

Reaction of 6-Methyluracyl Derivatives with Acetylacetone and Ethyl Acetoacetate

E. S. Krylova, V. E. Semenov, I. V. Galyametdinova,
D. R. Sharafutdinova, V. D. Akamsin, and V. S. Reznik

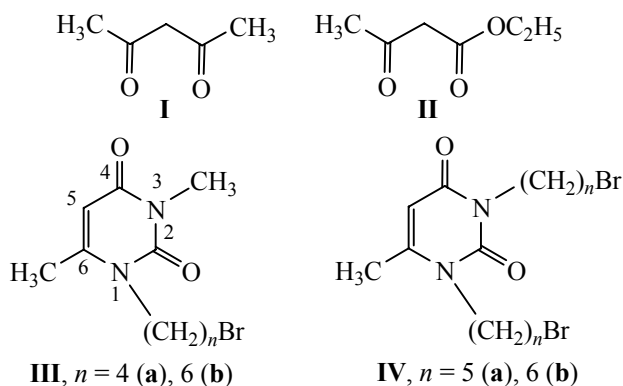
Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center, Russian Academy of Sciences,
ul. Arbuzova 8, Kazan, 420088 Tatarstan, Russia
e-mail: sve@iopc.knc.ru

Received July 9, 2009

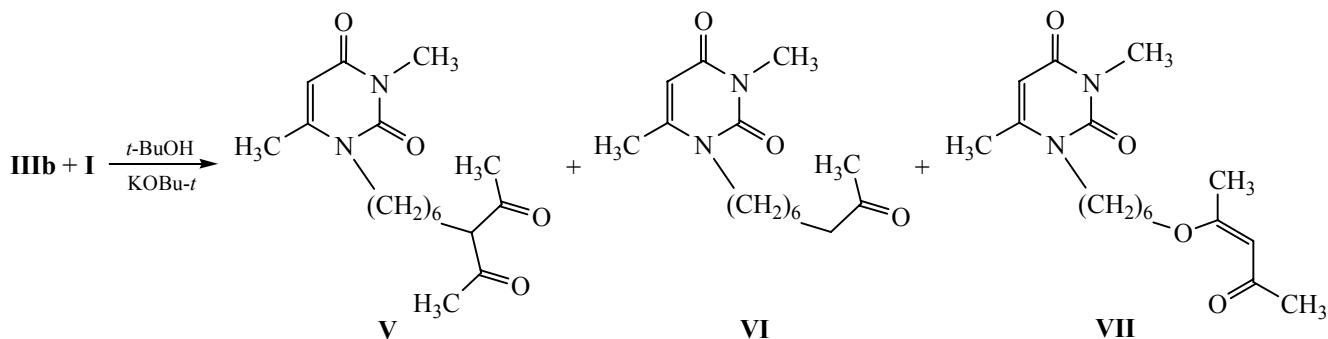
Abstract—Reaction of acetylacetone and ethyl acetoacetate with 1-(ω-bromoalkyl)-3,6-dimethyluracils and 1,3-bis(ω-bromoalkyl)-6-methyluracils lead to the formation of uracyl derivatives containing the ketone and ketoester fragments. Conditions leading to the highest yields of the compounds synthesized were found.

DOI: 10.1134/S1070363210070248

Reaction of β-diketones and β-ketoesters with ureas, guanidines, and amidines is the classic method for preparing pyrimidine derivatives [1]. If β-diketone or β-ketoester fragment is bound by means of some bridge, for example, of polymethylene chain, with the derivatives of nucleoside base, in particular, with uracyl derivatives, compound of such type may be used as starting reagents for the synthesis of a series of acyclic or macrocyclic pyrimidine derivatives. These substances may consist of the different number of pyrimidine fragments including the functional groups capable of formation of the coordination and hydrogen bonds with different charged and neutral substrates. With the purpose of synthesis of such compounds we have studied the reactions of acetylacetone **I** and ethyl acetoacetate **II** with 1-(ω-bromoalkyl)-3,6-dimethyluracils (**IIa**, **IIb**) and 1,3-bis(ω-bromoalkyl)-6-methyluracils (**IVa**, **IVb**).



