mole) of $LiAlH_4$ and 3 g (0.023 mole) of aluminum chloride in 50 ml of absolute ether. At the end of the addition the mixture was refluxed with stirring for 1 h, after which it was cooled, and 50 ml of ethyl acetate was added to it gradually. The resulting solution was poured into 100 ml of 20% sulfuric acid, and the mixture was filtered. The organic layer was separated, and the aqueous layer was washed twice with 50-ml portions of ether. The combined ether extracts were dried over sodium sulfate, and the solvent was evaporated to give colorless needles of 9H-9-(p-tolyl)-10-telluraanthracene with ml 163°C (from heptane–benzene) in 75-85% yield. Found: C 62.4; H 4.6%. $C_{20}H_{16}Te$. Calculated: C 62.6; H 4.4%.

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SYNTHESIS OF COMPOUNDS OF THE BICYCLO[2.2.1]HEPTANE SERIES THAT ARE FUSED WITH AN OXAZECINE RING

N. K. Levchenko, G. M. Segal', and I. V. Torgov

UDC 547.892

Derivatives of the bicyclo[2,2,1]heptane series that are condensed with an oxazecine ring were obtained. A number of transformations of the compounds obtained were realized. Data from the IR, NMR, and mass spectra that confirm the structures of the synthesized compounds are presented.

In the course of our research on the preparation of analogs of natural alkaloids we have realized the synthesis of polycyclic nitrogen-containing structures that have the norbornane skeleton. A number of compounds of this type have high spasmolytic [1], antiarrhythmic [2], hypotensive [3], or cardiotonic [4, 5] action. Several highly active natural alkaloids that contain 8-azabicyclo[3.2.1]octane and 9-azabicyclo[4.2.1]nonane systems can be included in this group of compounds [6].

We selected the accessible endo-5-norbornene-2,3-dicarboxylic acid anhydride (I), which is formed by the reaction of cyclopentadiene with maleic anhydride [7], as the starting compound. The corresponding imide (II) is formed smoothly in 65% yield when anhydride I is heated with urea by the method in [8]. The condensation of cyclopentadiene with maleinimide also makes it possible to obtain imide II; however, the yield of the adduct decreases in this case.

The reduction of imide II with lithium aluminum hydride leads to norbornene IIIa, condensed with a pyrrolidine ring. Compound IIIa was characterized in the form of the N-acetyl derivative (IIIb) and the benzenesulfonamide (IIIc).

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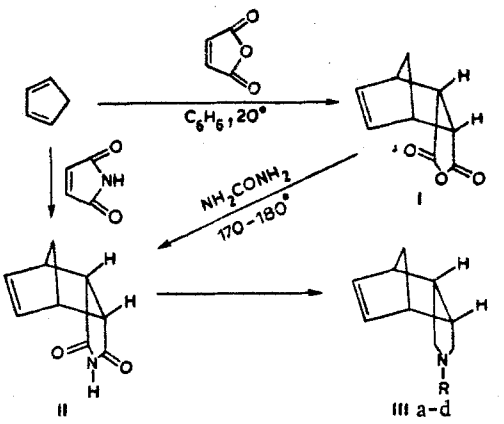


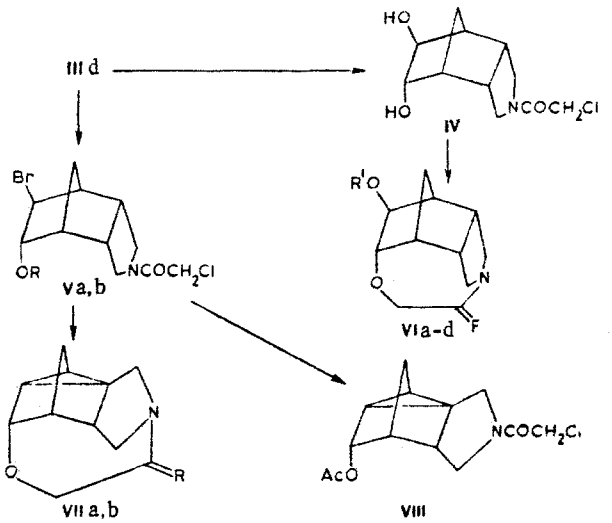
IIIa R=H; b R=$COCH_3$; c R=$SO_2C_6H_5$; d R=$COCH_2Cl$

Amine IIIa was then converted to chloroacetamide IIId — the key substance for the construction of an additional oxazecine ring. It has been shown [9-11] that carbocyclic compounds that have closely located hydroxy and chloroacetamido groupings may, upon treatment with sodium hydride, undergo intramolecular cyclization to give an oxazepine or oxazecine ring.

