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AMINOMETHYLATION OF 3-ARYL-7-HYDROXYCOUMARINS

S. P. Bondarenko[1], M. S. Frasinyuk[1]*, and V. P. Khilya[1]

The reaction of the analogs of natural 3-arylbenzopyran-2-ones with electrophilic reagents of aminal structure was studied. Substituted 8-aminomethyl-3-aryl-7-hydroxycoumarins were synthesized. The optimum conditions were determined for the production of 9-alkyl- and 9-(het)arylmethyl derivatives of 3-aryl-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-one in the series of analogs of natural 3-arylbenzopyran-2-ones.

Keywords: 9,10-dihydro-2H,8H-chromeno[8,7-*e*][1,3]oxazin-2-one, coumarin, C- and O-aminomethylation, electrophilic substitution.

Coumarins, which are widely represented among compounds of vegetable origin, have a wide spectrum of pharmacological activity. More than 30 types of biological activity have been found in coumarins [1]. An advantage of products from vegetable raw material is the low toxicity and the possibility of prolonged use without risk of the appearance of side effects. In this connection the urgency of seeking new methods of introducing pharmacophoric groups into the molecules of natural compounds and their analogs is constantly increasing.

The introduction of a basic amino group, which is a structural feature of alkaloids, is one prospective method of modifying the compounds. While continuing research into the reactivity of the analogs of natural 3-arylbenzopyrones we studied electrophilic substitution in the series of 3-aryl-7-hydroxycoumarins for the case of the aminomethylation reaction, by means of which it is possible to obtain derivatives of aliphatic tertiary amines and their water-soluble salts.

The initial substituted 3-aryl-7-hydroxycoumarins **1a-d** were obtained under the conditions of the Perkin reaction by the condensation of substituted phenylacetic acids with 2,4-dihydroxybenzaldehyde or 2,4-dihydroxyacetophenone in acetic anhydride in the presence of potassium acetate as base [2-7] followed by deacylation of the acetoxy derivatives.

As known, the aminomethylation of 7-hydroxybenzopyran-2-ones takes place at position 8 of the coumarin ring [8-14] or at position 6 if position 8 is occupied [14, 15]. The presence of an electron-withdrawing heterocyclic substituent at position 3 of the benzopyran ring significantly reduces the reactivity of such compounds to the action of electrophilic reagents [9-11], whereas electron-donating groups can favor reaction in other directions [8, 16-18]. In this connection it was interesting to study features of the aminomethylation of the analogs of natural coumarins containing electron-donating alkoxy groups in the 3-aryl substituent.

* To whom correspondence should be addressed, e-mail: mfras@i.kiev.ua.

[1]Taras Shevchenko Kiev National University, Kiev 01033, Ukraine.

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