Reaction of bromide **IIIb** with the compound **I** in the presence of NaOC₂H₅, KOC(CH₃)₃ or with sodium salt of compound **I** leads to the formation of several products. After performing the reaction of bromide **IIIb** with the compound **I** in boiling *tert*-butanol in presence of KOBu-*tert*. we managed to isolate pure compounds **V–VII** in 6, 14, and 2% yield respectively.



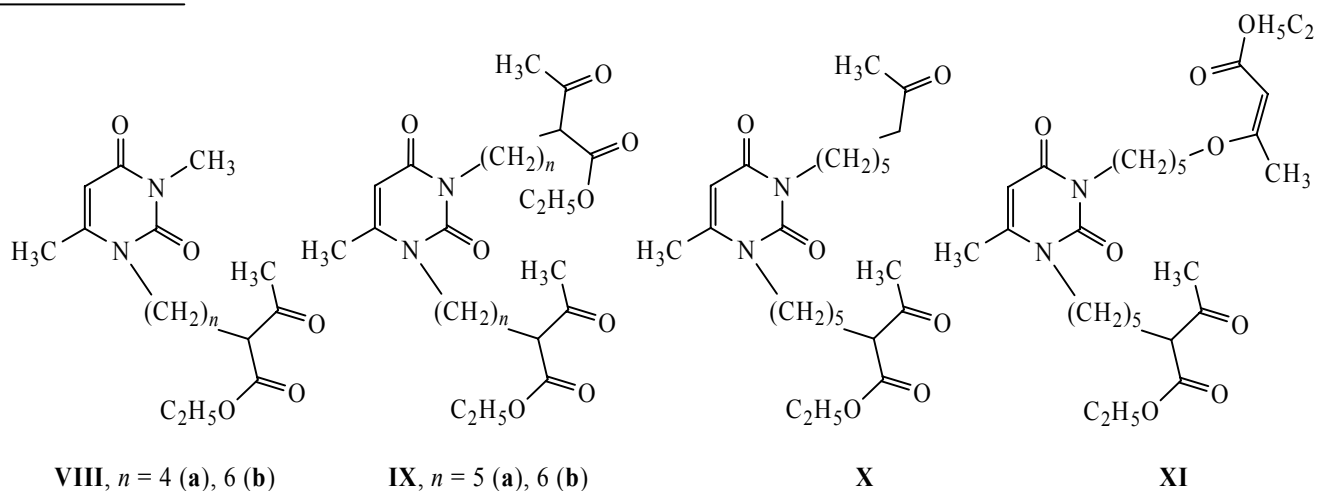
The composition of products of the reaction of bromide **IIIb** with the compound **I** and their ratio depends on the used solvent and base. Performing the reaction in dioxane in the presence of NaOC_2H_5 lead to isolation only of the starting bromide **IIIb**. Introduction of sodium salt of compound **I** in the reaction leads to formation of the product **VI** in 40% yield. Compounds **V**, **VII** were not found. Carrying out the reaction of bromide **IIIb** with compound **I** in butanol-1 in the presence of sodium ethylate leads to formation of compounds **V**, **VI** in 10 and 22% yield respectively.

Reaction of compound **IIIb** with the substance **I** is slow. Complete consumption of the starting reagent **IIIb** in different solvents according to TLC data was observed only after 50–60 h at boiling. It causes evidently the formation of the product **VI** arising from the ketonic cleavage of compound **V**. In its turn the formation of the products **V**, **VII** results from acetylacetone **I** existing as a mixture of keto-enol tautomers. Reaction of bromide **IIIb** with the ketonic form of compound **I** gives the product **VI**, and the reaction of its enol form leads to the product **VII**.

According to the IR and ^1H NMR data compound **V** exists mainly in the ketone form. In the IR spectrum of solution of the compound **V** in CHCl_3 intense bands of bond vibrations of carbonyl groups of the uracyl ring and the diketone fragment are registered at 1702 and 1657 cm^{-1} respectively. Broad unresolved base of

$\nu(\text{CH})$ lines in the range $2400\text{--}3100\text{ cm}^{-1}$ is absent as characteristic of the enol $\nu(\text{OH})$ structures [2]. In the ^1H NMR spectrum of compound **V** in CDCl_3 a triplet at 3.53 ppm and a multiplet at 1.83 ppm are observed. They belong to the proton of the keton form of diketone fragment and the protons of bridgine methylene groups at this fragment. In the ^1H NMR spectrum of compound **V** weak signal is observed at 16.7 ppm. It corresponds evidently to the OH group of enol form bound by strong intramolecular hydrogen bond. On the base of devinite intensity of this signal it may be concluded that the formation of the enol form of the compound **V** in CDCl_3 solution is approximately 2%. Note that these data seem unexpected because the part of enolic form in C-alkylsubstituted acetylacetones is rather large [3].