To realize this sort of transformation it was necessary to introduce an OH group with an endo orientation in the 8 or 9 position. The simplest method for this could be the synthesis of the corresponding trans-glycol (IV), which we also obtained by hydroxylation of an unsaturated chloroacetamide (IIId) with performic acid. Another possible synthetic variant could be the construction of an oxazacine ring through the trans-bromohydrin; of the two possible isomers, only that which had an endo-oriented OH group was necessary.

From data on the stereospecificity of the addition of the elements of HOBr to norbornene derivatives [12] and from the result of bromolactonization of 5-norbornenedicarboxylic acids [13] it is known that the Br cation in reactions involving addition to the double bond in such systems usually substitutes the exo position in the final compounds, while the OH group substitutes the endo position. In fact, in our case we obtained the trans-bromohydrin (Va) with the necessary configuration by treatment of amide IIId with N-bromoacetamide in aqueous perchloric acid. The Va structure follows from the subsequent transformations.

The action of sodium hydride on trans-glycol IV converts it smoothly to the corresponding lactam VIa, which we were subsequently able to reduce without isolation to hydroxy amine VIb, which was characterized in the form of benzoate VIc and 3,5-dinitrobenzoate VId.



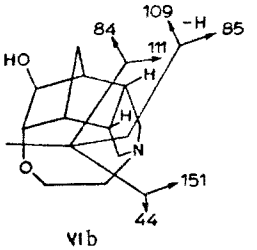
V a R=H; b R=$COCH_3$; VI a R=O, R'=H; b R=H_2, R'=H; c R=H_2, R'=COC_6H_5; d R=H_2, R'=$COC_6H_3(NO_2)_2$; VIIa R=O, b R=H_2

In the case of bromohydrin VA a similar sequence of transformations also leads to the formation of lactam VIIa and subsequently amine VIIb. However, elimination of the elements of HBr, which leads to the formation of a nortricyclene system, is observed along with cycli-

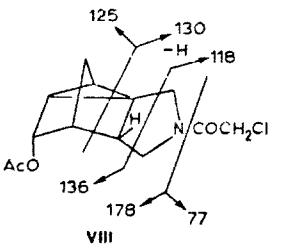
zation in the first step in this case. This sort of behavior is generally characteristic for 4(or 5)-halobornanes that have an endo orientation of the halogen atom [14, 15]. This fact may serve as an indirect confirmation of the structure of starting bromohydrin Va, while the formation of an oxazecine ring is a definite confirmation of its structure. This sort of cyclization is sterically impossible in the case of the isomeric trans-bromohydrin, which has oppositely oriented Br and OH groups.

Bromohydrin Va is evidently generally inclined to undergo HBr elimination reactions with the formation of a nortricyclene system. This transformation takes place, for example, even upon attempts to obtain bromohydrin acetate Vb; only N-chloroacetyl-4-azatetracyclo-5.2.1.$0^{2,6}$.$0^{2,9}$]-8(endo)-decanol acetate (VIII) is formed in this case in place of acetate Vb, even under mild acylation conditions (acetic anhydride, 20°C).

It should be noted that VIb, VIIa, VIIb, and VIII undergo similar fragmentation processes under electron impact, regardless of whether their structures contain a nortricyclene system:



VIb



VIII

According to preliminary tests carried out in the A. V. Vishnevskii Institute of Surgery of the Academy of Medical Sciences of the USSR (in the laboratory of Professor B. I. Khodorov), benzoate VIc has pronounced local-anesthetic action, while the corresponding 3,5-dinitrobenzoate VId is capable of modifying fast sodium pathways.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in alcohol were recorded with a Specord UV-vis spectrophotometer. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Varian XL-100 spectrometer with tetramethylsilane as the internal standard. The mass spectra were obtained with an MKh-1309 spectrometer with direct introduction of the samples into the ionization region; the ionizing-electron energy was 70 eV, and the sample vaporization temperature was 20-50°C. Preparative chromatography was carried out with columns filled with L 40 × 100 μm silica gel (Czechoslovakian SSR). The course of the reactions and the purity of the substances obtained were monitored on Silufol UV-254 plates.

Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic Acid Anhydride (I). A 10-g (0.152 mole) sample of freshly distilled cyclopentadiene was added at 6°C to a solution of 14.4 g (0.147 mole) of maleic anhydride in 100 ml of absolute benzene, and the mixture was stirred for 12 h. The precipitate was removed by filtration and washed with cold benzene to give 22 g (91%) of anhydride I with mp 160-161°C (from petroleum ether) (mp 160-161°C [7]).

4-Azatricyclo[5.2.$1^{2,6}$]dec-8-one-3,5-dione (II). A) A mixture of 2.48 g (0.015 mole) of freshly ground anhydride I and 10 g (0.167 mole) of urea was heated at 170-180°C until ammonia evolution ceased (1 h), after which it was cooled and triturated with water. The residue was removed by filtration to give 1.75 g (71%) of imine II with mp 193-194°C (from ethyl acetate) (mp 186-187°C [14]). IR spectrum (KBr pellet): 1690-1710 (broad band) and 1761 (CONHCO group); 3172 cm^{-1} (NH).

B) A solution of 1 g (15 mmole) of cyclopentadiene and 1.3 g (13 mmole) of maleinimide in 10 ml of absolute benzene was maintained at 20°C in an argon atmosphere in the presence of traces of boron trifluoride etherate for 24 h and at 35°C for 1 h. It was then cooled and treated with 50 ml of ether, and the precipitated crystals were removed by filtration to give 50 mg of imide II with mp 191-192°C (from ethyl acetate), which was completely identical to the sample obtained above.

4-Azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene (IIIa). A solution of 0.8 g (5.6 mmole) of imide II in 60 ml of absolute diglyme was added to a suspension of 1.2 g (35 mmole) of lithium aluminum hydride in absolute diglyme, and the mixture was stirred in an argon atmosphere at 45°C for 1 h. It was then heated at 120-130°C for 2 h, cooled to 20°C, and treated with 0.5 g

(0.115 mole) of lithium aluminum hydride. Heating was continued at 110-120°C for another 4 h, after which the mixture was cooled and treated with 100 ml of ethyl acetate. The organic layer was worked up to give 0.65 g (98%) of oily amine IIIa, which proved to be extremely labile in air, readily absorbed CO_2 from the air, and underwent resinification when it was stored outside a refrigerator. IR spectrum (film): 3450 (OH group) and 1637 cm^{-1} (—CH=CH—).

Treatment of amine IIIa with benzenesulfonyl chloride in pyridine (20°C, 12 h) gave stable benzenesulfonamide IIIc with mp 104-106°C (from ether) (mp 107-108°C [16]).

N-Acetyl-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene (IIIb). A mixture of 0.1 g (7.5 mmole) of freshly prepared amine IIIb, 2 ml of absolute pyridine, and 1 ml of acetic anhydride was maintained at 20°C for 12 h in an argon atmosphere, after which it was treated with water and acidified to pH 6.0 with dilute hydrochloric acid. The oily product was extracted with ether and chromatographed on silica gel with a mixture of petroleum ether and benzene (7:3) to give 0.7 g (54%) of acetamide IIIb (oil), which, according to thin-layer chromatography (TLC), was an individual substance [R_f 0.5, petroleum ether—benzene (7:3)]. IR spectrum (film): 1630 cm^{-1} (amide). PMR spectrum: 0.8 (2H, m, 2-H and 6-H), 2.08 (3H, s, $COCH_3$), 2.94 (2H, d, 1-H and 7-H, J = 9 Hz), 3.6-3.8 (4H, m, CH_2—N—CH_2), 6.22-6.24 (2H, m, CH=CH). Mass spectrum, m/e: 177 (M^+, 21%), 162 (M^+—CH_3, 70%), 149 (10%), 134 (M^+—$COCH_3$, 16%), 131 (21%), 105 (M^+—CH_3CON^+=CH_2—H, 100%), 78 (42%).

