yield 1.95 g (77%), mp 169–170°C, R_f 0.57 (chloroform–ethanol, 10:1). ^{1}H NMR spectrum, δ, ppm: 2.61 d (3H, NHC**H**$_3$, J = 4.6 Hz), 3.81–3.86 m (2H, OCH_2), 4.37–4.41 m (2H, OCH_2), 4.42 d (1H, =CH, J = 2.1 Hz), 5.34 s (2H, NCH_2), 6.69 br.q (1H, NH, J = 4.6 Hz), 7.49–7.57 m (2H, H_{arom}), 7.63–7.70 m (1H, H_{arom}), 7.92–7.97 m (2H, H_{arom}), 10.54 br.d (1H, NH, J = 2.1 Hz). Found, %: C 56.27; H 5.19; N 13.32. $C_{15}H_{17}N_3O_5$. Calculated, %: C 56.42; H 5.37; N 13.16.

2-[(6-Dimethylamino-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)methoxy]ethyl benzoate (5b). A mixture of 1.3 g (4 mmol) of compound **3** and 7.3 g (100 mmol) of diethylamine in 20 mL of chloroform was heated for 7 h under reflux. The solvent was distilled off, 30 mL of methanol was added to the residue, and the mixture was kept for 7–8 h in a refrigerator. The precipitate was filtered off and washed with methanol. Yield 0.8 g (55%), mp 126–128°C, R_f 0.46 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 1.05 t [6H, $N(CH_2C\mathbf{H}_3)_2$, J = 7.0 Hz], 3.08 q [4H, $N(C\mathbf{H}_2CH_3)_2$, J = 7.0 Hz], 3.98–4.03 m (2H, OCH_2), 4.38–4.43 m (2H, OCH_2), 5.01 d (1H, =CH, J = 1.8 Hz), 5.23 s (2H, NCH_2O), 7.41–7.48 m (2H, H_{arom}), 7.53–7.60 m (1H, H_{arom}), 7.94–7.99 m (2H, H_{arom}), 10.90 br.s (1H, NH). Found, %: C 59.71; H 6.41; N 11.38. $C_{18}H_{23}N_3O_5$. Calculated, %: C 59.82; H 6.41; N 11.63.

2-{[2,4-Dioxo-6-(piperidin-1-yl)-1,2,3,4-tetrahydropyrimidin-1-yl]methoxy}ethyl benzoate (5c). A mixture of 0.65 g (2 mmol) of compound **3** and 1.7 g (20 mmol) of piperidine in 30 mL of chloroform was heated for 30 min under reflux. The solvent was distilled off, 30 mL of aqueous methanol was added to the residue, and the precipitate was filtered off, and washed with water and diethyl ether. Yield 0.6 g (80%), mp 96–98°C, R_f 0.61 (benzene–ethyl acetate, 10:1). ^{1}H NMR spectrum, δ, ppm: 1.42–1.58 m (6H, $CH_2CH_2CH_2$), 2.87–2.95 m (4H, CH_2NCH_2), 3.90–3.95 m (2H, OCH_2), 4.38–4.42 m (2H, OCH_2), 5.00 br.s (1H, =CH), 5.19 s (2H, NCH_2O), 7.49–7.56 m (2H, H_{arom}), 7.63–7.69 m (1H, H_{arom}), 7.92–7.96 m (2H, H_{arom}), 11.04 br.s (1H, NH). Found, %: C 61.23; H 6.47; N 11.34. $C_{19}H_{23}N_3O_5$. Calculated, %: C 61.11; H 6.21; N 11.25.

6-(Morpholin-4-yl)pyrimidine-2,4(1*H*,3*H*)-diones 5d and 6 (*general procedure*). A mixture of 0.65 g (2 mmol) of compound **3** or **4** and 2 g (20 mmol) of morpholine in 20 mL of chloroform was heated for 3 h under reflux. The solvent was distilled off, 20 mL of methanol was added to the residue, and the mixture was kept for 4–5 h at room temperature. The precipitate was filtered off and washed with 10 mL of methanol.

2-{[6-(Morpholin-4-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl]methoxy}ethyl benzoate (5d). Yield 0.54 g (72%), mp 162–163°C, R_f 0.62 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 2.94–3.00 m (4H, CH_2NCH_2), 3.58–3.64 m (4H, CH_2OCH_2), 3.92–3.96 m (2H, OCH_2), 4.38–4.43 m (2H, OCH_2), 5.08 s (1H, =CH), 5.23 s (2H, NCH_2O), 7.50–7.56 m (2H, H_{arom}), 7.63–7.70 m (1H, H_{arom}), 7.92–7.96 m (2H, H_{arom}), 11.12 br.s (1H, NH). Found, %: C 57.41; H 5.31; N 11.40. $C_{18}H_{21}N_3O_6$. Calculated, %: C 57.59; H 5.64; N 11.19.

2-{[6-(Morpholin-4-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-3-yl]methoxy}ethyl benzoate (6). Yield 0.16 g (21%), mp 166–167°C, R_f 0.60 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 3.22–3.27 m (4H, CH_2NCH_2), 3.63–3.68 m (4H, CH_2OCH_2), 3.87–3.91 m (2H, OCH_2), 4.35–4.39 m (2H, $COOCH_2$), 4.75 s (1H, =CH), 5.26 s (2H, OCH_2N), 7.42–7.48 m (2H, H_{arom}), 7.53–7.60 m (1H, H_{arom}), 7.97–8.02 m (2H, H_{arom}), 10.64 s (1H, NH). Found, %: C 57.28; H 5.42; N 11.37. $C_{18}H_{21}N_3O_6$. Calculated, %: C 57.59; H 5.64; N 11.19.