Reaction of bromides **IIIa**, **IIIb**, **IVa**, **IVb** with ethyl acetoacetate **II** proceeds more smoothly as compared to acetylacetone **I**. Reaction of compound **II** with the bromides **IIIa**, **IIIb**, **IVa**, **IVb** in boiling dioxane in the presence of sodium ethylate gives ketoesters **VIIIa**, **VIIIb**; **IXa**, **IXb** in 63, 41, 61, and 52% yield respectively. The rest reaction products can be evidently derived from the ketonic cleavage and from the substitution of bromine atoms with the enolic form of compound **II**. The reaction of the ester **II** with dibromide **IVa** leads to the isolation of compounds which were described by structures **X**, **XI** on the basis of physicochemical data.



Using of dioxane as a solvent and sodium ethylate as a base seems optimal because using of sodium salt of compound **II** in the reaction with dibromide **IVa** leads to the formation of a mixture of hardly separable products, and in the other solvents in the

yield of β -ketoesters **VIIIa**, **VIIIb** and **IXa**, **IXb** decreases.

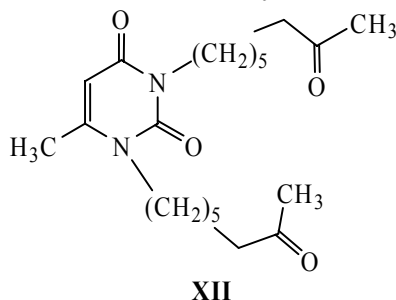
For example, performing the reaction of bromide **IIIa** with the compound **II** in DMF gives the product

VIIIa in 19% yield. Dibromide **IVa** reacts with compound **II** in ethanol and *tert*-butanol to form compound **IXa** in 23% and 37% yield respectively.

Compounds **VIIIa**, **VIIIb** and **IXa**, **IXb** are clearly identified with the help of the IR and ^1H NMR spectra. In their IR spectra intense absorption bands at 1740 cm^{-1} and 1240 cm^{-1} are observed. They are characteristic of vibrations of the C=O and C–O bonds of aliphatic esters respectively. Vibrations of the ester C=O groups are observed at higher frequencies as compared to $\nu(\text{C}=\text{O})$ of diketone **V**.

IR and ^1H NMR data show that ketoesters **VIIIa**, **VIIIb** and bis(ketoesters) **IXa**, **IXb** exist in solutions almost completely in the ketone form. No signs of the above-described enols are observed in the IR and ^1H NMR spectra of compounds **VIIIa**, **VIIIb** and **IXa**, **IXb**. Besides, in the ^1H NMR spectra of these products no signals of enol OH groups usually revealing at 14–16 ppm are observed.

Compounds **VIIIa**, **VIIIb** and **IXa**, **IXb** containing β -ketoester fragment enter the reactions characteristic of compound **II** and its alkylsubstituted derivatives. In particular, while treating with the diluted aqueous alkali solutions these substances undergo cleavage to give ketones **VI**, **XII** in 72–75% yield.



Hence, the reaction of acetylacetone and ethyl acetoacetate with 1-(ω -bromoalkyl)-5,6-dimethyluracils and 1,3-bis(ω -bromoalkyl)-6-methyluracils gives uracyl derivatives containing the ketone and ketoester fragments. The reaction with acetylacetone leads to a set of products formed in small yields, while the reaction with ethyl acetoacetate is more selective and gives target substances in moderate yields.

EXPERIMENTAL

^1H NMR spectra were taken on the Bruker Avance-400 spectrometer against internal TMS. Electron impact mass spectra were obtained on a Finnigan MAT-212 mass spectrometer at the resolution 1000. IR

spectra were recorded on a Bruker Vector 22 Fourier spectrometer under standard conditions in the range $4000\text{--}400\text{ cm}^{-1}$. Solid samples were prepared in KBr pellets. UV spectra were registered on a Specord UV-Vis (Karl Zeiss Jena) spectrophotometer.