N-Chloroacetyl-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene (IIId). An 18-ml (0.155 mole) sample of chloroacetyl chloride was added dropwise with stirring and in the presence of 1.2 g (0.03 mole) of magnesium oxide in an argon atmosphere to a cooled (to 0°C) solution of 3.8 g (28 mmole) of amine IIIa in 300 ml of dry chloroform, after which stirring was continued for another 12 h. The precipitate was removed by filtration, and the filtrate was evaporated to give 5.83 g (98%) of oil chloroacetamide IIId, which purified by percolation through a column filled with silica gel (chloroform) to give a substance with R_f 0.3 (ether). IR spectrum (film): 1630 cm^{-1} (amide). PMR spectrum: 3.4-3.6 (4H, m, CH_2—N—CH_2), 4.15 (2H, d, $COCH_2Cl$, J = 3 Hz), 6.25 (2H, m, —CH=CH—). Mass spectrum, m/e: 211 (M^+, 61%), 162 (M^+—CH_2Cl, 12%), 149 (16%) 134 (M^+—$COCH_2Cl$, 18%), 105 (M^+—$ClCH_2$—H, 36%), 91 (61%), 78 (100%).

N-Chloroacetyl-4-azatricyclo[5.2.1.$0^{2,6}$]decane-8(exo),9(endo)-diol (IV). A solution of 0.5 g (2.4 mmole) of chloroacetamide IIId in 5.2 ml of 98% formic acid and 1 ml of 36% Perhydrol was stirred at 20°C for 16 h; after which 20 ml of ether was added. The mixture was washed with water and a saturated solution of sodium bicarbonate, and the extract was evaporated to give 0.35 g (58%) of trans-glycol IV (oil), which was purified by percolation with a column filled with silica gel (ether). IR spectrum (film): 3400-3600 (broad band, OH) and 1660 cm^{-1} (amide). Mass spectrum, m/e: 245 (M^+, 20%), 213 (M^+—CH_4O, 36%), 199 (M^+—H_2O—CO, 32%), 181 (M^+—$2CH_4O$, 10%), 168 (M^+—$COCH_2Cl$, 62%), 150 (M^+—H_2O—$COCH_2Cl$, 28%), 135 (M^+—CH_4O—$COCH_2Cl$—H, 100%), 122 (24%), 104 (M^+—$2CH_4O$—$COCH_2Cl$, 64%).

4,8-Ethyleneoxy-4-azatricyclo[5.2.1.$0^{2,6}$]decan-8-(endo)-ol (VIb). A solution of 0.5 g (21 mmole) of sodium hydride in 150 ml of absolute tetrahydrofuran (THF) was added in an argon atmosphere to a solution of 0.35 g (14.2 mmole) of glycol IV in 10 ml of absolute THF, and the mixture was stirred at 20°C for 30 min and refluxed for 14 h. It was then cooled to 20°C and treated with 0.5 g (13.2 mmole) of lithium aluminum hydride in 50 ml of absolute ether, and the mixture was refluxed for another 8 h. Decomposition of the excess reagents with ethyl acetate yielded 0.23 g (82%) of oily amino alcohol VIb, which was purified by chromatography with a column filled with silica gel [chloroform—methanol (1:1)] to give a product with R_f 0.1 [benzene—acetone (5:1)]. IR spectrum (film): 3400-3500 (broad band, OH) and 1200 cm^{-1} ($CHOCH_2$). PMR spectrum: 0.82-0.9 (2H, m, 2- and 6-H), 1.29 (2H, m, 10-H_2), 1.75 (2H, m, 1- and 7-H), 1.77 (1H, s, OH), 3.6-3.7 [6H, m, CH_2—N—$(CH_2)_2$] 3.75 (1H, m, 9-H), 3.8 (2H, m, 12-H_2), 3.94 (1H, m, 8-H). Mass spectrum, m/e: 195 (M^+, 2%), 177 (M^+—H_2O, 60%), 151 (M^+—44, 96%), 120 (53%), 111 (89%), 109 (80%), 105 (65%) 85 (100%), 84 (85%), 66 (51%).

Amino alcohol VIb was characterized in the form of the hydrochloride with mp 112-115°C (from alcohol) and the perchlorate with mp 135-136°C (from alcohol). Benzoate VIc (oil), which gave a crystalline hydrochloride with mp 80°C (dec., from alcohol), and 3,5-dinitrobenzoate VId, with mp 230-232°C (from alcohol), which gave a nitrate with mp 88-89°C (from alcohol) and a hydrochloride with mp 100°C (dec., from alcohol), were obtained on the basis of amino alcohol VIb.

