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Dedicated to Full Member of the Russian Academy of Sciences B.A. Trofimov on his 70th anniversary

Hydroxyalkylammonium Salts of Organylsulfanyl(sulfonyl)acetic Acids—New Stimulators of Biological Processes

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Abstract—The article gives a survey of methods of synthesis and specific biological activity of hydroxyalkylammonium salts derived from organylsulfanyl(sulfinyl, sulfonyl)acetic acids which can be used as growth stimulators with respect to beneficial bacteria, yeasts, and fungi in large-scale biotechnology processes for manufacture of fodder and baker's yeasts and citric acid, barley sprouting for the preparation of brewer's malt, and breeding of silkworms.

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Tris(2-hydroxyethyl)ammonium salts of aroxyacetic acids of the general formula $ArOCH_2COO^- \cdot HN^+(CH_2CH_2OH)_3$ are highly effective biostimulators and medical agents. For example, Trekrezan [tris(2-hydroxyethyl)ammonium (2-methylphenoxy)acetate (**I**)] was approved as adaptogen with a broad spectrum of action [1]; in addition, it exhibits compatible hemopoiesis- and immunopoiesis-modulating activity; i.e., this compound represents a new class of immunomodulators [2–4].

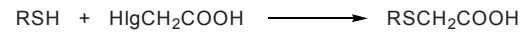
On the other hand, prior to our present work, no systematic studies on the synthesis, chemical transformations, and biological activity of sulfur-containing analogs of aroxyacetic acid hydroxyalkylammonium salts containing bi-, quater-, or sexivalent sulfur atom have been reported. Therefore, in the present article we made an attempt to attract researchers' attention to prospects in the chemistry and practical applications of organylsulfanyl(sulfinyl, sulfonyl)acetic acids and their salts with 2-hydroxyalkylamines of the general formula $RS(O)_nCH_2COO^- HN^+R^1R^2R^3$, where n = 0–2; R = Alk, Ar, Ht; $R^1 = HOCH_2CH_2$, R^2, R^3 = H, Alk, Ar, $HOCH_2CH_2$, $HOCH_2CH[CH(OH)C_6H_4NO_2\text{-}4]$, as new biologically active substances. For this purpose, we summarized the results of our studies in the fields of synthesis and biological activity of sulfur-containing alkanoic acids and their hydroxyalkylammonium salts. Hydroxyalkylammonium salts turned out to be almost nontoxic to mammalians and humans, and they showed pronounced growth-stimulating activity at very low concentrations (10^{-4}–10^{-10} wt %) toward beneficial bacteria, yeasts, and fungi used in large-scale biotechnology processes for manufacture of fodder and baker's yeasts and citric acid, barley sprouting for the preparation of brewer's malt, and breeding of silkworms.

On the basis of accessible large-scale initial compounds, namely chloroacetic acids, thiols, sulfanylacetic acid, nitro- and dinitrochlorobenzenes, arenesulfinates, isothiuronium salts, alkyl halides, and trichloroethylene we have developed convenient procedures for the synthesis of both organylsulfanyl(sulfinyl, sulfonyl)acetic acids having an aromatic or heterocyclic fragment at the sulfur atom and their derivatives.

Initial alkyl-, aryl-, and hetarylsulfanylacetic acids, both those described previously and hitherto unknown, were synthesized in up to 90% yield by reactions of the corresponding thiols with chloroacetic acid in aqueous alkali at 90–100°C (reaction time 1.5–2 h), i.e., according to the procedure most commonly used for the preparation of alkyl(aryl)sulfanylacetic acids [5] (Scheme 1).

2(4)-Nitro- and 2,4-dinitrophenylsulfanylacetic acids were obtained in high yield by reaction of fluoro-

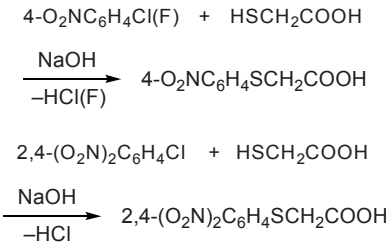
Scheme 1.



