2-(4-Alkoxybenzylamino- or Phenethylamino)-4-amino-6-chloromethyl-1,3,5-triazines (II, $X = CI$). The alcoholate prepared from sodium (3 g, 0.16 mole) and absolute methanol (20 ml) was cooled to $-70^\circ$C and methyl chloroacetate (2.7 g, 0.025 mole) was added dropwise with stirring. Compound I (0.025 mole) was then added, the mixture was stirred till it warmed up to room temperature and then left standing for another 5 h. The precipitate was filtered off and recrystallized from ethanol (Table 2).

2-(4-Alkoxybenzylamino- or Phenethylamino)-4-amino-6-cyanomethyl-1,3,5-triazines (II, $X = CN$). A solution of I (0.03 mole) and ethyl cyanoacetate (3.5 g, 0.03 mole) in methanol (25 ml) was left standing at room temperature for 35 h. The precipitate was filtered off and recrystallized from water (see Table 2).

2-(4-Alkoxyphenethylamino)-4-amino-6-$B$-aminoethyl-1,3,5-triazines (II, $X = CH_2NH_2$). To a mixture of lithium aluminum hydride (3.8 g, 0.1 mole) in tetrahydrofuran (100 ml) was added dropwise with stirring a solution of II ($X = CN$, n = 2) (17 g, 0.06 mole) in tetrahydrofuran (100 ml). The mixture was heated on a water bath for 30 h, and 40% sodium hydroxide solution (50 ml) was then added dropwise. The ether layer was separated, the solvent was evaporated, and the residue was recrystallized from ethanol (see Table 2).

LITERATURE CITED

SYNTHESIS AND THE BACTERIOCIDAL ACTIVITY OF FERROCENYLAMINOMETHYLPHOSPHONATES

V. I. Boev and Yu. L. Volyanskii

Organophosphorous compounds are widely used as insecticides. However, the physiological activity of these compounds is far from limited just to the insecticidal action. Organophosphorous compounds having herbicidal and fungicidal activity have been prepared and also used in both veterinary and medical practice [1]. Of particular interest is the possibility of obtaining bacteriocidal aminoalkyl organophosphorous compounds, the biological activity of which has not been studied much. The low toxicity of the aminoalkylphosphonic acids and their esters towards warm-blooded animals makes them particularly suitable for use as bacteriocidal agents [2].

In this work, we prepared and studied the bacteriocidal activity of a group of new organophosphorous compounds, i.e., ferrocenylaminomethylphosphonates. The synthesis of 22 compounds of this type was comparatively easy; they were prepared by condensing the readily available formyl- and acetylferrocenes with the phosphorous acid dialkylesters in the presence of various primary and secondary amines. The reaction was carried out by keeping the reaction mixture, containing equimolar quantities of the aldehyde or ketone, phosphorous acid dialkylester, and the amine for 7-10 days at room temperature. The corresponding ferrocenylaminomethylphosphonates are obtained under these conditions in quantitative yields. With heating, the yields of the expected compounds decreased considerably and a large quantity of resinous product formed instead.

The reaction products I-XXII are crystalline compounds, either yellow or light brown, easily soluble in organic solvents and insoluble in water. The structure of the ferrocenyl-aminomethylphosphonates (Table 1) was confirmed by the elemental analysis and IR spectra results.

The IR spectra of the above compounds show absorption bands at 1230-1260 cm⁻¹, corresponding to the stretching vibrations of the P=O group. Further absorption bands at 1150-1170 cm⁻¹, characteristic for the P-O-alkyl group vibrations, at 1290-1340 cm⁻¹ corresponding to the C-N bond vibrations are present [3]. The IR spectra of aminomethylphosphonates I-XXII also exhibit characteristic absorption at 800, 1000, 1100, and 1415 cm⁻¹, corresponding to the vibrations of the ferrocenyl ring [4]. The spectra of aminomethylphosphonates containing the aromatic amine residue show the absorption bands at 3300-3400 cm⁻¹ that are characteristic for the stretching vibrations of the N-H group, and also the bands typical of the benzene ring are present.

Experimental

Pharmacological

The bacteriocidal activity of the studied compounds towards certain strains of bacteria and fungi was studied using the method of culture propagation in a liquid culture medium [5]. It can be seen from Table 2 that the minimum bacteriocidal concentration of the above compounds towards Staphylococcus aureus (strain No. 209) and Anthracoid (strain No. 297) is from 15.62 to 125.0 mg/ml, towards Escherichia coli (strain No. 365), Salmonella typhosa (strain No. 495), and Proteus vulgaris (strain No. 409) is from 31.25 to 125.0 mg/ml, and towards Pseudomonas pyocyaneus (strain No. 128) is from 31.25 to 250.0 mg/ml. The above ferrocenyl-aminomethyl phosphonates show fungicidal activity towards Candida albicans (strain No. 688) at concentrations from 31.25 to 125.0 mg/ml. Some correlation between the magnitude of the bacteriocidal activity and the structure of the compounds was established. Thus, as the length of the group R increases the activity of the compounds decreases slightly (compounds IV and VIII). At the same time, branching of R practically does not effect the biological activity of the compounds (cf., for example, compounds XV and XVII, XIV and XVIII, etc.). The change of R¹ = H to CH₃ group also leads to a decrease in the bacteriocidal activity (compounds V and IX). The most active aminophosphonates were those prepared from aromatic amines; however, the bacteriocidal activity of resulting compounds depends only slightly on the basicity of the starting amines. The presence of the ferrocenyl radical in aminophosphonates, as compared to some other similar compounds [2] leads to an increase in the bacteriocidal activity. It is also of some interest to mention the nearly equal activity of the above compounds towards both gram-positive and gram-negative microorganisms.

Chemical

IR spectra of the compounds prepared were recorded in mineral oil suspensions using an IKS-14A spectrophotometer, employing the NaCl and LiF prisms.

Ferrocenylaminomethylphosphonates (I-XXII). A mixture of formyl- or acetylferrocene (0.005 mole) phosphorous acid dialkyl ester (0.005 mole) and the amine (0.005 mole) was heated until it became homogeneous and the mixture was then kept at room temperature for 7-10 days. During that time the reaction mixture either fully or at least partially crystallized out. Alcohol (10-15 ml) was then added and the mixture was again heated to redissolve the solids. On cooling, aminophosphonates II, XIII, and XI crystallized out. For other aminophosphonates, the alcohol solution was diluted with a few milliliters of water (till it became turbid) and the mixture was then left standing for 12 h at 0°C. Aminophosphonates that crystallized out were filtered, washed with water, and dried over phosphorous pentoxide.