

SHORT
COMMUNICATIONS

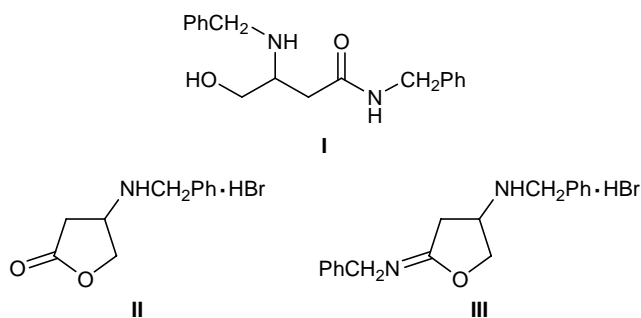
Lactonization of *N*-Benzyl-3-benzylamino-4-hydroxybutyramide under the Hofmann–Löffler Reaction Conditions

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N-Alkyl(or benzyl)-3-alkyl(or benzyl)amino-4-hydroxybutyramides are difunctional 1,3-nucleophiles possessing nonequivalent reaction centers: the hydroxy group is less nucleophilic than the NHR group. As we showed previously [1], alkaline hydrolysis of 3-alkylamino-4-hydroxybutyramides in an alcoholic medium leads to formation of 4-alkylaminobutanolides, most probably as a result of deamination followed by intramolecular dehydration. *N*-Halo-substituted amides are known to undergo rearrangement into 4-haloalkylamides whose subsequent cyclization readily gives the corresponding pyrrolidines, piperidines, and butyrolactones; apart from lactones, cyclic imidates are also formed [2, 3].



We have accomplished cyclization of *N*-benzyl-3-benzylamino-4-hydroxybutyramide (**I**) under the Hofmann–Löffler reaction conditions, i.e., by bromination in chloroform on heating under reflux. A crystalline solid separated from the reaction mixture. It was isolated and identified as 4-benzylaminotetrahydrofuran-2-one (**II**). According to the TLC and spectral data, the product was identical to that obtained by us previously [1]. The reaction mixture also contained

a small amount of a compound which showed in the IR spectrum an additional absorption band at 1710–1715 cm^{-1} . This band is typical of imidates having an exocyclic imino group (compound **III**).

4-Benzylaminotetrahydrofuran-2-one hydrobromide (II). A solution of 0.5 mol of bromine in 10 ml of chloroform was added dropwise under stirring to a solution of 1 mol of *N*-benzyl-3-benzylamino-4-hydroxybutyramide in 50 ml of chloroform, heated to the boiling point. When a solid product no longer precipitated (TLC monitoring of the consumption of the initial compound), the solvent was removed, and the residue was reprecipitated from ethyl acetate–ethanol (1:1) with ethyl acetate. The product (68%) was filtered off and washed with diethyl ether. Colorless crystals, mp 164–165°C. IR spectrum (mineral oil), ν , cm^{-1} : 1140, 1355, 1430 (C–O–C); 1575 (NH_2^+); 1770 (C=O); 2505 (NH_2^+); 3200 (NH). ^1H NMR spectrum (CF_3COOH), δ , ppm: 7.93 (2H, NH_2^+), 7.00 (5H, Ph), 4.43 (NH_2^+CH_2), 4.20 (1H, CH), 4.06 (2H, CH_2), 2.93 (2H, $\text{CH}_2\text{C=O}$). Found, %: C 48.71; H 5.20; Br 29.63; N 5.20. $\text{C}_{11}\text{H}_{14}\text{BrNO}_2$. Calculated, %: C 48.53; H 5.15; Br 29.41; N 5.15.

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