2-Methyl-2-(1-methyl-2-alkylthioethyl)-4-dimethylaminomethoxymethyl-1,3-dioxolanes (V, VI). Into a flask fitted with reflux condenser and a Dean and Stark attachment there were added III (0.05 mole), diethylamine (0.05 mole), paraformaldehyde (0.05), and p-toluenesulfonic acid (100-150 mg) in toluene (50 ml). The mixture was refluxed until water (0.9 ml) had collected. After drying the solution ($MgSO_4$) the solvent was distilled off and the product fractionated *in vacuo*. The yields and physical constants for V and VI are given in Table 1.

EXPERIMENTAL (PHARMACOLOGICAL)

The antibiotic activity of 1,3-dioxolanes was determined by the method of progressive dilution. The strains used in this work were: staphylococci, streptococci, *B. pyocyaneus*, *E. coli*, and anthracoids. The data obtained points to a sharp increase in the antibacterials' V and VI activity upon introduction of a tertiary nitrogen atom at position 4 of the heterocycle.

The acute toxicity of the compounds was studied in white mice and the LD_{50} claculated according to Kerber [2]. Preparations were introduced in increasing doses in 10% Tween-80. These experiments showed that all compounds were of low toxicity but that the toxicity was highest when the diethylamino group was introduced into the 1,3-dioxolane ring (Table 2).

LITERATURE CITED

1. M. D. Babakhanov, S. Sh. Shukurov, S. S. Sabirov, and M. D. Isobaev, Zh. Org. Khim., 16, 1093-1094 (1980).
2. M. L. Belen'kii, Elements of Quantitative Analysis of the Pharamacological Effect, 2nd Edition, [in Russian], Leningrad (1963), pp. 97-103.
3. A. N. Nikol'skaya, A. N. Volkova, E. P. Levanova, et al., Khim.-farm. Zh., No. 5, 82 (1978).
4. G. P. Sokolov, A. A. Kimenis, D. K. Kruskop, et al., Khim.-farm. Zh., No. 2, 10-13 (1972).
5. G. P. Sokolov, R. O. Vitolin', and S. A. Giller, Khim.-farm. Zh., No. 12, 70 (1973).

SYNTHESIS AND ANTIFUNGAL ACTIVITY OF SOME γ-IODOPROPARGYL ESTERS OF MONO- AND DICARBAMATES

A. G. Makhsumov and M. A. Atakhodzhaeva

UDC 615.282:[547.239+547.362].012.1

Data on the pharmacological activity of carbamate derivatives is given in the literature [1, 3]. Related preparations used in medical practice include meprotan (meprobamate), isoprotan, etc.

In a further search for biologically active carbamate derivatives, we synthesized previously-unknown γ-iodopropargyl esters of carbamic acids. They were prepared not by the hypohalide method [4], but directly by the substitution of metals by halogen in acetylides in dry ether solution according to the following scheme:

$$RNHC(O)OCH_2C{\equiv}CCu + I_2 \xrightarrow{\text{ether}} RNHC(O)OCH_2C{\equiv}CI$$

I: $R = C_6H_5$; II: $R = 2,4\text{-}Cl_2C_6H_4$; III: $R = \alpha\text{-}C_{10}H_7$; IV: $R = CH_3(CH_2)_{17}$; V: $R = IC{\equiv}CCH_2OC(O)NH(CH_2)_6$; VI: $R = IC{\equiv}CCH_2OC(O)NHC_6H_3(CH_3)\text{-}4$

The γ-iodopropargyl carbamates I-VI (cf. Table 1) are stable under ordinary conditions and are crystalline substances, easily soluble in organic solvents and insoluble in water.

The composition and structure of the compounds obtained were supported by data from elemental analysis and IR spectroscopy. The IR spectra of the γ-iodopropargyl carbamates showed absorption bands characteristic of the C≡C oscillation in the 2210 cm^{-1} region, of the N–H bond in the 3310 cm^{-1} region, and of the carbamate group in the 1710 cm^{-1} region.

Tashkent Medical Institute.

Translated from Khimiko-Farmatsevitcheskii Zhurnal, Vol. 19, No. 12, pp. 1455-1456, December, 1985. Original article submitted November 28, 1984.

0091-150X/85/1912-0855$09.50

TABLE 1. γ-Iodopropargyl Carbamates (I-VI).

No.	Yield, %	mp, °C	I %, Found	Empirical Formula	I %, Calculated
I	91,4	134	41,87 41,91	$C_{10}H_8INO_2$	42,19
II	93	101	34,22 34,25	$C_{10}H_6Cl_2INO_2$	34,32
III	93	123	36,05 36,12	$C_{14}H_{10}INO_2$	36,18
IV	91	78—80	26,50 26,53	$C_{22}H_{40}INO_2$	26,62
V	82	110	47,62 47,67	$C_4H_{10}I_2N_2O_4$	47,74
VI	90	86	47,13 47,17	$C_{15}H_{12}I_2N_2O_4$	47,21

The antifungal activity of the synthesized compounds was studied. Preliminary tests were carried out by diffusion in two-layered agar gels of 1, 5, and 10 mg suspensions of the preparations. Fungicidal and fungistatic doses were established in conformity with the approved USSR Health Ministry unified method for the determination of the sensitivity of micro-organisms to chemotherapeutic preparations. The fungicidal activity of the preparations was stuided on the following fungi: *Penicillium waksmani*, *Trichoderma ronihge*, *Alternaria fenius*, *Aspergillus flavus*, and *Fusarium monilforme*. The most effective of the series of tested compounds proved to be γ-iodopropargyl phenylcarbamate (I). A suspension of 1 mg in an agar gel test suppressed the growth of the indicated fungi in 20-38 mm zones.

In beef broth cultures, (Chapeka liquid medium), it was established that I, in dilutions of 1:4000, 1:8000, 1:16,000, and 1:64,000, in which the compound I content was 1250, 626, 362.5, and 90.625 μg/ml of nutritive medium, respectively, had activity against *Penicillium waksmani*, *Aspergillus flavus*, *Fusarium monilforme*, and *Trichoderma ronihge*.

Thus, our novel synthetic series of γ-iodopropargyl carbamates has effective anti-fungal activity [1].

EXPERIMENTAL

IR spectra were recorded on an UR-20 spectrometer (GDR) in KBr pellets.

γ-Iodopropargyl Phenylcarbamate (I). The starting copper acetylide (2.38 g, 0.01 mole) in a three-necked flask was stirred slowly while adding 400 ml of dry diethyl ether. Elemental iodine was added in portions with vigorous stirring until the solution remained colored, and the reaction mixture was then stirred for about ½ h at room temperature. The flask contents were then filtered, and the filtrate was purified by column chromatography to give 2.75 g 91.4%).

The other γ-iodopropargyl carbamates (II-IV) were prepared analogously (cf. Table 1).

LITERATURE CITED

1. US Patent 4,180,399 (1980).
2. Japanese Patent 5,425,027 (1979).
3. F. Pavanetto, M. Mazza, L. Montanari, and T. Modena, Farm. Ed. Sci., 34, 808-816 (1979).
4. Sh. Seki, K. Nichinata, T. Nakayama, and H. Ocana, Agr. Biol. Chem. (Tokyo), 27, 150 (1963).