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METHOD OF PREPARATION OF 3-(1-BENZIMIDAZOLONYL)PROPANOIC ACID

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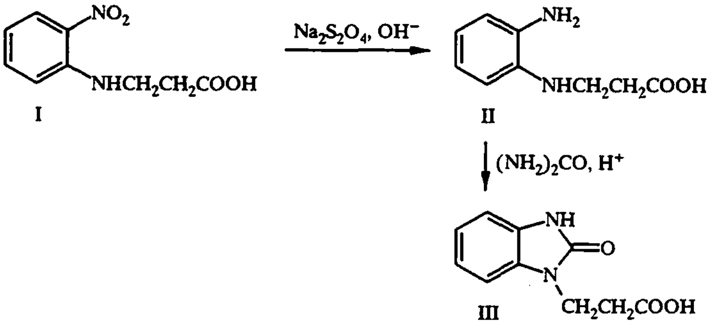
We proposed a method of synthesis of 3-(1-benzimidazolonyl)propanoic acid based on condensation of N-(2-aminophenyl)-β-alanine with urea. The reaction is conducted in acetic acid with subsequent treatment of the mixture with hydrochloric acid. N-(2-Aminophenyl)-β-alanine (II) cannot be synthesized directly from *o*-phenylenediamine and acrylic acid, since heterocyclization of intermediate amino acid II into tetrahydro-1,5-benzodiazepinone takes place together with the addition reaction [1]. N-(2-Aminophenyl)-β-alanine (II) was obtained by hydrogenation of N-(2-nitrophenyl)-β-alanine (I) with sodium dithionite in water–base medium.



Compound III is also formed when β-alanine II is melted with carbamide, but the yield does not exceed 35%.

The structure of the synthesized compounds was confirmed by the data from elemental analysis, and the IR, ^1H and ^{13}C NMR, and mass spectra.

N-(2-Aminophenyl)-β-alanine (II). Here 14.7 g (0.07 mole) of N-(2-nitrophenyl)-β-alanine (I), 8 g (0.2 mole) of sodium hydroxide, and 100 ml of water were heated to boiling. Sodium dithionite was added to the boiling solution in small portions until the red color disappeared (approximately 40-45 g). Reduction virtually ended after 20 min. The solution was neutralized to pH 7, cooled, and the crystals separated after standing for 10 h at 4°C were filtered and washed with water. Yield of 7.3 g (58%). mp = 119°C (with decomposition). ^1H NMR spectrum [$(CD_3)_2CO$]: 2.60 (2H, t, CH_2CO); 3.39 (2H, t, NCH_2); 3.4-4.6 (2H, br. s, NH_2), 6.0-6.7 (4H, m, arom. H).

3-(1-Benzimidazolonyl)propanoic Acid (III). Here 1.8 g (0.01 mole) of β-alanine II, 1.8 g (0.03 mole) of urea, and 10 ml of 90% acetic acid were boiled for 10 h, and the mixture was acidified with hydrochloric acid (1:1) and boiled for another 30 min. The liquid fractions were vacuum distilled, and 10 ml of water was poured on the residue and stirred. The sediment of compound III precipitated was filtered off and washed with water. Yield of 1.21 g (59%). mp = 186-188°C (from ethanol). IR spectrum: 1680, 1740 (CO). ^1H NMR spectrum (DMSO-D_6): 2.62 (2H, t, CH_2CO); 4.03 (2H, t, NCH_2); 6.9-7.3 (4H, m, arom. H); 10.85 (1H, s, NH); 12.31 (1H, s, OH). ^{13}C NMR spectrum (DMSO-D_6): 32.93 ($\underline{CH_2}CO$), 36.44 (NCH_2), 108.18 (C_7), 108.88 (C_4), 120.68 and 120.99 (C_5 and C_6), 128.44 (C_9), 130.19 (C_8), 154.22 (CO), 172.60 (COOH). M^+ 206.

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