9(endo)-Bromo-N-chloroacetyl-4-azatricyclo[5.2.1.$0^{2,6}$]decan-8(exo)-ol (Va). A 0.2-g (1.45 mmole) sample of freshly prepared N-bromoacetamide in 5 ml of dioxane, 0.1 ml of water,

and 0.2 ml of 10% $HClO_4$ were added to a solution of 0.3 g (1.41 mmole) of chloroacetamide IIId in 5 ml of dioxane, and the mixture was stirred at 20°C for 2 h. It was then treated with 20 ml of a saturated solution of NaCl and extracted with 200 ml of ethyl acetate. Evaporation of the extract yielded 0.3 g (63%) of bromohydrin Va (oil), which was purified by chromatography with a column filled with silica gel (elution with chloroform). IR spectrum (film): 3400-3600 (broad band, OH) and 1660 cm^{-1} (amide). Mass spectrum, m/e: no M^+ peak, 273 (M^+–Cl, 2%), 231 (M^+–$COCH_2Cl$, 6%), 228 (M^+–HBr, 8%), 210 (M^+–HBr–H_2O, 5%), 189 (M^+–119, 8%), 151 (228–77, 23%), 178 (M^+–130, 6%), 133 (210–77, 9%), 109 (228–119, 100%), 91 (71%), 79 (90%).

N-Chloroacetyl-4-azatetracyclo[5.2.1.$0^{2,6}$.$0^{2,9}$]decan-8(endo)-ol Acetate (VIII). A mixture of 0.1 g (0.32 mmole) of bromohydrin Va with 0.3 ml of acetic anhydride was stirred at 20°C for 48 h, after which it was diluted with 7 ml of water and 20 ml of ether. Workup of the organic layer gave 60 mg (76%) of acetate VIII (oil), which was purified by preparative TLC on silica gel (ether) to give a product with R_f 0.45. IR spectrum (film): 1750 (CH_3COO), 1680 (amide), and 1250 cm^{-1} (C–$OCOCH_3$). PMR spectrum: 0.86 (1H, d, 9-H, J = 3 Hz), 0.92 (1H, d, 1-H, J = 3 Hz), 1.29 (2H, m, 10-H_2), 1.7 (2H, m, 2- and 6-H), 2.21 (3H, s, $COCH_3$), 3.55 (4H, m, CH_2–N–CH_2), 3.74 (1H, m, 8-H), 4.2 (2H, d, $COCH_2Cl$, J = 3 Hz); the signals of olefin protons were absent. Mass spectrum, m/e: 225 (M^+, 28%), 178 (M^+–77, 26%), 165 (M^+–CH_3COOH, 36%), 136 (M^+–119, 41%), 130 (54%), 125 (M^+–130, 50%), 118 (42%), 105 (73%), 91 (77%), 66 (100%).

4,8-Ethyleneoxy-4-azatetracyclo 5.2.1.$0^{2,6}$.$0^{2,9}$]decan-11-one (VIIa). A 0.3-g (12.5 mmole) sample of sodium hydride was added in small portions in an argon atmosphere to a solution of 0.2 g (0.65 mmole) of bromohydrin Va in 50 ml of absolute THF, and the mixture was stirred for 2 h and refluxed for another 6 h. Ethyl acetate (100 ml) and 5 ml of water were added, and the organic layer was worked up to give 0.1 g (61%) of lactam VIIa (oil), which was purified by preparative TLC on silica gel [ether–chloroform (1:1)]. IR spectrum (film): 1730 (lactam) and 1180 cm^{-1} (CH–OCH_2). Mass spectrum, m/e: 191 (M^+, 9%), 163 (M^+–CO, 13%), 125 (M^+-66, 25%), 100 (M^+-91, 100%), 99 (71%), 91 (25%), 66 (30%).

