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SYNTHESIS OF MODIFIED LUPININ DERIVATIVES

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Abstract

The article presents the results of research aimed at the synthesis and study of various modified benzoyl esters of the alkaloid lupinin in order to find among them effective biologically active substances that have a certain superiority over known drugs. The main objectives of the study were: to develop a synthesis method, to establish the structure and configuration of synthesized compounds.

Keywords: *alkaloid, synthesis, lupinin, structure, bond, spectrum*

Introduction

One of the priority areas of bioorganic chemistry is the modification of molecules of natural compounds, in particular alkaloids. In this regard, lupinin alkaloids by their chemical structure belong to the most interesting class of compounds, among which there are substances with various combinations, for example, carbonic and heterocycles, conformational and optical isomers. Modification of the alkaloid molecule opens up wide opportunities for the search for highly effective, selective, stereospecific biologically active substances (Sadykov, A.S., Aslanov, X.A., Kushmuradov, Yu.K., 1975).

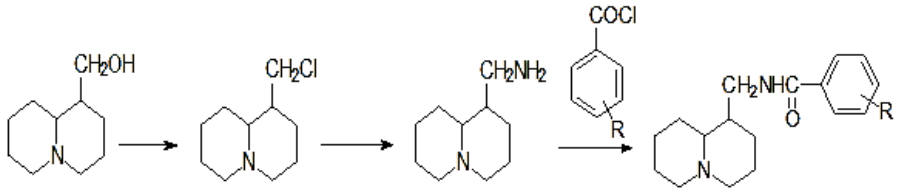
Among such alkaloids, lupinin (7a-hydroxymethyl-trans-quinolizidine) occupies an important place and is contained in significant quantities and is extracted from the Central Asian plant Anabasis aphylla L., belonging to the Chenopodiaceae family (Nasirov, S.H., Hazbievich, I.S., 1982.

Among the known derivatives of lupinin, its esters, which have pronounced antiviral, antitumor and hepatoprotective activity, are the most studied (Sadykov, A.S., Aslanov, X.A., Kushmuradov, Yu.K., 1975; Nasirov, S.H., Hazbievich, I.S., 1982; Tlegenov, R.T., 1991). Series of lupinine esters showed local anesthetic effect, antituberculous and anticholinesterase activity

(Nasirov, S.H., Hazbievich, I.S., 1982; Tlegenov, R.T., 1991).

Results and their discussion

In order to find new highly effective biologically active compounds among lupinin derivatives, we synthesized new derivatives of lupinin – its aminoesters. Synthesis was carried out according to this scheme:

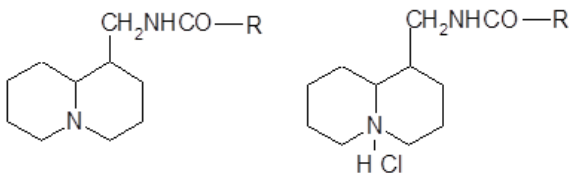


R = o-COC_6H_5; m-OCH_3; m-NO_2; p-NH_2; 2,4-Cl;

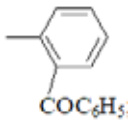
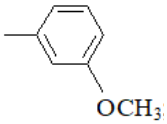
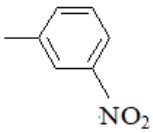
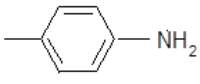
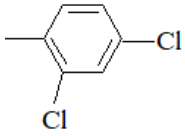
Of all the synthesized compounds, ortho-benzoyl-, 2,4-dichloro-p-amino substituted benzoylamidolupinins are crystalline substances with a yellowish tinge, and the rest are oily substances. The individuality of the synthesized compounds was controlled by thin-layer chromatography. Hydrochlorides were obtained by the action of dry hydrogen chloride. All hydrochlorides are obtained clean and do not require further cleaning. The characteristics of the synthesized compounds are given in Table 1.

The structure of the obtained substances is confirmed by the data of PMR, IR and mass spectra.

Table 1. *Physico-chemical characteristics of aminobenzoyl esters of aminolupinin (I) and their hydrochlorides (II)*