R = Pr, C_6H_{13}, Ph, 2-MeC_6H_4, 4-MeC_6H_4, 2-ClC_6H_4, 4-ClC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, 4-$F_3CC_6H_4$, 4-BrC_6H_4, 4-$O_2NC_6H_4$, 2,4-$Cl_2C_6H_3$, 2,5-$Cl_2C_6H_3$, 2-Me-4-ClC_6H_3, 3,4-$Me_2C_6H_3$, 2,4-$Me_2C_6H_3$, 3-(2-$HOCOC_6H_4NHCO)C_6H_4$, 3-(3-$HOCOC_6H_4NHCO)C_6H_4$, 1*H*-indol-3-yl, 1*H*-imidazol-2-yl, pyridin-2-yl, pyrimidin-2-yl, 5-butylpyrimidin-2-yl, quinolin-2-yl, purin-8-yl, 1,3-benzothiazol-2-yl, 2-thienyl.

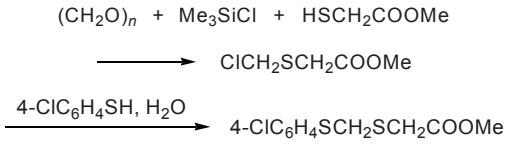
(chloro)-2(4)-nitrobenzenes or 2,4-dinitrochlorobenzene with sulfanylacetic acid at 80°C in alcoholic alkali (Scheme 2). According to the known procedure [6], 4-nitrophenylsulfanylacetic was synthesized in anhydrous medium in the presence of alkali metal [6].

Scheme 2.



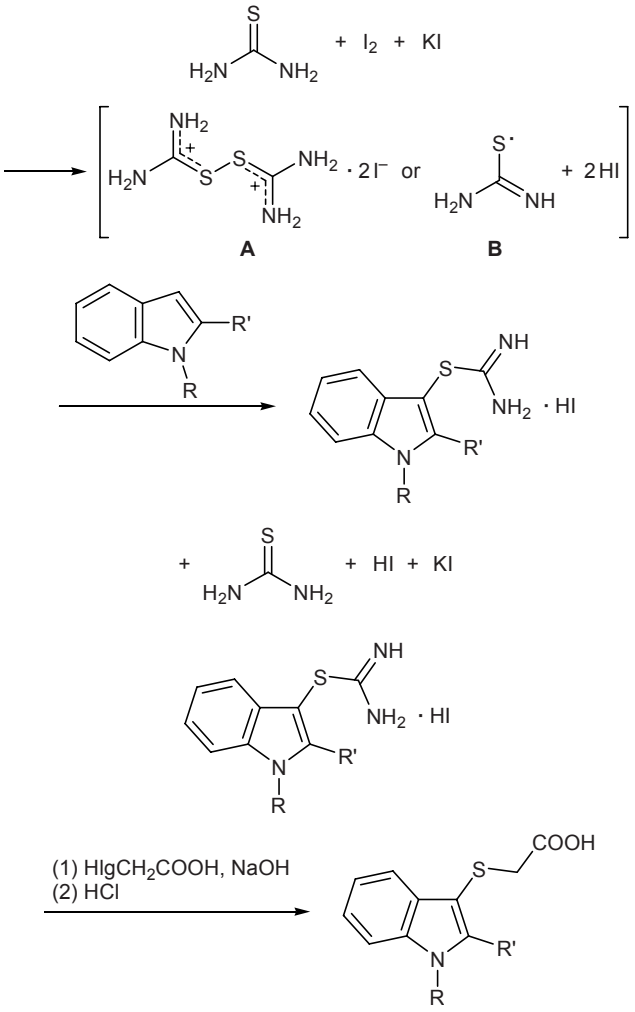
We have developed a procedure for the synthesis of highly reactive methyl (chloromethylsulfanyl)acetate by reaction of methyl sulfanylacetate with the system paraformaldehyde–chloro(trimethyl)silane and demonstrated prospects in using it for the preparation of (arylsulfanylmethylsulfanyl)acetic acids [7]. An example (the reaction with 4-chlorobenzenethiol) is shown in Scheme 3.

Scheme 3.



