On the basis of this experimental study it is evident that among the I-III, IV, and X type of compounds antiviral activity is possessed only by those which contained the triazo, hydroxy, and epoxy groups. Among the IV-VIII compounds, which possess the ester group, antiviral activity is shown only by those substances which contain the following two groups: two epoxide rings or one epoxide ring and double bond along with a methyl group on the six-member carbon ring and the ester group.

LITERATURE CITED

1. J. G. Boyer and F. K. Kanter, Usp. Khim., 26, No. 1, 54-95 (1957).
2. L. A. Mukhamedova, F. G. Nasybullina, and M. I. Kudryavtseva, Izv. Akad. Nauk SSSR, Ser. Khim., 2066-2069 (1977).
3. T. M. Malyshko, M. I. Kudrayvtseva, F. G. Nasybullina, et al., Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol., 24, 42-46 (1981).
4. L. A. Mukhamedova, T. M. Malyshko, and R. R. Shagidullin, Dokl. AN SSSR, 160, 1323-1326 (1965).
5. B. A. Arbuzov, Studies on the Isomeric Transformations of Bicyclic Terpene Hydrocarbons and Their Oxides [in Russian], Kazan' (1936), p. 209.
6. L. A. Mukhamedova, T. M. Malyshko, and M. V. Konoplev, Inventor's Certificate No. 320487; Oktrytiya, No. 34 (1971).
7. Z. Chabudzinski, Z. Rikowski, and H. Orszanska, Pol. J. Chem., 52, 767-774 (1978).
8. S. de Fazekas, S. Growth, G. S. Watson, and A. F. Reid, J. Immunol., 80, 215-224 (1958).
9. F. Link, in: Methods in Virology, K. Maramorosch and H. Koprowski, eds., New York, 4, 211-278 (1968).
10. V. I. Il'enko, Methods for testing and evaluating antiviral activity of chemicals against influenza virus. Instructions [in Russian], Leningrad (1977), pp. 12-15.

SYNTHESIS AND ANTIMICROBIAL PROPERTIES OF PHOSPHONIOSULFONAMIDES

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Since the discovery that some sulfonamides are able to lower the sugar content in blood and have a long-term action [1], the interest in these compounds has increased.

In the present work, experimental data are reported on the synthesis of phosphoniosulfonamides of different structure and on the study of their antimicrobial properties. No information on sulfonamides of triphenylphosphonium salts and their physiological activity is available in the literature.

Conditions were found under which β-acylallyl- and β-acylvinyltriphenylphosphonium salts, and bistriphenylphosphoniobutenone chloride and p-formylphenyltriphenylphosphonium bromide [2-6] condense at the carbonyl group with a series of sulfonamides commonly used in medicine (streptocide, ethazole, norsulfazole, sulfadimezine, sulfadimethoxine, etc). The formation of phosphoniosulfonamides takes place on heating equimolar amounts of the above phosphonium salts and the corresponding sulfonamides in alcohol. Phosphoniosulfonamides I-X were obtained by the condensation of β-acylvinyltriphenylphosphonium salts with sulfonamides by the reaction

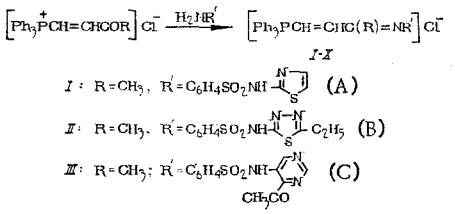

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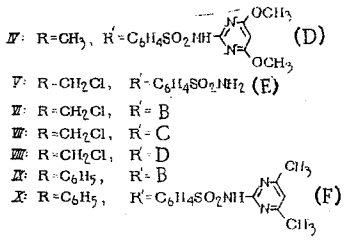
TABLE 1. Antimicrobial Activity of Phosphoniosulfonamides

