NEW N-SUBSTITUTED CYTISINE DERIVATIVES

R. A. Shaimardanov, S. Iskandarov,
and S. Yu. Yunusov

UDC 547.944/945

The widespread nature and high physiological activity of cytisine enables various N-substituted derivatives to be obtained from it for the purpose of establishing an interrelationship between structure and physiological activity. Numerous cytisine derivatives have been synthesized by condensing it with various alkyl halides, acid chlorides, amino acids, etc. [1-3].

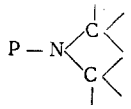
We have obtained N-substituted derivatives of cytisine and of N-(3-amino-2-hydroxypropyl)cytisine with dialkyl phosphites. For this purpose, 2 moles of cytisine was dissolved in a mixture of chloroform and carbon tetrachloride, and 1 mole of dialkyl phosphite was added. During the first few days, cytisine hydrochloride deposited. To complete the reactions, the mixture was left at room temperature for 7 days.

After the separation of the crystals from the mother liquor, chromatography on a column of silica gel (elution with a mixture of chloroform and methanol) gave the N-(dialkoxyphosphinyl)cytisines.

The treatment of N-(3-chloro-2-hydroxypropyl)cytisine [4] with conc. ammonia solution gave N-(3-amino-2-hydroxypropyl)cytisine, forming a crystalline hydrate with mp 233-234°C.

The condensation of N-(3-amino-2-hydroxypropyl)cytisine with dialkyl phosphites likewise gave its N'-dialkoxyphosphinyl derivatives. The physicochemical constants of the derivatives obtained are given in Table 1.

The structures of products (I)-(VII) were established by their IR, mass and NMR spectra. The IR spectra of (I)-(IV) show the presence in the substances of an α-pyridone ring (1660, 1565, and 1585 cm^{-1}),



grouping (810-820 cm^{-1}), and of a P–O–C (alkyl) group (990 cm^{-1}) [5]. In the IR spectrum of (V), in addition to the absorption of the α-pyridone fragment there are absorption bands showing the presence in the substance of OH and NH_2 groups (3380 and 3300 cm^{-1}, respectively).

TABLE 1

Substance	Comp.	$[\alpha]_D$, deg	R_f^*	n_D^{20}	Yield, % of theoretical
N-(diethoxyphosphinyl)cytisine (I)	$C_{15}H_{23}N_2PO_4$	−187,7	0,78	1,5395	84
N-(dipropoxyphosphinyl)cytisine (II)	$C_{17}H_{27}N_2PO_4$	−168,9	0,84	1,5304	57
N-(dibutoxyphosphinyl)cytisine (III)	$C_{19}H_{31}N_2PO_4$	−153,8	0,83	1,5110	97
N-(diisobutoxyphosphinyl)cytisine (IV)	$C_{19}H_{31}N_2PO_4$	−151,6	0,82	1,5135	62
N-(3-amino-2-hydroxypropyl)cytisine (V)	$C_{14}H_{21}N_3O_2$	−154,1	0,07	1,5616	Quantitative
N-[3-(dipropoxyphoshinylamino)-2-hydroxypropyl]cytisine (VI)	$C_{20}H_{34}N_3PO_5$	−98,1	0,89	1,5212	59
N-[3-(dibutoxyphosphinylamino)-2-hydroxypropyl]cytisine (VII)	$C_{22}H_{38}N_3PO_5$	−88,2	0,88	1,5115	63

*TLC on silica gel in the chloroform–methanol (4:1) system.

Order of the Red Banner of Labor Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 383-384, May-June, 1971. Original article submitted March 1, 1971.

By comparing the extinction coefficients of the absorption maxima in the UV spectra between 234 and 310 nm we determined the molecular weights of the products obtained. The structures of the cytisine derivatives obtained were also confirmed by the assignment and integration of the signals of the protons.

LITERATURE CITED

1. Z. P. Pakudina and S. Yu. Yunusov, Izv. Akad. Nauk UzSSR, Ser. Khim. Nauk, 2, 69 (1957).
2. S. B. Davidyants, É. M. Kryukova, I. N. Griginina, and K. T. Poroshin, Dokl. Akad. Nauk TadzhSSR, 1967, No. 1, 18.
3. G. Luputiu and L. Gilau, Arch. Pharm. (Weinheim), 302, No. 12, 943 (1969).
4. I. Primukhamedov, P. Ch. Gupta, Kh. A. Aslanov, and A. S. Sadykov, Khimiya Rastitel'nykh Veshchestv. Tr. TashGU, Tashkent, 3, No. 341, 102 (1968).
5. L. Bellamy, Infrared Spectra of Complex Molecules, 2nd ed., Methuen (1958).