Taking into account strong biological activity of indole derivatives, we have synthesized a series of indol-3-ylsulfanylacetic acids according to a novel procedure which does not require the use of unstable, allergenic, and difficultly accessible indolethioles. Indol-3-ylsulfanylacetic acids were obtained in up to 84% yield by reaction of chloroacetic acid with alkali and *S*-(1*H*-indol-3-yl)isothiuronium iodides generated *in situ* from the corresponding substituted indoles, thiourea, and iodine (ratio 1 : 2 : 1) in the presence of potassium iodide [8, 9] (Scheme 4). The products contained ~99% of the main substance, and no additional purification was necessary.

Scheme 4.

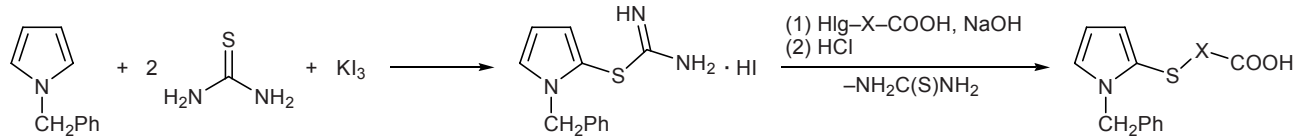


Hlg = Cl, Br; R = H, Me, $PhCH_2$; R′ = H, Me, Et.

Following the same approach, by reaction of 1-substituted pyrroles with iodine, thiourea, and halogen-substituted alkanoic acids, we synthesized for the first time α- and β-(1-benzyl-1*H*-pyrrol-2-ylsulfanyl)alkanoic acids in 59–68% yield (Scheme 5) [10]. Analogous bis[pyrrolylsulfanylacetic acids were obtained in 59–73% yield from *N*,*N*′-bridged dipyrroles, thiourea, potassium triiodide, and chloroacetic acid [10] (Scheme 6).

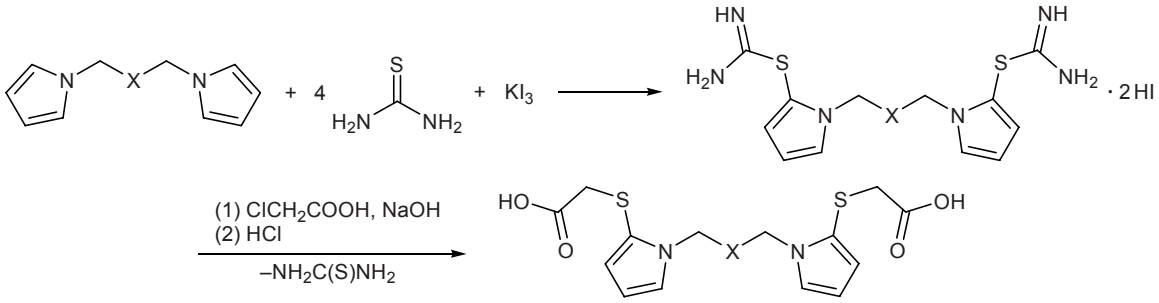
We also synthesized organylsulfinylacetic acids with a view to estimate the effect of the degree of oxidation of the sulfur atom on their biological activity. According to published data [11], the desired sulfoxides can be obtained in a low yield by oxidation of organylsulfanylacetic acid with potassium periodate or

Scheme 5.



Hlg = Cl, Br; X = CH_2, CH_2CH_2, CH(Me), CH(Et).

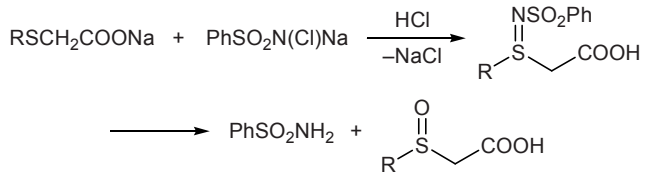
Scheme 6.