Uncorrected melting points were measured on a Boetius heating table. TLC was carried out on Silufol-254 plates, development with the UV light. Column chromatography was carried out on SiO_2 (0.06–0.2 mm).

All the solvents and reagents used were dried.

1-(4-Bromobutyl)-3,6-dimethyluracyl (**IIIa**), 1-(6-bromohexyl)-3,6-dimethyluracyl (**IIIb**), 1,3-bis(5-bromopentyl)-6-methyluracyl (**IVa**), and 1,3-bis(6-bromohexyl)-6-methyluracyl (**IVb**) were synthesized according to the described procedures [4–6]. Sodium acetylacetonate was prepared according to [2].

Reaction of bromide **IIIa** with the compound **I**.

a. A solution of 1.8 g of compound **I** in 5 ml of *tert*-butanol was added dropwise to the boiling solution of 1.3 g of KOBu-*tert* in 10 ml of *tert*-butanol. The mixture formed was stirred for 30 min and the solution of 3.8 g of compound **IIIb** in 25 ml of *tert*-butanol and 0.4 g of KI were added. Reaction mixture was boiled with stirring until the complete consumption of **IIIb** according to TLC data (52 h). After cooling the reaction mixture the solvent was evaporated until the 1/3 of starting volume, water was added, and the mixture obtained was extracted with chloroform (2×50 ml). The extract obtained was dried over MgSO_4 , filtered, and subjected to column chromatography on SiO_2 . The column was washed in succession with petroleum ether, with 1:1 diethyl ether–petroleum ether mixture, and then with diethyl ether. Evaporation of diethyl ether fractions gave 0.49 g of **1-(8-oxononyl)-3,6-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (VI)**, yield 14%, mp 85°C . IR spectrum (KBr), ν , cm^{-1} : 3099 [$\nu(\text{C}^5\text{--H})$], 2938, 2866, 1432, 1366, 724 [ν , $\delta(\text{CH}_3)$, CH_2], 1738, 1702 1658 [$\nu(\text{C}=\text{O})$, $\nu(\text{C}^4=\text{O})$, $\nu(\text{C}^2=\text{O})$], 1623, 1535, 1471 (uracyl ring), 1322, 1210, 1037, 970 [$\nu(\text{NCN})$, C–C, C–N]. ^1H NMR spectrum (CDCl_3), δ , ppm (*J*, Hz): 1.35 m (8H, 4CH_2), 1.64 m (2H, CH_2), 2.13 (3H, CH_3), 2.24 s (3H, $\text{C}^6\text{--CH}_3$), 2.42 t (2H, CH_2 , $^3J_{\text{HH}}$ 7.3), 3.32 s (3H, NCH_3), 3.79 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.7), 5.58 s (1H, $\text{C}^5\text{--H}$). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 281 [$M + 1$] $^+$ (5), 280 [M] $^+$ (26), 265 [$M - 15$] $^+$ (69), 223 (65), 195 (25), 167 (22), 154 (81), 153 (30), 140 (96), 110 (22), 96 (100). Found, %: C 64.29; H 8.55; N 10.02.