Compound	Yield, %	mp. °C	St. aureus		Salm. typhi		Salm. typhimurium		B. anthracoides		P. vulgaris		E. coli		P. aeruginosa		K. rhinoseleromatis	
			MBsC	MBcC	MBsC	MBcC	MBsC	MBcC	MBsC	MBcC	MBsC	MBcC	MBsC	MBcC	MBsC	MBcC	MBsC	MBcC
I	52	154—156	15,6	125	500	500	500	G	125	500	125	500	250	G	500	G	G	G
II	50	160—164	62,5	125	250	500	500	G	500	G	500	G	G	G	G	G	G	G
III	67	—	31,2	125	125	500	500	G	500	G	500	G	500	G	G	G	125	G
IV	63	180—182	31,2	125	62,5	125	500	G	G	G	500	G	500	G	G	G	500	G
V	64	201—203	31,2	125	500	500	500	500	500	500	500	125	500	500	G	G	250	500
VI	60	205—207	125	500	250	500	500	G	500	G	G	G	G	G	G	G	500	G
VII	40	214—216	31,2	125	62,5	500	500	G	500	G	500	G	500	G	G	G	G	G
VIII	58	222—225	62,5	125	62,5	500	500	G	500	G	500	G	G	G	G	G	G	G
IX	54	160—162	500	500	250	500	G	G	250	G	125	G	G	G	G	G	G	G
X	50	169—171	125	250	250	500	500	500	500	500	250	500	G	G	G	G	500	G
XI	62	160—162	15,6	125	250	500	250	500	500	500	250	500	250	G	500	G	250	500
XII	51	182—184	7,8	31,2	250	500	250	500	62,5	250	31,2	125	250	500	250	500	250	G
XIII	50	154—157	5,6	500	250	500	250	500	250	500	250	500	500	G	500	G	250	500
XIV	40	147—150	3,9	31,2	250	500	500	500	500	62,5	500	125	500	125	500	125	125	500
XV	74	174—196	62,5	500	500	500	500	500	500	G	500	500	G	G	G	G	500	G
XVI	61	—	3,9	15,6	250	500	250	500	125	500	62,5	250	250	500	125	500	31,2	125
XVII	70	192—194	7,8	7,8	125	500	250	500	31,2	125	31,2	62,5	250	500	250	500	125	500
XVIII	42	187—190	15,6	125	250	500	250	500	250	500	250	500	500	G	500	G	62,5	250
XIX	78	140—142	31,2	125	125	500	500	G	500	G	250	G	500	G	G	G	250	G
XX	46	—	7,8	15,6	250	500	250	500	250	500	62,5	125	125	500	500	G	125	G
XXI	—	—	15,6	15,6	15,6	31,2	500	G	62,5	125	31,2	125	250	500	250	G	62,5	250

Notes. 1) MBsC — minimal bacteriostatic concentration (in μg/ml); MBcC — minimal bactericidal concentration (in μg/ml); G — growth of microorganism in the presence of 500 μg/ml of preparation. 2) Quantitative analysis data for compounds I-XXI for Hal, N, and S correspond to the formulas of these compounds and are within the permissible errors.



Phosphoniosulfonamides XI-XIV were prepared similarly by the condensation of β-acetylallyltriphenylphosphonium chloride with the sulfonamides

$$[Ph_3\overset{+}{P}CH_2C(=CH_2)COCH_3]\overset{-}{Cl} \xrightarrow{H_2NR} [Ph_3\overset{+}{P}CH_2C(=CH_2)C(CH_3)=NR]\overset{-}{Cl}$$

XI:R = E; XII:R = A; XIII:R = B; XIV:R = F

Reaction of β-chloroacetylvinyltriphenylphosphonium chloride with a twofold excess of sulfonamides takes place both at the carbonyl group and at the chloromethyl group, and leads to the formation of a bis-substitution product. Thus, compound XV was synthesized by the reaction of this salt with a twofold excess of streptocide

$$[Ph_3\overset{+}{P}CH=CHCOCH_2Cl]\overset{-}{Cl} \xrightarrow{H_2NR} [Ph_3\overset{+}{P}CH=CHC(=NR)CH_2NHR]\overset{-}{Cl}$$

XV:R = E

Compounds XVI-XX were obtained by condensing bistriphenylphosphoniobutenone chloride with the sulfonamides according to the scheme:

$$[Ph_3\overset{+}{P}CH=CHCOCH_2\overset{+}{P}Ph_3]2\overset{-}{Cl} \xrightarrow{H_2NR} [Ph_3\overset{+}{P}CH=CHC=(-NR)CH_2\overset{+}{P}Ph_3]2\overset{-}{Cl}$$

XVI — XX

XVI:R = E; XVII:R = A; XVIII:R = B; XIX:R = C; XX:R = F.

Phosphoniosulfonamide XXI was synthesized by reacting p-formylphenyltriphenylphosphonium bromide with sulfadimezine:

$$[Ph_3\overset{+}{P}C_6H_4CHO]\overset{-}{Br} \xrightarrow{H_2NR} [Ph_3\overset{+}{P}C_6H_4CH{-}NR]\overset{-}{Br}$$

XXI:R = F

The phosphoniosulfonamide chlorides I-XXI synthesized (see Table 1) are yellow brown crystalline compounds, which are stable under normal conditions, sparingly soluble in water, soluble in alcohol, acetone, and other polar organic solvents.

