SYNTHESIS AND PROPERTIES OF 2-(BENZOYILAMINO)(1-R-2-OXOINDOLIN-3-YLIDENE)ACETIC ACID ETHYL ESTERS

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Introduction. Analysis of scientific and patent literature testifies that research of biologically active compounds among derivatives of 2-oxoindoline is promising. They include the well-known amino acids (tryptophane), neurohormone serotonine, series of natural alkaloids and synthetic drugs (indomethacin, dimecarbin).

Aim. The aim of the research is the synthesis of a new group of chemical compounds – 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethyl esters as potentially biological active substances.

Materials and methods. While studying of the research objects in order to prove the structure and purity of the substances synthesized the physical and chemical methods given in the State Pharmacopeia of Ukraine were applied.

Melting points were determined by the capillary method at “PTM (M)” apparatus. The elemental analysis of Nitrogen content was carried out the help of an automatic analyser “CNH”, model EA 1108 “Carlo Erba”.

IR-spectra were registered by a “Tensor 27” device in KBr tablets, the concentration of the substance − 1%.

^{1}H NMR spectra of the compounds synthesized were recorded on a Varian Mercury VX-200 (200 MHz) spectrophotometer. The solvent is DMSO-D_6, the internal standard is tetramethylsilane (TMS).

Data of elemental analysis correspond to the calculated ones.

2-(Benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acid ethyl ester (3a).

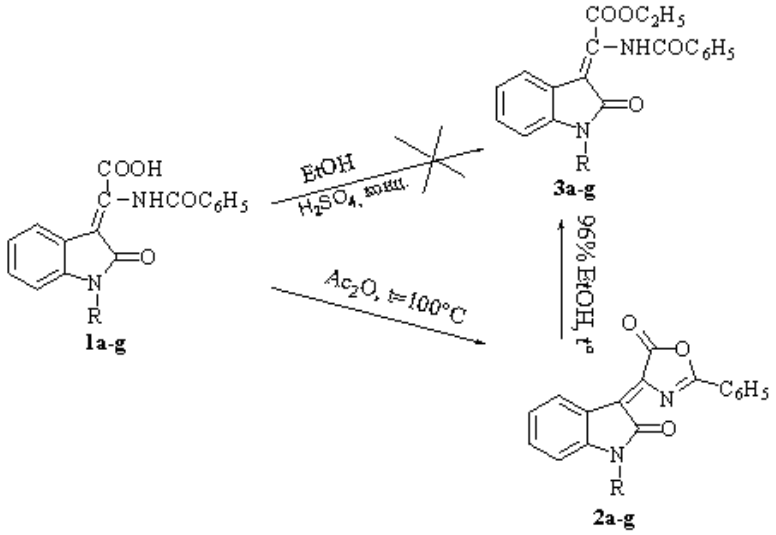
Method A. Boil 2.9 g of the solution of (0.01 Mole) of 1-R-3-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)-1,3-dihydro-2*H*-indole-2-one (**2a**) in 200 ml of absolute ethanol for 6 hours. Then add 100 ml of water to the reaction mixture and continue to heat for 30 minutes. Filter the precipitate obtained, wash with water, dry and recrystallize from ethanol. The yield is 3.10 g (92.5%). The melting point is 176-177°C. Compounds (**3b-g)** were obtained in the same manner.

Method B. Boil 2.9 g of the solution of (0.01 Mole) of 1-R-3-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)-1,3-dihydro-2*H*-indole-2-one (**2a**) in 50 ml of 96% ethanol on water bath for 1 hour. In 2 hours filter the precipitate obtained, wash with ethanol, dry and recrystallize from ethanol. The yield is 3.29 g (98%). The melting point is 176-177°C. Compounds (**3b-g)** were obtained in the same manner.

The mixed sample of compounds obtained by methods A and B does not lead to melting point depression, their ^{1}H NMR spectra are identical.

Results and discussion. An attempt to obtain 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethyl esters through esterification was unsuccessful. Even after a long boiling of the appropriate acids in absolute ethanol in the presence of concentrated sulphuric acid the starting compounds were isolated from the reaction mixture.

Taking into consideration alternative ways to obtain 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethyl esters, for their synthesis interaction of ethanol with 1-R-3-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)-1,3-dihydro-2*H*-indole-2-ones (**2a-g)** was proposed, in their turn, they were synthesized by heating of acids (**1a-g)** on boiling water bath with the excess of acetic anhydride (Scheme).



Based on the method described in scientific literature, alcoholysis of 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids azlactone is carried out with its long-term boiling (not less than 6 hours) using 10 times excess of absolute ethanol. We have proposed a preparative method for synthesis of 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethylic esters; it has significant advantages comparing to the current method, namely the use of 96% ethanol in the ratio of 1:4 and heating of the reaction mixture for one hour.

Ethyl esters of 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids (**3a-g)** after crystallization from ethanol are yellow crystalline substances with precious melting points that are soluble while heating in ethanol, dioxane, DMFA, DMSO.

Conclusions. 1. A new method for 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethylic esters has been developed and their synthesis has been performed.

2. The structure of the compounds synthesized has been confirmed by IR-, ^{1}H NMR – spectroscopy.