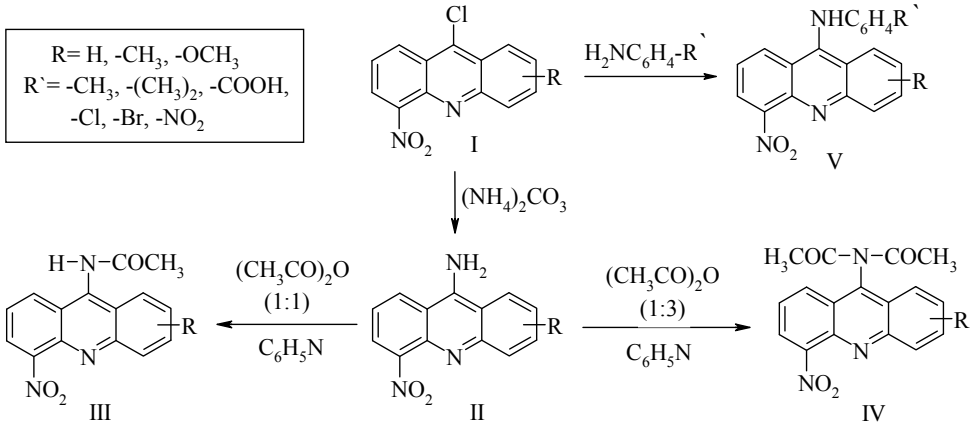
SYNTHESIS, PHYSICAL-CHEMICAL PROPERTIES, BIOLOGICAL ACTIVITY OF 9-ACETYL- AND 9-N-ARYLAMINO-DERIVATIVES OF 5-NITROACRIDINES

Yeromina H.O., Isaev S.G.
The National University of Pharmacy, Kharkiv, Ukraine
e-mail: medchimia@mail.ru

Derivatives of acridine are well-known for their antimicrobial properties. Their action is conditioned by ability to contact with nucleic acids that predetermines their influence on genetic elements of bacteria. These circumstances defined the necessity of further expansion of chemical and pharmacological study of the 9-acetyl- and 9-N-arylaminoderivates of 5-nitroacridine not investigated earlier (scheme):



In the interaction of 9-chloracridines (I) and ammonium carbonate the corresponding 9-aminoacridines (II) were synthesized. Acetylation of 9-aminoacridines (II) was carried out by heating them with acetic anhydride in pyridine medium in the ratio 1:1 or 1:3. Respectively 9-monoacetylaminoacridines (III) and 9-diacetylaminoacridines (IV) were obtained as a result. In the interaction of 9-chloracridines (I) and aromatic amines 5-nitro-9-N-arylaminoacridines (V) were obtained. The synthesis of 5-nitro-9-N-arylaminoacridines (V) was established experimentally to be more expedient to be conducted in the dioxane medium in the presence of hydrochloric acid. The advantages of the developed method are: exception of toxic phenol from the synthesis, reduction of the experiment time, a high yield of the desired product.

The structure of compounds (II-V) synthesized was confirmed by elemental, IR-, NMR-, UV-spectral analysis and their individuality has been proven by thin-layer chromatography.

According to classification by K.K. Sydorov the derivatives of 5-nitroacridine belong to the compounds with low toxicity, their DL_{50} is higher than 2500 mg/kg at intragastric introduction. Synthesized compounds (III-V) possess antimicrobial, antifungal, anti-inflammatory, cholagogue activities.