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SHORT COMMUNICATIONS

Dedicated to Full Member of the Russian Academy of Sciences N.S. Zefirov on His 70th Anniversary

2,3,4,5,6,7,8,9-Octahydro-1*H*-pyrido[4,3-*b*]azepines. Synthesis and Properties

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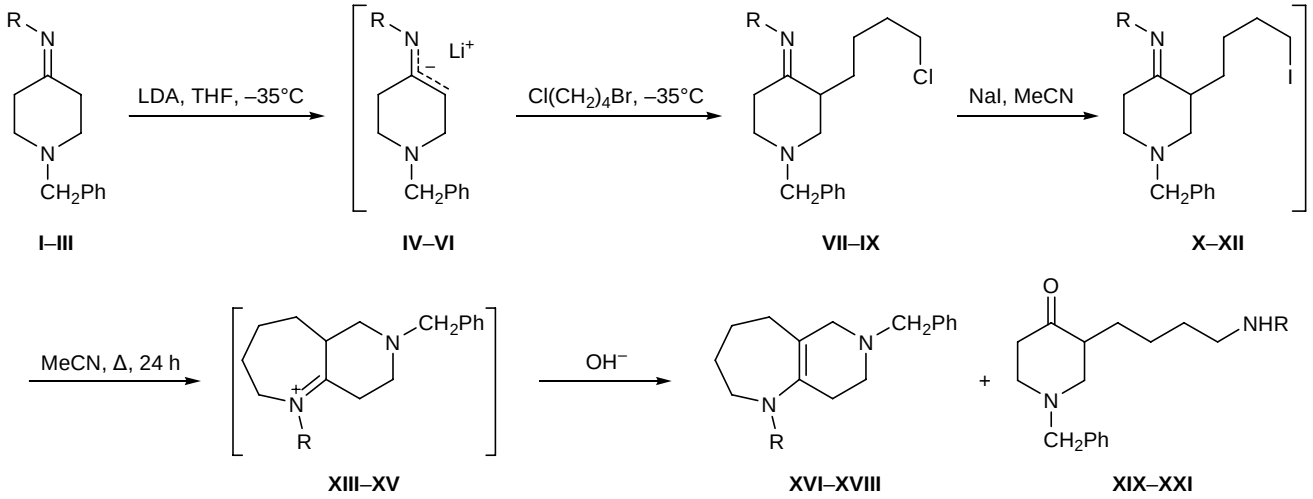
The synthesis and chemical properties of 1,7-disubstituted 2,3,4,5,6,7,8,9-octahydro-1*H*-pyrido[4,3-*b*]azepines were studied. These compounds belong to a new heterocyclic system containing an endocyclic enamine fragment. Compounds **XIII**–**XV** were synthesized via a series of consecutive reactions including lithiation of 4-iminopiperidines **I**–**III** with lithium diethylamide, alkylation of lithium salts **IV**–**VI** with 1-bromo-4-chlorobutane, nucleophilic substitution of the chlorine atom in 3-(4-chlorobutyl)imines **VII**–**IX** by iodine, and intramolecular cyclization of 3-(4-iodobutyl)imines **X**–**XII** to target 1,7-disubstituted pyrido[4,3-*b*]azepinium salts **XIII**–**XV** by heating in boiling acetonitrile. All these reactions were carried out without isolation of intermediate products **VII**–**XV**.

We planned to obtain seven-membered enamines **XVI**–**XVIII** according to the procedure developed by us previously for the preparation of their six-membered analogs, 1,2,3,4,5,6,7,8-octahydro-1,6-naphthyridines [1].

However, no cyclization of intermediate **VII** (R = Ph) to desired azepine **XVI** occurred under the conditions optimal for the synthesis of 1,6-naphthyridines. We succeeded in obtaining azepinium salt **XIII** only via cyclization of the corresponding iodide **X** which was prepared by nucleophilic substitution of the chlorine atom in 1-benzyl-3-(4-chlorobutyl)-4-phenyliminopiperidine (**VII**) by iodine on heating with NaI in boiling acetonitrile. 6-Benzyl-1-phenyl-2,3,4,5,6,7,8,9-octahydro-1*H*-pyrido[4,3-*b*]azepine (**XVI**) was isolated by treatment of salt **XIII** with alkali. The structure of enamine **XVI** was determined on the basis of the GC–MS data, MALDI spectra (using positive and negative ion registration), and ^{1}H and ^{13}C NMR



I, **IV**, **VII**, **X**, **XIII**, **XVI**, **XIX**, R = Ph; **II**, **V**, **VIII**, **XI**, **XIV**, **XVII**, **XX**, R = *p*-MeC_6H_4; **III**, **VI**, **IX**, **XII**, **XV**, **XVIII**, **XXI**, R = *p*-$MeOC_6H_4$.

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spectra. We also found that compound **XVI** undergoes opening of the seven-membered ring during isolation and chromatographic purification on silica gel to give 3-(4-phenylaminobutyl)-1-benzylpiperidin-4-one (**XIX**). Analogous transformations of azepines **XVII** (R = *p*-MeC_6H_4) and **XVIII** (R = *p*-$MeOC_6H_4$) into δ-amino ketones **XX** and **XXI** occurred even at a higher rate. Thus we revealed that newly synthesized 1,7-disubstituted 2,3,4,5,6,7,8,9-octahydro-1*H*-pyrido-[4,3-*b*]azepines **XVI**–**XVIII** readily undergo hydrolytic cleavage of the seven-membered ring with formation of previously unknown 1-substituted 3-(4-aminobutyl)piperidin-4-ones **XIX**–**XXI**.

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