$C_{15}H_{24}N_2O_3$. Calculated, %: C 64.26; H 8.63; N 9.99. From the subsequent diethyl ether fractions 0.25 g of **1-(7-acetyl-8-oxononyl)-3,6-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (V)** was isolated. Yield 6%, mp 78–80°C. Found: m/z 322.1890 $[M]^+$. $C_{17}H_{26}N_2O_4$. Calculated: M 322.1893. IR spectrum (CCl_4 , c 3.9 mmol), ν , cm^{-1} : 2962, 2929, 2859, 1434, 1418, 1364 [ν , $\delta(CH_3)$, CH_2], 1708, 1672 [$\nu(C=O)$, $\nu(C^4=O)$, $\nu(C^2=O)$], 1626, 1549, 1470 (uracyl ring), 1262, 1095, 1017 [$\nu(NCN)$, C–C, C–N]. UV spectrum ($CHCl_3$), λ , nm (ϵ): 268(3.83), 300 (3.45). 1H NMR spectrum ($CDCl_3$), δ , ppm (J , Hz): 1.26–1.37 m (4H, 2 CH_2), 1.65 m (4H, 2 CH_2), 1.83 m (2H, CH_2), 2.17 s (6H, 2 CH_3), 2.24 s (3H, C^6-CH_3), 3.32 s (3H, NCH_3), 3.53 t (1H, CH, $^3J_{HH}$ 7.2), 3.79 t (2H, NCH_2 , $^3J_{HH}$ 7.3), 5.59 s (1H, C^5-H). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 323 $[M + 1]^+$ (8), 322 $[M]^+$ (39), 307 $[M - 15]^+$ (39), 265 (30), 223 (63), 195 (60), 167 (36), 141 (96), 140 (97), 110 (18), 96 (97), 43(100). Found, %: C 63.25; H 8.16; N 8.66. $C_{17}H_{26}N_2O_4$. Calculated, %: C 63.33; H 8.13; N 8.69. From the subsequent diethyl ether fractions 0.06 g (2%) of **1-(7-oxa-8-methyl-8-en-9-acetylacetonyl)-3,6-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (VII)** was isolated as an oil. 1H NMR spectrum ($CDCl_3$), δ , ppm: 1.36–1.44 m (4H, 2 CH_2), 1.65–1.70 m (4H, 2 CH_2), 2.13 s (3H, CH_3), 2.15 s (3H, CH_3), 2.25 s (3H, C^6-CH_3), 3.32 s (3H, NCH_3), 3.76–3.84 m (4H, NCH_2 , OCH_2), 5.44 s (1H, CH), 5.59 s (1H, C^5-H). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 323 $[M + 1]^+$ (5), 322 $[M]^+$ (19), 307 $[M - 15]^+$ (34), 265 (31), 223 (54), 209 (56), 195 (24), 181 (65), 141 (99), 140 (93), 96 (98), 43 (100). Found, %: C 63.24; H 8.19; N 8.75. $C_{17}H_{26}N_2O_4$. Calculated, %: C 63.33; H 8.13; N 8.69.

b. To a solution of 1.5 g of compound **IIIb** in 50 ml of butanol-1, 3 ml of compound **I** and a solution of 0.12 g of sodium in 5 ml of ethanol were added. The reaction mixture was refluxed with stirring until the complete consumption of the starting substance **IIIb** according to TLC data (60 h). After cooling the reaction mixture was filtered, the filtrate was concentrated and subjected to column chromatography on SiO_2 . The column was washed in succession with 1:1 diethyl ether–petroleum ether mixture, and then with diethyl ether. From the diethyl ether fractions 0.3 g of compound **VI** was isolated. Yield 22%. From the subsequent diethyl ether fractions 0.16 g (10%) of the product **V** was isolated.

c. To a solution of 1.5 g of compound **IIIb** in 100 ml of dioxane 0.61 g of freshly prepared sodium

acetylacetonate was added, and the reaction mixture was refluxed with stirring until the complete consumption of the starting substance **IIIb** according to TLC data (46 h). After cooling the reaction mixture was filtered, the filtrate was concentrated and subjected to column chromatography on SiO_2 .

The column was washed in succession with 1:1 diethyl ether–petroleum ether mixture, and then with diethyl ether. From the diethyl ether fraction 0.62 g (44%) of compound **VI** was isolated.

