

DISCUSSIONS

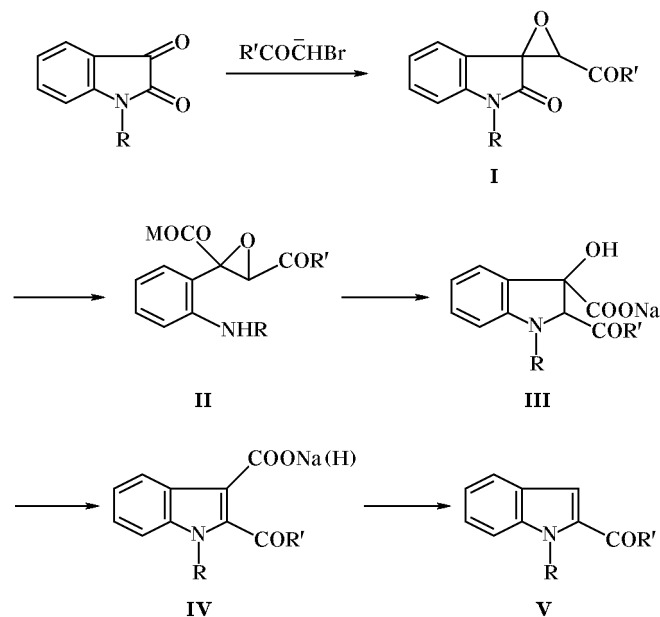
On the Synthesis of 2-Acylindoles by the Darzens Condensation

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Radul *et al.* recently reported [1] on the N-alkylation of unsubstituted and substituted isatins with α -bromo ketones in benzene and toluene in the presence of bases (pyridine, triethylamine, K_2CO_3). These reactions led to formation of the corresponding N-acetyl- and N-phenacylisatins which are used as starting compounds in the dihydroindole-dione-indole rearrangement. A disadvantage of the proposed procedure is poor solubility of initial isatins in the above solvents. In addition, high reactivity of the carbonyl group in the β -position and ready generation of anions from bromo ketones by the action of bases favor the Darzens condensation, and separation of the products by preparative thin-layer chromatography is difficult because of their similar mobilities in different solvent systems.



R = H, Alk.; R' = Alk, Ar, Ht; M = K, Na.

It should be noted that the Darzens condensation, which readily occurs in DMF in the presence of K_2CO_3 [2] or NaH, is the first stage in the synthesis of 2-acylindoles and that epoxy ketones **I** are nothing but a latent form of epoxy acid salts **II**; the latter are products of intermolecular condensation of *ortho*-aminobenzoylformic acids with halomethyl ketones, which does not occur under usual conditions. Structure **I** is hidden by the isatin ring; its opening in alkaline or superbasic medium [DMSO–water (9:1)–NaOH (5–10%)] leads to the explicit form, hydroxy acid **III**.

Thus, for the intermolecular condensation to occur it is necessary to attach the $R'COCH_2$ fragment of halomethyl ketone to C³ of the isatin molecule before ring opening. Therefore, the Darzens condensation is an intramolecular version of this process.

Taking into account that the same 2-acylindoles **IV** are formed from the Darzens condensation products **I** and from 1-[2-oxoalkyl(aryl, heteryl)]-2,3-dihydroindole-2,3-diones in the dihydroindole-dione-indole rearrangement [3], there is no need of suppressing the first of these via reduction of the solvent polarity; moreover, it can be regarded as a simple procedure for transformation of isatins into 3-(1,2-dioxoethyl)dihydroindol-2-ones **V**.*

REFERENCES

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* As in Russian original.—Publisher