REPLACEMENT OF A PIPERIDINE RESIUDE BY A HALOGEN IN 3-AMINO-4-PIPERIDINOQUINOLINE-2-CARBOXYLIC ACID

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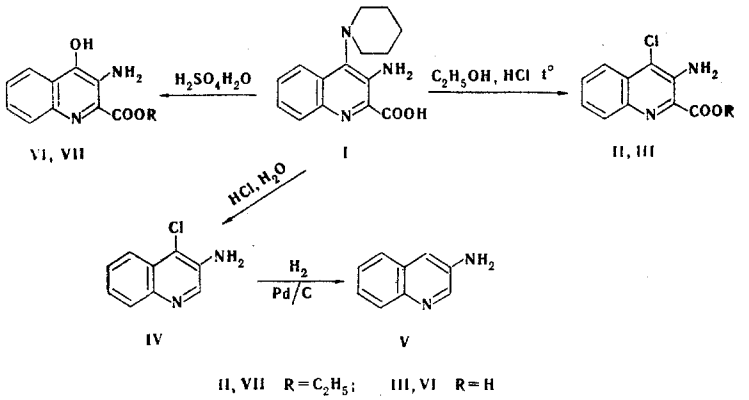
In a study of the properties of 3-amino-4-piperidinoquinoline-2-carboxylic acid (I) [1] it was found that it is possible to replace the piperidine residue in it by chlorine. Thus ethyl 3-amino-4-chloroquinoline-2-carboxylate (II) with mp 97-98° (from aqueous alcohol), is formed when dry HCl is bubbled into a refluxing solution of I in ethanol; the PMR spectrum of II (in CCl_4) does not contain signals of the protons of the CH_2 groups of the piperidine ring but does contain multiplets of the protons of the benzene ring (7.4 and 7.8 ppm). Saponification of acid II with 3% aqueous NaOH solution gave acid III with mp 154-155° (from water). The piperidine residue is also replaced by chlorine when I is heated in dilute hydrochloric acid, but the carboxyl group is split out under these conditions to give 3-amino-4-chloroquinoline (IV) with mp 142-143° (from 3-aminoquinoline (V) with mp 84° (from benzene–petroleum ether), and by reductive dehalogenation in alcoholic alkali in the presence of Pd/C. Heating acid I in 50% sulfuric acid gave 3-amino-4-hydroxyquinoline-2-carboxylic acid (VI) with mp 267-268° (purified by reprecipitation through the Na salt), which was converted to the corresponding ester (VII), with mp 174-175° (from aqueous alcohol), by heating in ethanol with simultaneous bubbling of HCl into the solution. The experimental results make it possible to assume that protonation of I takes place at the nitrogen atom of the piperidine residue, inasmuch as the presence of a positively charged piperidinium residue in the 4 position should facilitate nucleophilic substitution at the ring C_4 atom to a considerable degree.



II, VII R = C_2H_5; III, VI R = H

The results of elementary analysis of the compounds obtained in this study are in agreement with the calculated values. The IR spectrum of V was in agreement with the literature data.

LITERATURE CITED

1. N. E. Britikova, L. A. Belova, O. Yu. Magidson, and A. S. Elina, Khim. Geterotsikl. Soedin., 131 (1974).

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