CONDENSATION OF ACETANILIDE AND N-PHENYLBUTYROLACATAM WITH γ-BUTYROLACTONE

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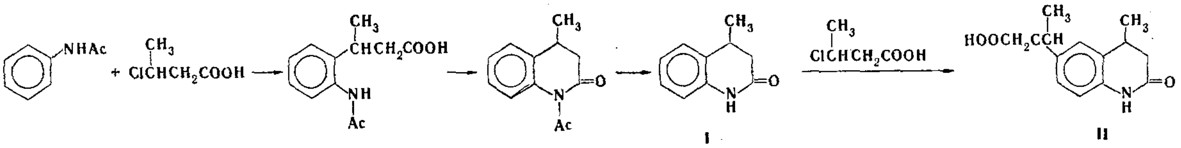
1,2,3,4-Tetrahydro-2-quinolone and β-6-(1,2,3,4-tetrahydro-2-quinolonyl)butyric acid were obtained by condensation of acetanilide with γ-butyrolactone in the presence of aluminum chloride. β-n-(N-phenylbutyrolactamyl)butyric acid was obtained by carboxyalkylation of N-phenylbutyrolactam with γ-butyrolactone.

We have previously demonstrated the possibility of C-alkylation of benzimidazolone and its derivatives with γ-lactones to give 3,4-benzimidazolonylbutyric acids and their derivatives [1, 2]. Benzimidazoline, which can be considered to be an acylated aromatic amine, proved to be very stable and did not undergo cleavage. In a continuation of our studies of the alkylation of nitrogen-containing aromatic compounds with lactones, we studied the condensation of acetanilide and N-phenylbutyrolactam with γ-butyrolactone. The effect of amide and lactam groupings on the direction of alkylation and the behavior of such a labile alkylating agent as γ-butyrolactaone under the conditions of the Friedel–Crafts reaction was examined.

The formation of β-(p-acetamidophenyl)butyric acid during the reaction of equimolecular amounts of acetanilide and butyrolactone in the presence of three equivalents of anhydrous aluminum chloride was reported in [3]. However, we have shown that 1,23,4-tetrahydro-2-quinolone (I) and β-6-(1,2,3,4-tetrahydro-2-quinolonyl)butyric acid (II) are formed when the benzimidazolone-lactone ratio is different (1:2) and the mixture is heated to 90-120°C under the conditions of the Friedel–Crafts reaction.

One of the possible paths of formation of 1,2,3,4-tetrahydro-2-quinolone is alkylation of acetanilide with β-chlorobutyric acid (the formation of intermediate β-chlorobutyric acid from butyrolactone under the influence of a twofold to threefold excess of $AlCl_3$ was proved by special experiments) in the o-position with subsequent cycloacylation. Under these conditions, the product of the further alkylation of I – β-6-(1,2,3,4-tetrahydro-2-quinolonyl)butyric acid (II) – is also formed in the presence of excess butyrolactone.



Thus six-membered heterocyclic nitrogen compounds are formed under the conditions that we found; this may be of interest as a method for the one-step synthesis of 1,2,3,4-tetrahydro-2-quinolone derivatives.

The alkylation of γ-butyrolactone with N-phenylbutyrolactam in the presence of anhydrous aluminum chloride gives β-(p-butyrolactamylphenyl)butyric acid (III).

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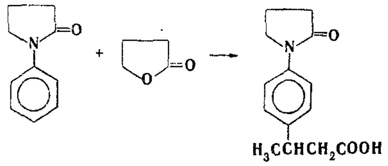
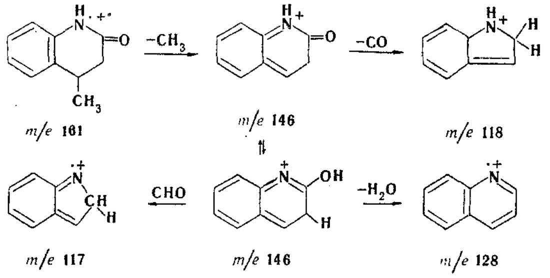


III

The structures of I-III were proved unambiguously by data from the IR, PMR, and mass spectra. The IR spectrum of I contains a band at 760 cm^{-1}, which is characteristic for an o-substituted aromatic ring, amide bands at 1686 cm^{-1} (amide I band) and 1590 cm^{-1} (amide II band), and bands at 3200, 2960, and 2930 cm^{-1}, which are related to the valence vibrations of the aromatic ring C–H bonds [4]. The mass spectrum contains a molecular ion peak with m/e 161, the magnitude of which corresponds to the empirical formula, and peaks of fragments with m/e 146, 128, 118, and 117, the possible paths for the formation of which are presented in the scheme. The proposed sequence of the fragmentations are confirmed by the presence of peaks of the corresponding metastable ions in the spectrum.