X = $(CH_2)_4$, 1,4-C_6H_4.

hydrogen peroxide in acetic anhydride at room temperature. Organylsulfinyl-substituted carboxylic acids were also obtained by reaction of sulfanylacetic acid with *N*-chlorobenzenesulfonamide sodium salt in aqueous alkali [12]. However, these procedures ensured poor yields of the target products which contained considerable amounts of impurities. We have developed a procedure for the synthesis of arylsulfinylacetic acids with high yield and purity by reaction of arylsulfanylacetic acids with an equimolar amount of *N*-chlorobenzenesulfonamide sodium salt in anhydrous acetone, followed by acid hydrolysis of intermediate S-amination products (Scheme 7).

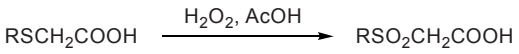
Scheme 7.



R = Bu, Ph, 4-ClC_6H_4.

Arylsulfonylacetic acids can be prepared by oxidation of arylsulfanylacetic acids with excess oxidant; however, these reactions often give mixtures of products. We have developed a procedure for selective oxidation of arylsulfanylacetic acids to the corresponding sulfones using 30% hydrogen peroxide in glacial acetic acid at a ratio of 1:2:2. The process included two steps: in the first step, the mixture was kept for 3–24 h at room temperature, and in the second, it was heated for 15 min under reflux. In such a way we succeeded in improving the yield of arylsulfonylacetic acids to 65–93% and their purity [13, 14] (Scheme 8). 4-Methyl- and 4-chlorophenylsulfonylacetic acids were also synthesized in up to 70% yield by oxidation of the corresponding arylsulfanylacetic acids with 30% hydrogen peroxide in acetic anhydride.

Scheme 8.

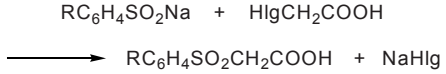


R = Ph, 4-MeC_6H_4, 4-ClC_6H_4, 4-FC_6H_4, 4-$O_2NC_6H_4$, 2,4-$Cl_2C_6H_3$, 2,5-$Cl_2C_6H_3$, 2-Me-4-ClC_6H_3.

The most convenient preparative procedure for the synthesis of arylsulfonylacetic acids and their esters, which excludes the use of thiols, is condensation of sodium arenesulfinates with chloroacetic acid or its esters. By varying the reactant ratio, temperature, reaction time, and solvent we found the optimal conditions for the condensation: aqueous sodium hydroxide (pH 10), 100°C, reaction time 1 h. These conditions ensured isolation of highly pure arylsulfonylacetic acids in 85–93% yield [13, 14] (Scheme 9).

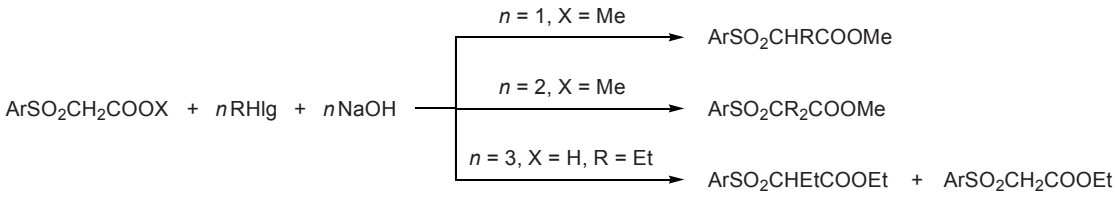
α-(Arylsulfonyl)alkanoic acids were obtained in 73–85% yield by alkylation of arylsulfonylacetic acids

Scheme 9.



R = H, 4-Me, 4-Cl.

Scheme 10.

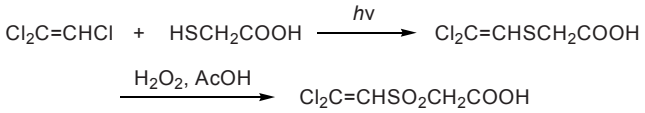


Ar = Ph, 4-MeC_6H_4, 4-ClC_6H_4; R = Et, *i*-Pr, Bu, $PhCH_2$; Hlg = Cl, Br.

with alkyl halides or benzyl chloride in the presence of sodium hydroxide. Depending on the reactant ratio, either the corresponding mono- or dialkyl derivatives were formed [14] (Scheme 10).