4,8-Ethyleneoxy-4-azatetracyclo[5.2.1.$0^{2,6}$.$0^{2,9}$]decane (VIIb). A) A 0.1-g (0.52 mmole) sample of lactam VIIa was added to a suspension of 0.55 g (14.5 mmole) of lithium aluminum hydride in 50 ml of absolute dioxane, and the mixture was refluxed for 18 h. Workup as in the preparation of amine IIIa gave 30 mg of amine VIIb (oil), which was purified by chromatography with a column filled with silica gel (chloroform) to give a product with R_f 0.1 [TLC, benzene–acetone (5:1)]. IR spectrum (film): 1175 cm^{-1} (CH–OCH_2). Mass spectrum, m/e: 177 (M^+, 8%), 133 (M^+–44, 28%), 111 (M^+–66, 72%), 91 (33%), 85 (78%), 66 (75%). PMR spectrum: 0.84 (1H, d, 9-H, J = 3 Hz), 1.7 (2H, m, 2- and 6-H), 3.7 (8H, H atoms attached to C_3, C_5, C_{11}, and C_{12}), and 4.1 ppm (1H, m, 8-H). Amine VIIb was characterized in the form of the hydrochloride with mp 100-102°C (from alcohol).

B) A solution of 0.1 g (0.5 mmole) of hydroxy amine VIb in 20 ml of absolute benzene was refluxed with 0.2 ml (2 mmole) of freshly distilled $SOCl_2$ for 6 h (monitoring by TLC), after which the mixture was cooled to 20°C and poured into ice water. Excess potassium carbonate was added, and the mixture was extracted with ether. Workup of the extract gave 60 mg (66%) of amine VIIb (oil), which gave a hydrochloride with mp 98-100°C.

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ENAMINES.

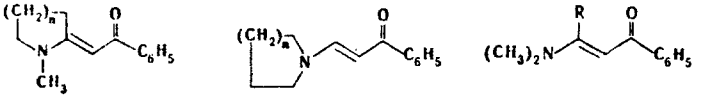
8.* POLAROGRAPHIC STUDY OF THE REACTIONS OF A NUMBER OF ENAMINO KETONES WITH NUCLEOPHILIC REAGENTS

S. S. Kiselev, M. K. Polievktov, and V. G. Granik

UDC 542.938:547.743.1'822.3'891

The hydrolysis and hydrazinolysis of cyclic enamino ketones of the pyrrolidine, piperidine, and hexahydroazepine series, as well as their noncyclic analogs, were investigated. It is shown that these processes have several principles in common. A bell-shaped dependence of k_{obs} on the pH of the medium is characteristic for hydrolysis; the reaction of the enamino ketones with hydrazine hydrate in absolute ethanol is accelerated in the presence of p-toluenesulfonic acid. It is shown that the rates of hydrolysis and hydrazinolysis depend on the size of the saturated azaheteroring and change in the order 6 > 5 > 7. A possible mechanism for the processes in which the slow step is C-protonation and(or) attack by the nucleophilic reagent in the "enamine" α position is discussed.

The reactions of enamino ketones with nucleophilic reagents at the present time constitute an extremely promising and convenient approach to the synthesis of various classes of heterocyclic compounds [2-5]. We have previously [1, 6] used polarography to investigate the hydrolysis of cyclic enamino ketones Ia-c, which was selected as a model reaction for the study of the reaction of these compounds (or their cations) with nucleophilic partners.



Ia-c IIa-c IIIa,b

I a n=1; b n=2; c n=3; III a R=H; b R=CH_3

It was recently demonstrated by PMR spectroscopy that the behavior of enamino ketones Ia-c and their noncyclic analog IIIb with respect to protonating agents differs substantially from the behavior (under the same conditions) of enamino ketones of a different type (IIa-c, IIIa) in which a CH_2 link or a CH_3 group is absent in the "enamine" α position [7].

In conformity with this, the aim of the present research was to investigate the dependence of the rate of hydrolysis of enamino ketones IIa-c and IIIa on the properties of the medium and the ring size and to compare data on the hydrolysis of two series of enamino ketones (Ia-c, IIIb and IIa-c, IIIa). In addition, in the present paper we compare the results of a study of the hydrolysis with data on the heterocyclization of IIa-c and IIIa (in the case of the synthesis of 3-phenylpyrazole by the reaction of these enamino ketones with hydrazine). The dependence of the hydrolysis of enamino ketone IIIa on the pH is presented in Fig. 1. It is apparent from Fig. 1 that the general form of the observed dependence corresponds to the results previously obtained for other enamino ketones [1, 6]. The curve has a bell-shaped

*See [1] for Communication 7.

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