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NEW LACTON-HETEROCYCLES SYNTHESIS ON BASE OF 2-(2-ETHOXY-3-BROMOPROPYL)-2-ETHOXYCARBONYL-4-BUTANOLIDE

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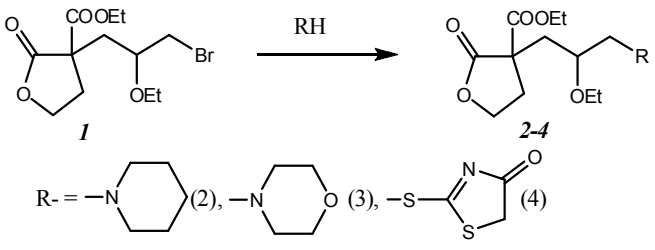
Interaction of 2-(2-ethoxy-3-bromopropyl)-2-ethoxycarbonyl-4-butanolide with piperidines, morpholines and rodanines lead to the formation of new lacton--heterocycles.

***Keywords*:** piperidine, morpholine, rodanine, lacton.

Introduction. The insertion of ethoxy-group in the lactone ring is actual as they are widely used nowadays in pharmaceutical preparations, as vynyline, acitretine, galidore [1], dimedrol and so on [2], which possess alkoxy group in their structure. Piperidine, morpholine, rodanin and their derivatives are widely used in medical practice as tranquilizer, synthetic narcotic analgesics. They also possess antibacterial, anticonvulsive, antituberculous activities. From chemical point of view they could represent further synthetic interest as condensation agents in the synthesis of very different organic compounds [3–4].

As a continuation of our previous work dedicated to the chemical transformations of ethoxybromlactone and with the aim to syntheses of new potent biological active lactone-heterocycles on their base, the interaction of 2-(2-ethoxy--3-brompropyl)-2-ethoxycarbonyl-4-butanolides [5] with piperidine, morpholine and rodanine was investigated. The combinations of these compounds were realized and the optimal conditions for high yields of targeted products have been developed.

It was established, that it is reasonable to realize the reactions in molar ratio 1:2 of initial compounds in the anhydrous ether solution during 1–2 hours, and after corresponding processes the targeted products can be separated.



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NMR and IR spectral data confirm structures of new compounds 2–4 that can be interesting for practical and theoretical reasons in medicine and pharmacology, as well as a synthons in fine organic synthesis of complicated compounds. The elemental analyses matched the calculated composition. TLC analysis controlled the purity of the synthesized compounds.

Experimental Part. NMR spectra were registered at 30^0C on spectrometer Varian Mercury-300 (300 and 75 *MHz* for ^1H and ^{13}C respectively), solvent DMSO-d_6. IR spectra were recorded on spectrophotometers Specord 75IR from thin films or mulls in mineral oil. The homogeneity and purity of products were checked by TLC on Silufol UV-254 plates, development in iodine vapor.

*2-(3-Bromo-2-Ethoxypropyl)-2-Ethoxycarbonyl-4-Butanolide (**1**)*. Solution of 14.85 *g* (0.075 *mol*) 2-allyl-2-ethoxycarbonyl-4-butanolide in 45 *ml* ethanol at $0–5^0C$ were added dropwise 12 *g* (0.075 *mol*) brome in 10 *ml* benzen. It was left 60 *h* at room temperature. Then the reaction mixture was removed from the HBr and excess solvent, the residue was distilled. Yield 10 *g* (41 %), bp152–155^0C/ 2 *mm* Hg, n_D^{20} 1.4930; R_f 0.49 (EtOH:*n*–C_6H_{14}=1:1). Found, %: Br 24.89. $C_{12}H_{19}BrO_5$. Calculated, %: Br 24.72. IR spectrum, *v*, cm^{-1}: 1780 (C=O, lactons); 1730 (C=O, COOEt); 1140–1180 (C–O–C). ^1H NMR spectrum, *δ*, *ppm*: 1.10 t (3H, $\underline{CH_3}CH_2O$); 1.29 t (3H, $\underline{CH_3}CH_2OC=O$); 2.13 d.d (2H, $\underline{CH_2}CHO$); 2.29 m (1H, CH_2 in lactons); 2.54 m (1H, CH_2 in lactons); 3.25 m (1H, $\underline{CH}O$); 3.31 m (1H, CH_2Br); 3.56 m (1H, CH_2Br); 3.88 q (2H, $CH_3\underline{CH_2}O$); 4.21 q (2H, $CH_2OC=O$); 4.32 m (2H, CH_2O in lactons).