1-(5-Ethoxycarbonyl-6-oxoheptyl)-3,6-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (VIIIa). To a solution of 1.4 g of compound **IIIa** in 50 ml of dioxane 3 ml of compound **II** and a solution of 0.15 g of sodium in 2 ml of absolute ethanol were added. The reaction mixture was refluxed with stirring for 7 h. After cooling the mixture obtained was filtered, the filtrate was concentrated and subjected to column chromatography on SiO_2 . The column was eluted successively with petroleum ether, with 1:1 petroleum ether–diethyl ether mixture, and then with diethyl ether. From the diethyl ether fractions 1 g (63%) of compound **VIIIa** was isolated as an oil. Found, m/z 322.1683 $[M]^+$. $C_{16}H_{24}N_2O_5$. Calculated: M 324.1685. IR spectrum, ν , cm^{-1} : 2972, 2938, 2866, 1432, 1366, 724 [ν , $\delta(CH_3)$, CH_2], 1738, 1702, 1658 [$\nu(C=O)$, $\nu(C^4=O)$, $\nu(C^2=O)$], 1623, 1535, 1471 (uracyl ring), 1322, 1243, 1210, 1152, 1095, 1036, [$\nu(NCN)$, C–C, C–N, C–O–C]. 1H NMR spectrum ($CDCl_3$), δ , ppm (J , Hz): 1.28 t (3H, CH_3 , $^3J_{HH}$ 7.0), 1.35–1.39 m (2H, CH_2), 1.66–1.70 m (2H, CH_2), 1.86–1.88 m (2H, CH_2), 2.24 c (3H, CH_3), 2.25 s (3H, C^6-CH_3), 3.32 s (3H, NCH_3), 3.43 t (1H, CH, $^3J_{HH}$ 7.4), 3.80 t (2H, NCH_2 , $^3J_{HH}$ 7.8), 4.21 q (2H, OCH_2 , $^3J_{HH}$ 7.0), 5.60 s (1H, C^5-H). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 325 $[M + 1]^+$ (12), 324 $[M]^+$ (54), 279 $[M - 45]^+$ (40), 195 (100), 140 (97), 96 (98), 43 (83). Found, %: C 59.25; H 7.44; N 8.61. $C_{16}H_{24}N_2O_5$. Calculated, %: C 59.24; H 7.46; N 8.64.

1-(7-Ethoxycarbonyl-8-oxononyl)-2,6-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (VIIIb) was prepared under the above-described conditions from 1.69 g of compound **IIIb**, 0.15 g of sodium and 3 ml of compound **II**. Yield 0.8 g (41%), oil. Found m/z 352.1999 $[M]^+$. $C_{18}H_{28}N_2O_5$. Calculated: M 352.1998. IR spectrum (CCl_4 , c 20 mmol), ν , cm^{-1} : 2970, 2934, 2860, 1432, 1366 [ν , $\delta(CH_3)$, CH_2], 1740, 1709, 1671 [$\nu(C=O)$, $\nu(C^4=O)$, $\nu(C^2=O)$], 1634, 1548, 1469 (uracyl ring), 1242, 1210, 1181, 1148, 1095, 1035 [$\nu(NCN)$, C–C, C–N, C–O–C]. UV spectrum (CCl_4), λ , nm (ϵ):

296 (4.18). ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.27 t (3H, CH_3 , $^3J_{\text{HH}}$ 7.0), 1.36 m (4H, 2 CH_2), 1.61–1.65 m (2H, CH_2), 1.82–1.85 m (2H, CH_2), 2.22 s (3H, CH_3), 2.24 s (3H, $\text{C}^6\text{--CH}_3$), 3.32 s (3H, NCH_3), 3.36 t (1H, CH, $^3J_{\text{HH}}$ 7.4), 3.78 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.8), 4.20 q (2H, OCH_2 , $^3J_{\text{HH}}$ 7.0), 5.58 s (1H, $\text{C}^5\text{--H}$). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 353 [$M + 1$] $^+$ (3), 352 [M] $^+$ (8), 337 [$M - 15$] $^+$ (23), 223 (72), 140 (98), 96 (100), 41 (76). Found, %: C 61.37; H 7.98; N 7.91. $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_5$. Calculated, %: C 61.34; H 8.01; N 7.95

