REACTION OF ISATIN WITH BROMO KETONES UNDER INTERPHASE-CATALYSIS CONDITIONS

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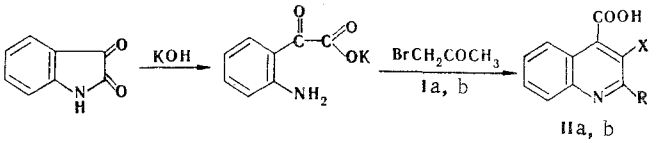
UDC 547.831.9'756.07

A multistep method for the preparation of 2-acylindole-3-carboxylic acids that consists in the alkylation of isatin with bromo ketones and subsequent recyclization of the alkylation products in alkaline media is known [1, 2].

An attempt to improve this method by means of alkylation of isatin under interphase-catalysis conditions unexpectedly led to the production of quinoline-4-carboxylic acids. Evidently under the selected conditions, of the two possible competitive processes, viz., alkylation of isatin by the bromo ketone and hydrolysis of isatin, the latter proceeds more rapidly. This reaction pathway also leads to the production of quinoline structures as a result of condensation of the product of hydrolysis of isatin with bromo ketones (the Pfitzinger reaction).



I, II a R=CH_3; b R=C_6H_5; II a X=OH; b X=Br

Thus 2-methyl-3-hydroxy- (IIa) [in 86% yield with mp 260°C (dec., reprecipitation from 20% aqueous sodium hydroxide by means of acetic acid) or 2-phenyl-3-bromoquinoline-4-carboxylic acid (IIb) (in 88% yield with mp 248-250°C) was obtained by heating (at 60-70°C) 0.1 mole of isatin and 0.15 mole of the bromo ketone (Ia or Ib) in a mixture of benzene with 50% aqueous potassium hydroxide in the presence of catalytic amounts of tetraethylammonium bromide.

Similar results were obtained when dimethylformamide(DMF)—methylene chloride—50% aqueous potassium hydroxide and DMF—potassium carbonate were used.

The results of elementary analysis and the PMR and mass spectra were in agreement with the protonated structures.

Rapid and complete nucleophilic substitution of bromine, which leads to the production of only hydroxy derivative IIa, is observed when bromoacetone (Ia) is used, while bromine is retained completely in the quinoline IIb molecule in the case of bromoacetophenone (Ib).

LITERATURE CITED

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0009-3122/82/1808-0871$07.50