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SYNTHESIS OF FORMONONETIN ANALOGS

S. P. Bondarenko, M. S. Frasinyuk, and V. P. Khilya

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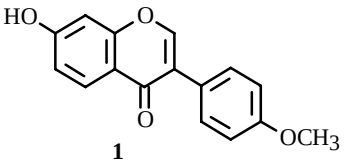
Derivatives of the natural isoflavone formononetin were synthesized. Acylation and alkylation of the phenolic hydroxyls and the chromone ring were investigated.

Key words: isoflavonoids, alkylation, aminomethylation, acylation.

The search for new highly effective bioregulators among modified analogs of natural isoflavones is very promising. They are used in medical practice [1] owing to the broad spectrum of physiological activity and low toxicity.

Isoflavonoids containing a methoxy in the para-position of ring B are used as natural antioxidants [2] and for prophylaxis of cardiovascular diseases [3] and breast [4] and prostate [5] cancers.

The natural isoflavonoid formononetin (7-hydroxy-4′-methoxyisoflavone) (**1**) possesses hypolipidemic activity [6] and lowers the cholesterol, triglyceride, phospholipid, and β-lipoprotein levels in blood [7, 8].



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In order to modify formononetin, we performed alkylation, acylation, and aminomethylation of isoflavones **2**-**5** [9-12].

Alkylation in acetone in the presence of freshly calcined potash produced 7-phenyloxy- and 7-phenylallyloxyisoflavones and ethyl 4-oxo-4*H*-chromenyl-7-hydroxyacetate (**6**-**8**).

Acylation of 7-hydroxyisoflavones proceeded readily in pyridine at room temperature. The acylating reagents were chlorides of naturally occurring acids (trimethylgallic, veratric, cinnamic, benzodioxolcarboxylic) and heterocyclic acids (substituted 3-benzofurancarboxylic, furan- and thiophenecarboxylic). Esters of methanesulfonic and carbonic acids of isoflavones were synthesized by reactions with methanesulfonylchloride and ethylchloroformate. Urethanes were prepared by acylation of N,N-disubstituted carbamoyl chlorides.

Mannich bases (**22**-**29**) were prepared by C-alkylation of the chromone ring. Aminomethyl derivatives of 7-hydroxyisoflavones were synthesized using various aminals based on piperidine or piperazine. Reaction of an equivalent amount of aminal in boiling dioxane led to aminomethylation of the chromone ring in the 8-position.

Taras Shevchenko Kiev University, 252033, Kiev, ul. Vladimirskaya, 64, fax (380) 442 351 273, e-mail: mfras@i.kiev.ua. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 277-280, July-August, 2003. Original article submitted July 23, 2003.

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