The reaction of compounds **IVa** and **II** was carried out under the conditions of synthesis of compound **VIIIa** using 2.0 g of compound **IVa**, 0.23 g of sodium and 6 ml of compound **II**. From the first diethyl ether fractions 0.15 g (6%) of **1-(6-ethoxycarbonyl-7-oxononyl)-3-(6-oxa-7-methyl-7-en-8-ethoxycarbonyloctyl)-6-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (XI)** was obtained as an oil. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.25 m (6H, 2 CH_3), 1.38 m (4H, 2 CH_2), 1.64 m (4H, 2 CH_2), 1.82–1.92 m (4H, 2 CH_2), 2.21 s (3H, CH_3), 2.23 s (3H, CH_3), 2.24 s (3H, $\text{C}^6\text{--CH}_3$), 3.36 t (1H, CH, $^3J_{\text{HH}}$ 7.4), 3.78 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.8), 3.88–3.92 m (4H, NCH_2 , OCH_2), 4.12 q [2H, $\text{C}(\text{O})\text{OCH}_2$, $^3J_{\text{HH}}$ 6.7], 4.18 q [2H, $\text{C}(\text{O})\text{OCH}_2$, $^3J_{\text{HH}}$ 7.2], 5.49 s (1H, CH), 5.56 s (1H, $\text{C}^5\text{--H}$). Found, %: C 61.92; H 8.00; N 5.27. $\text{C}_{27}\text{H}_{42}\text{N}_2\text{O}_8$. Calculated, %: C 62.05; H 8.10; N 5.36. From the subsequent diethyl ether fractions 1.53 g (61%) of **1,3-bis(6-ethoxycarbonyl-7-oxooctyl)-6-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (IXa)** was obtained as an oil. Found: m/z 522.2939 [M] $^+$. $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_5$. Calculated: M 522.2941. IR spectrum, ν , cm^{-1} : 2970, 2936, 2861, 1433, 1362, 726 [ν , $\delta(\text{CH}_3)$, CH_2], 1739, 1713, 1661 [$\nu(\text{C}=\text{O})$, $\nu(\text{C}^4=\text{O})$, $\nu(\text{C}^2=\text{O})$], 1622, 1536, 1467 (uracyl ring), 1241, 1210, 1152, 1096, 1026, [$\nu(\text{NCN})$, C–C, C–N, C–O–C]. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.27 m (6H, 2 CH_3), 1.34–1.37 m (4H, 2 CH_2), 1.61–1.64 m (4H, 2 CH_2), 1.82–1.85 m (4H, 2 CH_2), 2.21 s (6H, 2 CH_3), 2.23 s (3H, $\text{C}^6\text{--CH}_3$), 3.37–3.42 m (2H, 2 CH), 3.77 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.8), 3.89 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.5), 4.16–4.21 m (4H, 2 OCH_2), 5.60 s (1H, $\text{C}^5\text{--H}$). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 523 [$M + 1$] $^+$ (28), 522 [M] $^+$ (10), 493 [$M - 29$] $^+$ (60), 363 (43), 279 (60), 237 (47), 195 (65), 167 (55), 140 (67), 127 (83), 96 (86), 43 (100). Found, %: C 61.95; H 8.12; N 5.32. $\text{C}_{27}\text{H}_{42}\text{N}_2\text{O}_8$. Calculated, %: C 62.05; H 8.10; N 5.36. From the subsequent diethyl ether fractions 0.1 g (4%) of **1-(6-ethoxycarbonyl)-3-(7-oxooctyl)-6-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine X** was obtained as an oil. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): ^1H NMR spectrum

(CDCl_3), δ , ppm (J , Hz): 1.28 t (3H, CH_3 , $^3J_{\text{HH}}$ 7.0), 1.34 m (6H, 3 CH_2), 1.58–1.64 m (4H, 2 CH_2), 1.83–1.86 m (2H, CH_2), 2.13 s (3H, CH_3), 2.21 s (3H, $\text{C}^6\text{--CH}_3$), 2.42 t (2H, CH_2 , $^3J_{\text{HH}}$ 7.0), 3.38 t (1H, CH, $^3J_{\text{HH}}$ 7.2), 3.77 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.8), 3.89 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.7), 4.17–4.19 q (2H, OCH_2 , $^3J_{\text{HH}}$ 7.2), 5.55 s (1H, $\text{C}^5\text{--H}$). Found, %: C 63.86; H 8.55; N 6.19. $\text{C}_{24}\text{H}_{38}\text{N}_2\text{O}_6$. Calculated, %: C 63.97; H 8.50; N 6.22.