Sulfonylacetic acids having a heterocyclic fragment were synthesized via heterocyclization of (2,2-dichlorovinylsulfonyl)acetic acid which was prepared by radical sulfurization of trichloroethylene with sulfanylacetic acid and subsequent oxidation of (2,2-dichlorovinylsulfanyl)acetic acid [15] (Scheme 11).

Scheme 11.

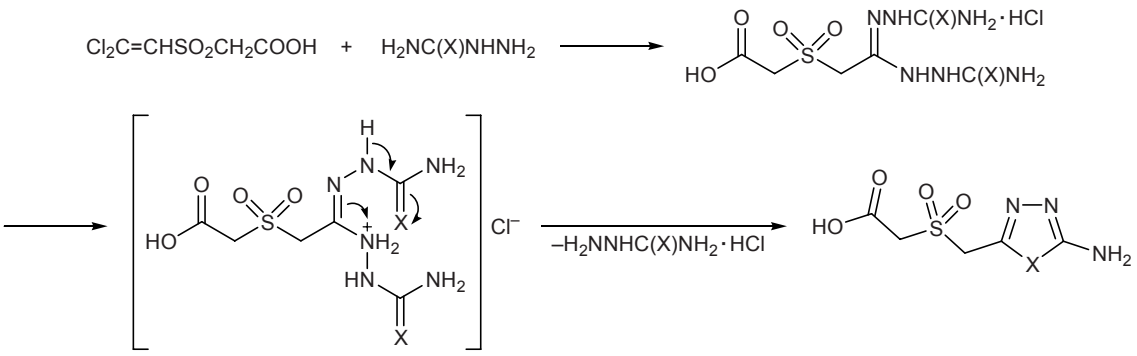


(2,2-Dichlorovinylsulfonyl)acetic acid reacted with difunctional O,S,N-nucleophiles (such as semicarbazide, thiosemicarbazide, and aminoguanidine) to give 5-amino-1,3,4-oxadiazol-2-yl-, 5-amino-1,3,4-thiadiazol-2-yl-, and 5-amino-1,3,4-triazol-2-ylmethylsulfonylacetic acids [16] (Scheme 12).

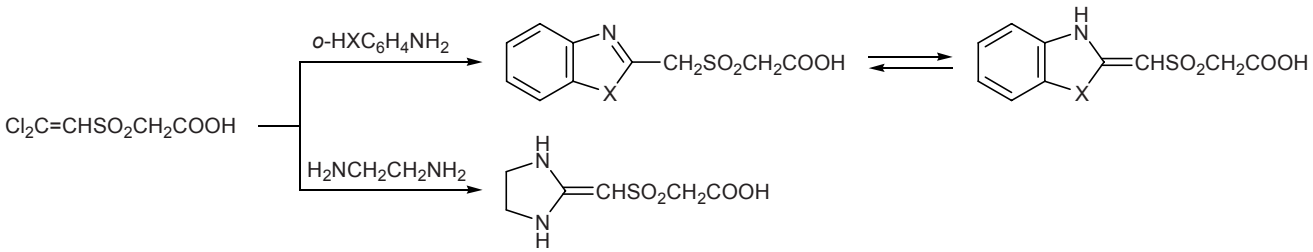
Likewise, reactions of (2,2-dichlorovinylsulfonyl)-acetic acid with 2-aminophenol, benzene-1,2,-diamine, and 2-aminobenzenethiol led to the formation of 1,3-benzoxazol-2-yl-, benzimidazol-2-yl-, and 1,3-benzothiazol-2-ylmethylsulfonylacetic acids, respectively [16] (Scheme 13). In the reaction with sodium sulfide nonahydrate we obtained bis-sulfanyl acetic acid having a 1,3-dithiole ring [16] (Scheme 14).

Organylsulfanyl(sulfinyl, sulfonyl)acetic acids were converted into the corresponding hydroxyalkylammonium salts with a view to test the products for biological activity. The salts were prepared by treatment of the acids with equimolar amounts of mono-, bis-, and tris(2-hydroxyethyl)amines, 2-(dimethylamino)- and

Scheme 12.