An absorption band at 825 cm^{-1}, which is characteristic for a 1,2,4-substituted aromatic ring, a band at 1740 cm^{-1}, which corresponds to the carbonyl of a carboxyl group, amide bands at 1650 and 1580 cm^{-1}, and a broad band at 2500-3400 cm^{-1}, which corresponds to the hydroxyl group of a carboxyl group in the dimeric form [4], are observed in the IR spectra of II.

The methylene group of the side chain and the methylene group of the heteroring coincide and appear as a four-proton quartet at δ 2.8-3.1 ppm in the PMR spectrum (in CF_3COOH), while two methylene groups give a two-proton multiplet at δ 3.4 ppm. A distinct six-proton doublet of two methyl groups (J =7 Hz) is observed at stronger field (1.45 ppm). The protons of the phenyl ring appear as a complex multiplet at δ 7.1-7.5 ppm.

The IR spectrum of III contains bands at 825 and 852 cm^{-1}, which are characteristic for a 1,4-substituted aromatic ring, bands at 1730 and 1646 cm^{-1}, which are related to carboxyl and amide carbonyl groups, respectively, and a broad band at 3400-3500 cm^{-1}, which corresponds to a hydroxyl group of a carboxyl group in the dimeric form [4]. The protons of the methyl and methylene groups of the side chain appear in the PMR spectrum (in CF_3COOH) as doublet with chemical shifts of 1.47 ppm (J =7 Hz) and 2.91 ppm (J =8 Hz), respectively: the methylidyne group appears as multiplet at δ 3.55 ppm. The methylene groups of the heteroring appear as triplets at δ 4.3 ppm (CH_2–N) and δ 3.2 ppm ($CH_2C=O$) and a multiplet at δ 2.55 ppm (CCH_2C). The protons of the phenyl ring appear as a symmetrical singlet at δ 7.6 ppm.

EXPERIMENTAL

The IR spectra of KBr pellets were recorded with a UR-20 spectrometer with NaCl and LiF prisms. The PMR spectra were recorded with a JNM-4H-100 spectrometer at 34° and an operating frequency of 100 MHz. The standard was tetramethylsilane. The mass spectrum was recorded with an MKh-1303 spectrometer.

1,2,3,4-Tetrahydro-2-quinolone (I). A 64.0-g (0.47 mole) sample of anhydrous aluminum chloride was added in small portions to a mixture of 21.6 g (0.15 mole) of acetanilide and 20.8 g (0.24 mole) of butyrolactone in 380 ml of tetrachloroethylene. The temperature of the mixture was then raised gradually to 95° in the course of 1.5 h, and the mixture was then heated at this temperature for 4 h. It was then cooled and decomposed with 200 ml of cold (0°) 17% hydrochloric acid, and the solvent was removed by steam distillation. The residual dark-red solution was extracted with 200 ml of ether, the ether was removed from the extract, and the solid residue was treated with hot sodium carbonate solution and filtered. Cooling of the sodium carbonate solution gave 1,2,3,4-tetrahydro-2-quinolone in 10% yield as a white crystalline substance with mp 96-97° (from water). Found: C 74.6; H 6.85%. $C_{10}H_{11}NO$. Calculated: C 74.51; H 6.88%.

β-6-(1,2,3,4-Tetrahydro-2-quinolonyl)butyric Acid (II). Acidification (to pH 1) of the sodium carbonate solution after separation of I yielded β-6-(1,2,3,4-tetrahydro-2-quinolonyl)butryic acid as a white crystalline substance with mp 233-235°. The yield was 3% of the theoretical value. Found: C 68.1; 68.3; H 7.02; 7.04; N 5.27; 5.28%. $C_{14}H_{17}NO_3$. Calculated: C 67.99; H 6.92; N 5.66%.

β-(p-butyrolactamylphenyl)butyric Acid (III). A 40-g (0.09 mole) sample of anhydrous $AlCl_3$ was added in small portions at room temperature with vigorous stirring in the course of 1.5 h to a suspension of 16.1 g (0.1 mole) of N-phenylbutyrolacatam, 8.6 g (0.1 mole) of γ-butyrolactone in 150 ml of tetrachloroethylene. The mixture was stirred for 30 min at room temperature and for 3 h at 95°. It was then cooled and decomposed with a mixture of 100 ml of concentrated HCl, 100 ml of water, and 50 g of ice. The solvent was removed by steam distillation, the residue was cooled, and the resulting dark-brown oil was dissolved in hot sodium bicarbonate solution. The warm bicarbonate solution was decolorized with activated charcoal and acidified to pH ~2-3 with dilute hydrochloric acid. The crystalline precipitate was recrystallized from water to give 60% of a product with mp 176.5°. Found: C 68.1; H 7.02; N 5.28% $C_{14}H_{17}NO_3$. Calculated: C 67.99; H 6.93; N 5.66%.

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