

CONJUGUÉS ALCALOÏDE FLAVONOÏDES ALKALOID-FLAVONOID CONJUGATES

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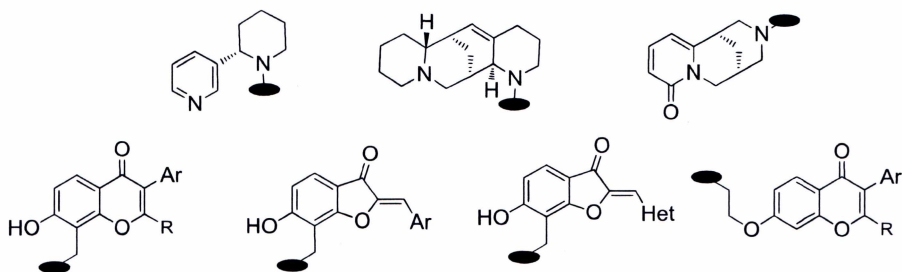
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Biologically active compounds of plant origin that are presently known are extremely varied. Nevertheless, the development of methods for synthesizing and modifying natural compounds is becoming more and more critical. The alkaloid-flavonoid conjugates are interesting as the combination of two pharmacophores in a single molecule.

It should be noted, the accrossing of biosynthetic pathways of alkaloids and flavonoids in a plants leads to formation secondary methabolites, which are contain both fragments. The most known of the similar compounds are *Sophora tonkinensis* alkaloids Tonkinenesin A and Tonkinenesin B, which possess anti-proliferative activity [1].



The interaction of 7-isoflavonoids with alkaloids in Mannich reaction was studied for the synthesis of semi-synthetic related alkaloid-flavonoid conjugates. The possibility of applying of cytosine, anabasine, and aloperine as amine was shown for aminomethylation of 7-hydroxyisoflavones, 6-hydroxyaurones, and related 6-hydroxy-3-hetarylbenzofuran-3-ones with paraformaldehyde. In all cases using of 4-(dimethylamino)pyridine was required. The aminomethylation of 7-hydroxyisoflavones with alkaloids was regioselective and led to formation of 8-alkaloid-methyl-7-hydroxyisoflavones. The similar reaction with 6-hydroxyaurones and their hetero analogues led to 7-aminomethyl substituted benzylideno 6-benzofuran-3-ones.

Another way for the synthesis of alkaloid-isoflavone conjugates was alkylation of cytosine or aloperine with 7-(2-bromoethoxy)isoflavones, which were obtained by alkylation with 1,2-dibromoethane. In this cases C₂-linked hybrids were obtained.

Thus, we synthesized various derivatives containing flavonoid and cytosine, aloperin, or anabasine moieties connected by one or two methylene groups in the position 8 or in O-7 of the chromone ring respectively. Another type of alkaloid-flavonoid conjugates are presented as 7-aminomethyl-6-hydroxyaurones.

1. X.-N. Li, Z.-Q. Lu, S. Qin, H.-X. Yan, M. Yang, S.-H. Guan, X. Liu, H.-M. Hua, L.-J. Wu, D.-A. Guo, *Tetrahedron Lett.*, 2008,49, 3797.