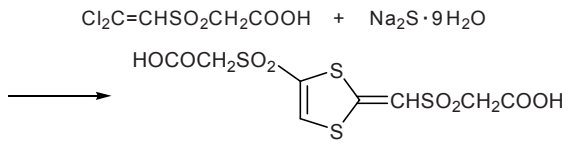


Scheme 13.



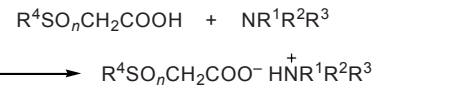
X = O, S, NH.

Scheme 14.



2-(diethylamino)ethanols, and 2-amino-1-(4-nitrophenyl)propane-1,3-diol in alcohol on heating at 60–70°C until complete dissolution, and their yields ranged from 70 to 90% [13, 14, 17–23] (Scheme 15).

Scheme 15.



n = 0–2; $R^1 = R^2 = R^3 = HOCH_2CH_2$; R^1 = H, $R^2 = R^3 = HOCH_2CH_2$; $R^1 = R^2$ = H, $R^3 = HOCH_2CH_2$; $R^1 = R^2$ = Me, $R^3 = HOCH_2CH_2$; $R^1 = R^2$ = H, R^3 = 4-$O_2NC_6H_4CH(OH)$-$CH(CH_2OH)$; R^4 = Pr, C_6H_{13}, Ph, 4-XC_6H_4 (X = Me, MeO, Cl, Br, F, F_3C, O_2N), 2-XC_6H_4 (X = Me, HOCO, CHO), 2-X-4-YC_6H_3 (X = Me, Y = Cl; X = Y = Cl; X = Y = O_2N), 2,5-$Cl_2C_6H_3$, 1-R^5-1*H*-indol-3-yl (R^5 = H, Me, $PhCH_2$), benzimidazol-2-yl, pyridin-2-yl, pyrimidin-2-yl, 5-butylpyrimidin-2-yl, quinolin-2-yl, purin-8-yl, 1,3-benzothiazol-2-yl, 2-thienyl.

Biological activity of organylsulfanyl(sulfonyl)acetic acid hydroxyalkylammonium salts. Biological screening performed for the first time in collaboration with authorized institutes showed that more than 80 hydroxyalkylammonium salts exhibit a broad spectrum of biological activity, being almost nontoxic. These salts display antiaggregation, membrane-stabilizing [17, 18], antiinflammatory, analgesic [19, 20], cardioprotective [21], immunomodulating [22], and hypocholesteremic activity [23] and inhibit peroxide oxidation of lipids [17]. Strong cancerostatic activity of tris(2-hydroxyethyl)ammonium arylsulfanyl- and arylsulfonylacetates was recently reported [24], so that their further study is promising from the viewpoint of design of new drugs. Among the examined hydroxyalkylammonium salts, the most challenging are compounds **I**–**XX** (see table).

Growth-stimulating activity. Hydroxyalkylammonium salts of organylsulfanyl(sulfonyl)acetic acids are highly effective stimulators of biological processes. All hydroxyalkylammonium salts **I**–**XX** may be regarded as nontoxic (LD_{50} = 1340–6000 mg/kg). They are active at very low concentrations, and their growth-stimulating activity is universal. In addition, they are stable on storage and are accessible due to developed procedures for their synthesis.

The effect of compounds **I**–**IV** on *Bacillus mucilaginosus* (*Bm*) and *Staphylococus Cowan* (*SC*) was studied. These microorganisms provide a highly efficient protein–vitamin–enzyme additive to forage (*Bm*) [25] and are used in the manufacture of a valuable medical agent, protein A (*SC*). Addition of an aqueous solution of compound **I**–**IV** with a concentration of 10^{-4} to 10^{-8} wt % to nutrient medium for *Bm* induced a 22–44% gain of the biomass. Compound **IV** turned out to be the most effective toward *SC*: the gain of the biomass reached 28.8%. The use of these stimulators makes it possible to avoid addition of expensive vitamins and amino acids (cysteine, tryptophane, etc.). Compounds **I**–**IV** accelerate by 30–35% the growth of meningococci over liquid and solid nutrient media, which may be utilized for express diagnostics of meningitis. They also affect the growth of bacteria responsible for lignin composting [26].