The antimicrobial activity of the compounds towards certain pathogenic and conditionally pathogenic types of bacteria and fungi was determined by the method of double serial dilutions in liquid culture medium [7].

Activity of compounds I-XXI was shown towards all test microbes studied. Antimicrobial activity was shown towards gram-positive bacteria (*St. aureus, B. anthracoides*); in experiments with *St. aureus*, bacteriostatic action was noticed generally in concentrations from 3.9 to 62.5 μg/ml. Gram-negative bacteria (*E. coli, Salmonella typhimurium, S. typhi, K. rhinoseleromatis, P. aeruginosa, Pr. vulgaris)* were found to be slightly sensitive towards the compounds studied.

Our experiments have shown that compounds XII, XIV, XVI, XVII, XX, XXI have the highest antimicrobial activity. The lowest antimicrobial activity was found in compounds VI, IX, X, etc., which had inappreciable action on *St. aureus*, while gram-positive bacteria were practically insensitive towards them.

EXPERIMENTAL CHEMICAL PART

Phosphoniosulfonamides I-XXI were obtained by the same method, which for compound I consists in the following: A solution of 0.84 g of phosphonium salt and 0.6 g of norsulfazole in 20 ml of alcohol is refluxed for 6 h. The solvent is evaporated in vacuo, and the

residue is dissolved in chloroform, and compound I is precipitated by adding a few portions of ether. For compounds V-VIII, the reaction mixture is refluxed for 2 h, and for compounds XI-XIV, 17 h. Phosphoniosulfonamide XXI is obtained similarly to compound I, using DMFA as the solvent; the mixture is refluxed for 5 h. Data for compounds I-XXI are listed in Table 1.

LITERATURE CITED

1. A. Walter, Chemotherapia (Basel), 6, 161 (1963); Farm. Pol., 17, 173 (1961).
2. M. I. Shevchuk, I. V. Megera, N. A. Burachenko, et al., Zh. Org. Khim., 10, 167 (1974).
3. M. I. Shevchuk, S. T. Shpak, and A. V. Dombrovskii, Zh. Obshch. Khim., 45, 2143 (1975).
4. I. V. Megera, L. B. Lebedev, and M. I. Shevchuk, Zh. Obshch. Khim., 51, 54-58 (1981).
5. M. I. Shevchuk, V. P. Rudi, I. V. Megera, et al., Zh. Obshch. Khim., 51, 1024-1028 (1981) (1981).
6. M. I. Shevchuk, I. V. Megera, and O. M. Bukachuk, in: Conference on Chemistry of Organophosphorus Compounds in Honor of the 100th Birthday Anniversary of Academician A. E. Arbuzov, Kiev (1977), p. 135.
7. S. M. Navashin and I. P. Fomina, Handbook on Antibiotics [in Russian] Moscow (1974), pp. 36-45.

DERIVATIVES OF AMINOPHENYLACETIC ACID AND THEIR ANTINEOPLASTIC ACTIVITY

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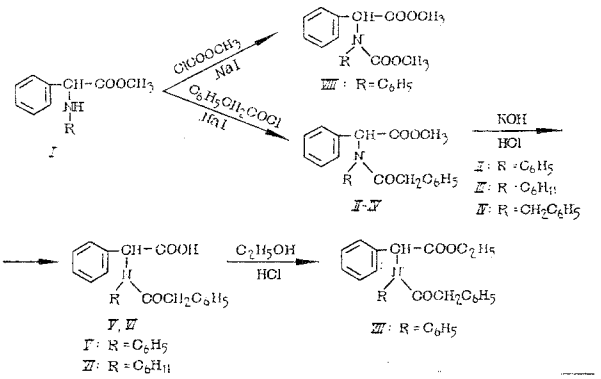
N-Acetyl derivatives of a number of amino acids, possessing antileukemic activity, have been described in the literature [1]. To expand the spectrum of N-acetyl derivatives of amino acids and to seek new substances with antileukemic activity we synthesized N-phenacetyl derivatives of N-substituted aminophenylacetic acids, as well as their methyl and ethyl esters and the methyl ester of N-phenyl-N-carbomethoxyphenylacetic acid (II-VIII), according to the following scheme:



Compounds II-IV were synthesized by the reaction of the methyl ester of N-monosubstituted aminophenylacetic acids I [2] with phenylacetyl chloride. The methyl esters II and III were saponified with an aqueous solution of potassium hydroxide to the corresponding acids V and VI.

Since the ethyl ester of α-aminophenylacetic acid was obtained in a negligible yield, the corresponding N-phenacetyl derivative VII was synthesized by esterification of the acid V. Compound VIII was produced by the reaction of I with the methyl ester of chlorocarbonic acid.

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