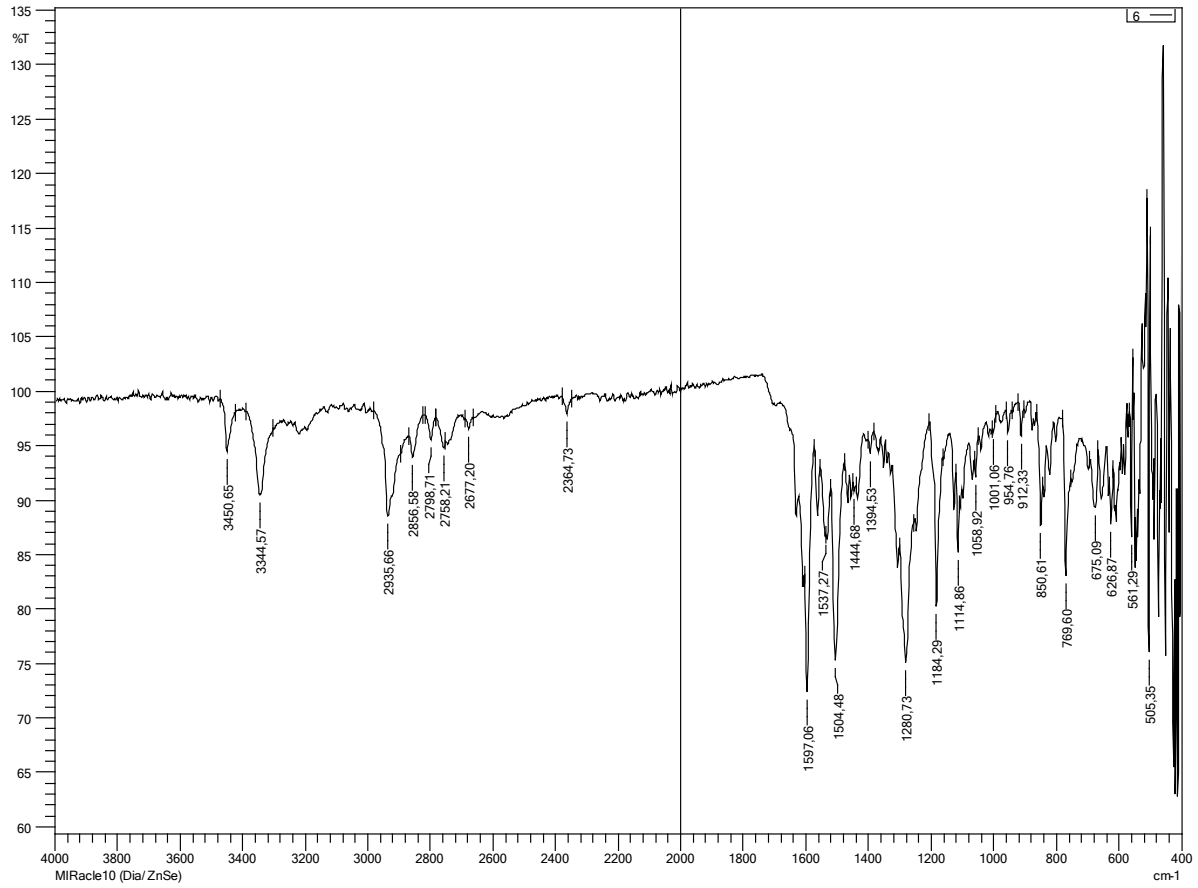


I II

№	R	Exit,%	Melting point, °C (I)	R_f	Melting point,°C (II)
1		68.0	167–169	0.92	hygroscope
2		59.0	87–89	0.54	142–143
3		79.0	oil	0.68	hygroscope
4		59.6	147–149	0.28	83–85
5		59.8	158–160	0.33	hygroscope

In the IR spectrum (1–5) there are intense absorption bands characteristic of functional groups (ϒ, cm^{-1}): 3350––3450 cm^{-1} (–NH-group); 1250–1190 cm^{-1} (– C - N -); 1590–1610 cm^{-1} (– C = C-aromatic core); 1610–1700 cm^{-1} (– N - C = 0) and 2800–2650 cm^{-1} (trans-quinolizidine system).

Figure 1. *IR spectrum of p-aminobenzoyl ether of aminolupinin*



In the PMR spectra of aminobenzoyl esters of aminolupinin (1–5), there is a complex signal in the region of 3.7–3.9 p.p.m. (2H, m) of the CH_2-N fragment. Signals of aromatic protons are observed at 7.6––7.9 p.p.m. (4H, m). in the region of 1.1––2.2 p.p.m. (14H, m, CH_2), signals belonging to protons of the quinolizidine fragment are noted. The positions of the other signals depend on the specific type of substituent. All the obtained spectra confirm the structure of the synthesized derivatives of aminobenzoyl esters of aminolupinin.

In the mass spectra of these compounds there are peaks with m/e 167, 152, 136, 124, 98, and etc., characteristic of alkaloids with a trans-quinolizidine system.

Conclusions

Thus, some lupinin derivatives with substituted benzoic acids bound by an amide bond and their hydrochlorides were synthesized. Their physico-chemical constants are determined. Based on the study of the IR, PMR and mass spectra of the obtained compounds, their structure has been established.

Modified derivatives of the lupinin alkaloid may offer great prospects in the search for biologically active substances with high efficiency, selectivity and stereospecificity.

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