*2-(2-Ethoxy-3-Piperidinylpropyl)-2-Ethoxycarbonyl-4-Butanolide (**2**)*. Mixture of 3.5 *g* (10 *mmol*) compound **1** and 1.7 *g* (20 *mmol*) piperidine in 10 *ml* of diethyl ether, the mixture was stirred for 2 *h* at $30–35^0C$. Filtered, the solvent was evaporated from the filtrate in vacuum. Yield 2.8 *g* (86%), n_D^{20} 1.5138; R_f 0.49 (C_6H_{14}:EtOH:H_2O=0.2:1.0:0.6). Found, %: N 4.55. $C_{17}H_{29}NO_5$. Calculated, %: N 4.28. IR spectrum, *v*, cm^{-1}: 1770 (C=O, lactons); 1730(C=O, COOEt); 1130–1150 (C–O–C). ^1H NMR spectrum, *δ*, *ppm*: 1.11 t (3H, $OCH_2\underline{CH_3}$); 1.28 t (3H, $COOCH_2\underline{CH_3}$); 1.46–1.68 m (6H, CH_2, piperidine); 2.11 dd (2H, CH_2–lactone); 2.20–2.70 m (8H, CH_2N, CH_2 in lactons); 3.07 m (1H, CHO); 3.88 q (2H, $O\underline{CH_2}CH_3$); 4.21 q (2H, $COO\underline{CH_2}CH_3$); 4.24 tt (1H, CH_2O in lactons); 4.35 tt (1H, CH_2O in lactons).

*2-(2-Ethoxy-3-Morpholinylpropyl)-2-Ethoxycarbonyl-4-Butanolide (**3**)*. Mixture of 3.5 *g* (10 *mmol*) compound **1** and 1.74 *g* (20 *mmol*) morpholine in 10 *ml* of diethyl ether, was stirred for 2 *h* at $30–35^0C$. Filtered, the solvent was evaporated from the filtrate in vacuum. Yield 2.94 *g* (74%), mp $197–198^0C$, R_f 0.5 (C_6H_{14} : EtOH = 0.3 : 2.5). Found, %: N 4.51. $C_{16}H_{27}NO_6$. Calculated, %: N 4.25. IR spectrum, *v*, cm^{-1}: 1770 (C=O, lactons), 1735(C=O, COOEt), 1230 (C–O–C). ^1H NMR spectrum, *δ*, *ppm*: 1.10 t (3H, $OCH_2\underline{CH_3}$); 1.29 t (3H, $COOCH_2\underline{CH_3}$); 2.12 dd (2H, CH_2–lactone); 2.29 td (2H, CH_2 in lactons); 2.37 dd (1H, CH_2N); 2.54 td (2H, CH_2 in lactons); 2.62 dd (1H, CH_2N); 2.67 m (4H, CH_2N in morpholine); 3.07 m (1H, CHO); 3.65 m (4H, $O\underline{CH_2}$ in morpholine); 3.88 q (2H, $O\underline{CH_2}CH_3$); 4.21 q (2H, $COO\underline{CH_2}CH_3$); 4.25 t.t. (1H, CH_2O in lactons); 4.35 tt (1H, CH_2O in lactons).

*2-(2-Ethoxy-3-(4-Oxo-4,5-Dihydrothiazol-2-Ylthio)propyl)-2-Ethoxycarbonyl--4-butanolide (**4**)*. Mixture of 3.5 *g* (10 *mmol*) compound **1** and 2.66 *g* (20 *mmol*)

rodanine in 20 *ml* of diethyl ether was stirred for 5 *h* at 30–35^0*C*. Filtered, the solvent was evaporated from the filtrate in vacuum. Yield 2.7 *g* (74%), mp 178^0*C*; R_f 0.59 (C_6H_{14} : EtOH:$CHCl_3$ = 2.0 : 0.2 : 0.1). Found, %: N 3.48. $C_{15}H_{21}NO_6S_2$. Calculated, %: N 3.73. IR spectrum, *v*, cm^{-1}: 1770 (C=O, lactons); 1740 (C=O, COOEt); 1675 (N–C=O); 1640 (C=N); 1130–1150 (C–O–C). ^{1}H NMR spectrum, *δ*, *ppm*: 1.10 t (3H, $OCH_2\underline{CH_3}$); 1.29 t (3H, $COOCH_2\underline{CH_3}$); 2.12 dd (2H, CH_2–lactone); 2.29 td (1H, CH_2 in lactons); 2.54 td (1H, CH_2 in lactons); 2.88 m (1H, CH_2S); 3.11 m (1H, CHO); 3.14 m (1H, CH_2S); 3.88 q (2H, $O\underline{CH_2}CH_3$); 4.05 s (1H, SCH_2C=O); 4.21 q (2H, $COO\underline{CH_2}CH_3$); 4.25 tt (1H, CH_2O in lactons); 4.36 tt (1H, CH_2O in lactons).

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