FORMATION OF ETHERS OF PSEUDOBASES FROM SALTS OF THE QUATERNARY ALKALOIDS SANGUINARINE AND HELERITRINE

O. N. Tolkachev, O. E. Lasskaya, and G. A. Maslova

UDC 547.944/945

It is known from the literature that the bases of quaternary ammonium alkaloids exist in equilibrium with the carbinolamine forms [1-3]. On reaction with hydroxyl-containing solvents, they are converted into the corresponding ethers of the pseudobases. The latter are readily formed during the dissolution of the bases or on their crystallization from the corresponding solvents. The ethers of the pseudobases can be identified fairly reliably from the signals of alkoxy groups and from the proton geminal to the alkoxy group in the NMR spectrum (Table 1). Their purity is also determined by potentiometric titration (Table 2).

We isolated sanguinarine and heleritrine from plant raw materials by a known method in the form of the sparingly water-soluble hydrogen sulfates, which are readily separated from the accompanying tertiary alkaloids [4].

In the potentiometric titration of the hydrogen sulfates of these alkaloids it was observed that the samples always contained a certain amount of material not titrated by alkali, the amount of which increases as the substances were recrystallized from aqueous solutions of alcohols. The concentration of nontitratable impurities in samples of the combined hydrogen sulfates of sanguinarine and heleritrine as a function of the number of crystallizations from 48% ethanol are given below:

No. of crystallization from 48% ethanol	1	2	3	4
Concentration of untitratable impurities in the samples, %	7.30	11.75	25	28

TABLE 1. Chemical Shifts of the Ethyl Ethers of the Pseudobases of Sanguinarine and Heleritrine

Compound	NCH_3	$(OCH_3)_2$	CH_2O_2	H-C-OR	Aromatic protons
Ethoxydihydroheleritrine	2,65* s	3,82 s 3,88 s	5,85 s (2H)	5,61 s	7,03 s, 7,58 s, 6,94 d, 7,36 d, 7,52 d, 7,69 d, (J=8 Hz)
Ethoxydihydrosanguinarine	2,68 s	—	5,88 s (4H)	5,42 s	7,05 s, 7,59 s, 6,85 d, 7,34 d, 7,41 d, 7,68 d (J= 8 Hz)

*s) singlet; d) doublet (chemical shifts given in the δ scale).

All-Union Scientific-Research Institute of Medicinal Plants. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 615-617, September-October, 1975. Original article submitted July 16, 1974.

TABLE 2. Results of the Potentiometric Titration of the Ethyl Ethers of the Pseudobases of Sanguinarine and Heleritrine

Compound	Metrological data				
	n	$\bar{x}$	$s_{\bar{x}}$	$E_{0,95}$	E_{rel}
Ethoxydihydrosanguinarine	5	99,15	0,10	0,28	0,30
Ethoxydihydroheleritrine	5	99,10	0,21	0,58	0,63

To study the nature of the untitratable impurities, they were separated by extraction with aprotic organic solvents and were then identified by chromatographic comparison and also by means of their NMR spectra with standard specimens of alkoxydihydrosanguinarine and alkoxydihydroheleritrine. In this way it was shown that ethoxydihydrosanguinarine and ethoxydihydroheleritrine are formed from their salts on reacting with alcohols or solvents containing them. Since sanguinarine reacts with alcohol more readily than heleritrine, in the unpurified samples including both alkaloids the alkoxydihydrosanguinarine is always formed in predominating amounts.

The dissimilar rates of reaction with alcohols of the hydrogen sulfates of sanguinarine and heleritrine are due to the different electron densities on the carbon atom subjected to nucleophilic attack because of the contributions to conjugation with the aromatic ring of the substituents in the 9-10 position. The unshared pairs of the oxygen atoms of the methylenedioxy group are almost parallel to the π-orbitals of the aromatic ring, and consequently, are conjugated with the latter, while the methoxy groups of heleritrine are only partially conjugated with the ring as the result of rotation about the C–O bonds. The difference in conjugation can be seen clearly from the electronic absorption spectra of these alkaloids in the visible region (sanguinarine absorbs at longer wave lengths than heleritrine).

Hence, it may be assumed that the ethers of the pseudobases of these alkaloids isolated by different authors from natural sources [5, 6] are artefacts, judging from the methods used for their isolation.

EXPERIMENTAL

The NMR spectra were taken on a Varian HA-100 instrument ($CDCl_3$, 0 – HMDS). The purity of the compounds was checked in a thin layer of "Silufol" silica gel [diethyl ether–petroleum ether–methanol (35:15:3) system]. The elementary analyses of the compounds agreed with the calculated figures.

The amounts of ethoxydihydro derivatives of sanguinarine and heleritrine in the samples were determined quantitatively by titrating their acetic acid solutions with a 0.01 N solution of perchloric acid in acetic acid using an LP-58 potentiometer with glass and calomel electrodes. The control experiment was performed in parallel. 1 ml of a 0.01 N solution of perchloric acid corresponds to 0.00377 g of ethoxydihydrosanguinarine and to 0.00393 g of ethoxydihydroheleritrine.

The amount of the combined hydrogen sulfates of sanguinarine and heleritrine in the preparation was determined by titrating aqueous solutions of the preparation with 0.1 N aqueous caustic soda in an LP-58 potentiometer with the same electrodes. 1 ml of 0.1 N caustic soda solution corresponds to 0.04374 g (average molecular weight; the preparation contains the alkaloids in approximately equal proportions) of the combined hydrogen sulfates of sanguinarine and heleritrine.

SUMMARY

It has been shown that the sulfates of the quaternary alkaloids sanguinarine and heleritrine react with alcohols to form the corresponding ethers of the pseudobases.

LITERATURE CITED

1. J. Slavik and L. Slaviková, Collection Czech. Chem. Commun., Vol. 25, No. 6, 1667 (1960).
2. V. Šimanek, V. Preininger, S. Hegerová, and F. Šantavý, Collection Czech. Chem. Commun., 37, 2746 (1972).

3. V. Shimanek [Simanek], The Chemistry of Plant Substances [in Russian], Tashkent (1972), p. 95.
4. V. A. Chelombit'ko and D. A. Murav'eva, Khim. Farmatz. Zh., 49 (1968).
5. D. B. MacLean, D. E. F. Gracey, J. K. Saunders, R. Rodrigo, and R. H. F. Manske, Canad. J. Chem., 47, No. 11, 1951 (1969).
6. F. G. Tarto and I. A. Mensah, Phytochem., 9, No. 4, 911 (1970).