1,3-Bis(7-ethoxycarbonyl-8-oxononyl)-6-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (IXb) was obtained analogously to compound **VIIIa** from 1.5 g of compound **IVb**, 0.14 g of sodium, and 3 ml of compound **II** as an oil. Yield 0.90 g (51%). IR spectrum (CCl_4 , c 3.9 mmol), ν , cm^{-1} : 2980, 2935, 2860, 1432, 1357 [ν , $\delta(\text{CH}_3)$, CH_2], 1741, 1717, 1667 [$\nu(\text{C}=\text{O})$, $\nu(\text{C}^4=\text{O})$, $\nu(\text{C}^2=\text{O})$], 1625, 1544, 1467 (uracyl ring), 1242, 1209, 1179, 1097, 1034 [$\nu(\text{NCN})$, C–C, C–N, C–O–C]. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.27 m (6H, 2 CH_3), 1.34 m (8H, 4 CH_2), 1.60 m (4H, 2 CH_2), 1.80–1.84 m (4H, 2 CH_2), 2.21 s (3H, $\text{C}^6\text{--CH}_3$), 2.22 s (6H, 2 CH_3), 3.36–3.41 m (2H, 2CH), 3.75–3.79 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.7), 3.87–3.91 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.7), 4.16–4.22 m (4H, 2 OCH_2), 5.55 s (1H, $\text{C}^5\text{--H}$). Found, %: C 63.27; H 8.33; N 5.01. $\text{C}_{29}\text{H}_{46}\text{N}_2\text{O}_8$. Calculated, %: C 63.25; H 8.42; N 5.09.

1,3-Bis(8-oxononyl)-6-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine (XII). To a solution of 0.9 g of compound **IXa** in 3 ml of ethanol 50 ml of 1% water solution of sodium hydroxide was added, and the reaction mixture was boiled for 11 h. After cooling the solution was acidified with hydrochloric acid to pH 4 and extracted with CH_2Cl_2 (3 \times 50 ml). The extract was dried over magnesium sulfate, and solvent was removed to give 0.47 g (72%) of compound **XII** as an oil. Found m/z 378.2520 [M] $^+$. $\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_4$. Calculated: M 378.2518. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.34 m (8H, 4 CH_2), 1.57–1.64 m (8H, 4 CH_2), 2.12 s (3H, CH_3), 2.13 s (3H, CH_3), 2.23 s (3H, $\text{C}^6\text{--CH}_3$), 2.39–2.44 m [4H, 2 $\text{C}(\text{O})\text{CH}_2$], 3.78 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.7), 3.89 t (2H, NCH_2 , $^3J_{\text{HH}}$ 7.7), 5.56 s (1H, $\text{C}^5\text{--H}$). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 379 [$M + 1$] $^+$ (55), 378 [M] $^+$ (14), 363 [$M - 15$] $^+$ (34), 335 [$M - 43$] $^+$ (45), 321 (87), 253 (91), 209 (71), 195 (79), 167 (59), 140 (83), 126 (97), 96 (100), 43 (89). Found, %: C 63.59; H 9.00; N 7.48. $\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_4$. Calculated, %: C 63.64; H 9.05; N 7.40.

Compound **VI** was obtained analogously to the product **XII** from 0.63 g of compound **IIIb**. Yield of compound **VI** 0.38 g (75%).

ACKNOWLEDGMENTS

The work was carried out with the financial support of Russian Foundation for Basic Research (project no. 07-03-00392) and the program no 18 of the Presidium of Russian Academy of Sciences.

REFERENCES

1. Brown, D.J., *The Pyrimidines. Supplement II*, New York: Wiley, 1985, p. 21.
2. Pod'yachev, S.N., Sudakova, S.N., Galiev, A.K., Mustafina, A.R., Syakhaev, V.V., Shagidullin, R.R., Bauer, I., and Konovalov, A.I., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 2006, no. 11, p. 1926.
3. Martin, F.D., Fernelius, C.W., and Shamma, M., *J. Am. Chem. Soc.*, 1959, vol. 41, no. 1, p. 130.
4. Semenov, V.E., Voloshina, A. D., Toroptzova, E.M., Kulik, N.V., Zobov, V.V., Giniyatullin, R.Kh., Mikhailov, A.S., Nikolaev, A.E., Akamsin, V.D., and Reznik, V.S., *Eur. J. Med. Chem.*, 2006, vol. 41, no. 9, p. 1093.
5. Semenov, V.E., Galiullina, L.F., Lodochnikova, O.A., Kataeva, O.A., Chernova, A.V., Efremov, Y.Y., Latypov, S.K., and Reznik, V.S., *Eur. J. Org. Chem.*, 2007, vol. 2007, no. 27, p. 4578.
6. Semenov, V.E., Akamsin, V.D., and Reznik, V.S., *Zh. Obshch. Khim.*, 2007, vol. 77, no. 8, p. 1353.