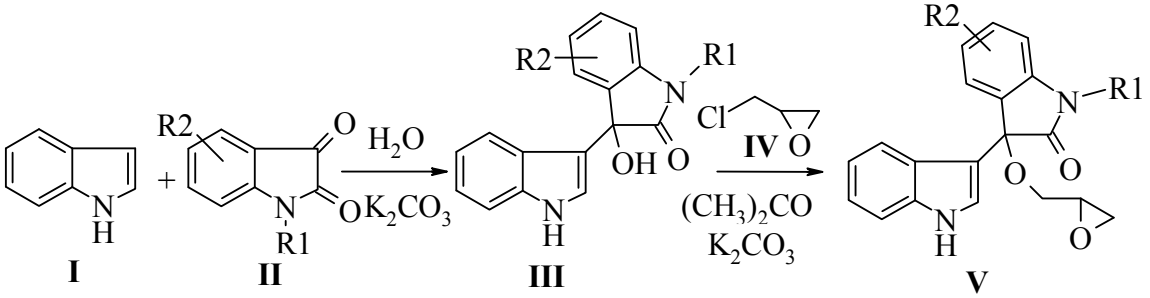
SYNTHESIS OF 3-HYDROXYINDOLINE-2-ONES

Grygoriv G. V., Redkin R. G., Syumka E. I., Shemchuk L. A., Chernykh V. P.
The National University of Pharmacy, Kharkiv, Ukraine
galkagrigoriv@gmail.com

Indole core is common for wide variety of biologically active compounds. Oxindoles are particularly well-known among them due to their broad spectrum of bioactivity. Thus, oxindoles reveal antibacterial, antifungal, antitumor, analgesic, antihypoxic and other types of activities. Therefore scientists are interested in the development of new efficient ways to synthesize oxindole derivatives.

Nowadays isatin is one of lead molecules for designing oxindoles. Its' reactive keto-carbonyl group readily undergoes condensation reactions under mild conditions. Such properties give useful opportunities for developing safe and economical green chemistry methods.

To synthesize 3-hydroxyindoline-2-one the reaction of isatin (I) and indole (II) (the molar ratio 1:1) was used. As a solvent we used water. Potassium carbonate was added to the reaction mixture in a molar equivalent. The reaction proceeded under reflux (50 – 60°C) and with stirring for 4 hours.



The reaction product (III) – a light yellow amorphous precipitate – was recrystallized from water. On the average 80% yield was obtained.

Prolongation of the reaction time did not increase the yield.

Obtained 3-hydroxyindoline-2-one can be subsequently used in different kinds of reactions: O-alkylation, C-alkylation, cycloaddition reactions with aldehydes and aminoacids etc.

However the attempt to alkylate 3-hydroxyindoline-2-one with epichlorohydrin (IV) in order to obtain product V wasn't successful. The reaction was carried out under reflux (50 – 60°C), using acetone as a solvent, in the presence of potassium carbonate.

Such difficulties may occur due to the possible competitive N-alkylation reaction in the oxindole core. That's why we are interested in additional research involving N-substituted isatins.

Moreover, according to the last researches in oxindoles area, condensation cycloaddition reactions of 3-hydroxyindoline-2-one give great synthetic opportunities to create spirocyclic compounds, that are expected to possess different types of biological activity.

Consequently, synthesis of 3-hydroxyindoline-2-one derivatives remains the key purpose of our future researches.