2-{[6-(Allylamino)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl]methoxy}ethyl benzoate (5e). A solution of 2.3 g (40.4 mmol) of allylamine in 20 mL of chloroform was added to a solution of 1.0 g (3 mmol) of compound **3** in 30 mL of chloroform, and the mixture was heated for 3–4 h under reflux. The mixture was evaporated, 20 mL of methanol was added to the residue, and the precipitate was filtered off and washed with 5 mL of methanol. Yield 0.7 g (67%), mp 131–132°C, R_f 0.41 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 3.64–3.69 m (2H, OCH_2), 3.90–3.94 m (2H, OCH_2), 4.42–4.45 m (3H, NHC**H**$_2$, =CH), 5.10 d.q (1H, =CH_2, J = 10.3, 1.6 Hz), 5.19 d.q (1H, =CH_2, J = 17.3, 1.6 Hz), 5.44 s (2H, NCH_2O), 5.76 d.d.t (1H, =CH, J = 17.3, 10.3, 5.1 Hz), 6.49 br.t (1H, NH, J = 5.5 Hz), 7.43–7.49 m (2H, H_{arom}), 7.55–7.61 m (1H, H_{arom}), 7.96–8.00 m (2H, H_{arom}), 10.34 br.s (1H, NH). Found, %: C 59.43; H 5.27; N 12.31. $C_{17}H_{19}N_3O_5$. Calculated, %: C 59.12; H 5.54; N 12.17.

1-[(2-Hydroxyethoxy)methyl]-6-(methylamino)-pyrimidine-2,4(1*H*,3*H*)-dione (7a). Gaseous methylamine was passed at 0 to –1°C through a solution of 3.2 g (0.01 mol) of compound **5a** in 50 mL of methanol until the initial compound disappeared (TLC). The

precipitate was filtered off and recrystallized from water. Yield 1.45 g (66%), mp 209–210°C, R_f 0.58 (chloroform–methanol, 1:1). ^{1}H NMR spectrum, δ, ppm: 2.74 d (3H, NCH_3, J = 4.6 Hz), 3.51–3.60 m (4H, OCH_2CH_2O), 4.43 d (1H, =CH, J = 1.6 Hz), 4.47 br.t (1H, OH, J = 4.7 Hz), 5.30 s (2H, NCH_2), 6.50 q (1H, N**H**CH_3, J = 4.6 Hz), 10.26 br.s (1H, NHCO). Found, %: C 44.37; H 6.42; N 19.53. $C_8H_{13}N_3O_4$. Calculated, %: C 44.64; H 6.09; N 19.52.

6-(Allylamino)-1-[(2-hydroxyethoxy)methyl]-pyrimidine-2,4(1*H*,3*H*)-dione (7b). A 1 N solution of sodium methoxide, 0.3 mL, was added to a solution of 0.35 g (1 mmol) of compound **5e** in 10 mL of anhydrous methanol, and the mixture was heated under reflux until the initial compound disappeared (TLC). The solvent was distilled off, the residue was treated with 10 mL of water, and the mixture was washed with 20 mL of chloroform. The aqueous phase was acidified with aqueous HCl, and the precipitate was filtered off and recrystallized from water. Yield 0.23 g (95%), mp 179–180°C, R_f 0.65 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 3.53–3.60 m (4H, OCH_2CH_2O), 3.74 t.t (2H, C**H**$_2$NH, J = 5.4, 1.6 Hz), 4.46 d (1H, =CH, J = 1.6 Hz), 4.47 br.s (1H, OH), 5.17 d.q (1H, =CH_2, J = 10.3, 1.6 Hz), 5.26 d.q (1H, =CH_2, J = 17.2, 1.6 Hz), 5.35 s (2H, NCH_2O), 5.83 d.d.t (1H, =CH, J = 17.2, 10.3, 5.4 Hz), 6.61 t (1H, N**H**CH_2, J = 5.4 Hz), 10.30 br.s (1H, NHCO). Found, %: C 49.91; H 6.47; N 17.53. $C_{10}H_{15}N_3O_4$. Calculated, %: C 49.78; H 6.27; N 17.42.

2-[(2,4-Dioxo-1,2,3,4-tetrahydropyrido[2,3-*d*]-pyrimidin-1-yl)methoxy]ethyl benzoate (8). A mixture of 0.35 g (1 mmol) of compound **5e**, 0.18 g (1 mmol) of $PdCl_2$, and 2 mL of water in 20 mL of dioxane was stirred for 8 h at 60–70°C under a stream of oxygen. The mixture was filtered and evaporated to dryness, 20 mL of chloroform was added to the residue, and the mixture was evaporated again. Methanol, 20 mL, was added to the solid residue, and the precipitate was filtered off and washed with cold methanol. Yield 0.15 g (44%), mp 164–166°C, R_f 0.60 (benzene–acetone, 1:1). ^{1}H NMR spectrum, δ, ppm: 3.97–4.01 m (2H, OCH_2CH_2OCO), 4.36–4.41 m (2H, OCH_2CH_2OCO), 5.76 s (2H, NCH_2), 7.26 d.d (1H, Py, J = 7.7, 4.8 Hz), 7.38–7.45 m (2H, H_{arom}), 7.52–7.58 m (1H, H_{arom}), 7.90–7.94 m (2H, H_{arom}), 8.32 d.d (1H, Py, J = 7.7, 1.9 Hz), 8.62 d.d (1H, Py, J = 4.8, 1.9 Hz), 11.72 br.s (1H, NH). Found, %: C 59.67; H 4.31; N 12.17. $C_{17}H_{15}N_3O_5$. Calculated, %: C 59.82; H 4.43; N 12.31.

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