Salts **I** and **V**–**XII** at a concentration of 10^{-6} to 10^{-10} wt % induce growth of *Saccharomyces cerevisiae* yeast which is an indispensable component for the manufacture of bakery foods and medical agents and an important source of vitamins and enzymes; the biomass yield increases by 6–17.2%, and the productivity, by 7–14% (the data were obtained using desthiobiotin as reference [27]). Procedures for the preparation and application of tris(2-hydroxyethyl)ammonium 4-chlorophenylsulfonylacetate (**XII**) at a concentration of 10^{-6} to 10^{-8} wt % have been developed. This compound is safe, and it shows no cytotoxic, teratogenic, allergenic, or mutagenic effect. It was approved for the application in food industry.

Baker's yeasts prepared with the use of growth stimulators exhibit enhanced enzymatic activity and vigor. Fermenting activity of yeasts obtained with the use of new stimulators was assayed by the intensity of fermentation of saccharose and maltose. After 2 h, standard yeasts showed loss in activity (by 9.3% in saccharose and by 9.5% in maltose). By contrast, increased fermenting activity was observed for the experimental yeasts (by 4.5 and 6.2%, respectively). Insofar as maltose fermentation determines the main bread-making parameters (such as specific volume and porosity), their values increase by 2.5%.

Compounds **I**–**XX** were also tested for growth-stimulating activity with a view to obtain protein-rich microorganisms. In these tests, the nutrient medium contained sources of carbon, nitrogen, and phosphorus, potassium and magnesium salts, and microelements. As source of carbon, liquid paraffins, alcohols, fatty

Hydroxyalkylammonium salts of organylsulfanyl(sulfonyl)acetic acids $R^4S(O)_nCH_2COO^-\ HN^+R^1R^2R^3$

Compound no.	*n*	R^1	R^2	R^3	R^4
I	0	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	Ph
II	0	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	2-MeC_6H_4
III	0	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	4-ClC_6H_4
IV	0	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	4-BrC_6H_4
V	0	Me	Me	$HOCH_2CH_2$	4-ClC_6H_4
VI	0	H	H	4-$O_2NC_6H_4CH(OH)CH(CH_2OH)$	4-ClC_6H_4
VII	0	Me	Me	$HOCH_2CH_2$	2,4-$(O_2N)_2C_6H_3$
VIII	0	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	1*H*-Indol-3-yl
IX	0	Me	Me	$HOCH_2CH_2$	1*H*-Indol-3-yl
X	0	Et	Et	$HOCH_2CH_2$	1*H*-Indol-3-yl
XI	2	H	H	4-$O_2NC_6H_4CH(OH)CH(OH)$	4-MeC_6H_4
XII	2	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	4-ClC_6H_4
XIII	0	H	$HOCH_2CH_2$	$HOCH_2CH_2$	4-MeC_6H_4
XIV	0	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	2,4-$Cl_2C_6H_3$
XV	0	H	H	4-$O_2NC_6H_4CH(OH)CH(CH_2OH)$	2,4-$(O_2N)_2C_6H_3$
XVI	0	H	H	$HOCH_2CH_2$	2,4-$(O_2N)_2C_6H_3$
XVII	0	Me	Me	$HOCH_2CH_2$	4-$O_2NC_6H_4$
XVIII	2	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	4-MeC_6H_4
XIX	2	H	H	4-$O_2NC_6H_4CH(OH)CH(CH_2OH)$	4-ClC_6H_4
XX	2	$HOCH_2CH_2$	$HOCH_2CH_2$	$HOCH_2CH_2$	4-ClC_6H_4

acids, or carbohydrates were added. Compounds **I**–**XX** were added to the nutrient medium at a very low concentration (10^{-4} to 10^{-8} wt %). The cultivation was performed under stirring and aeration. The substrates were yeasts of the *Candida* (*C. sake, C. tropicalis, C. guilliermondii, C. parapsilosis, C. salmonicala, C. utilis, C. boidinii*), *Hansenula*, *Torulopsis*, and other families, as well as bacteria of the *Pseudomonas*, *Methylomonas*, and *Acetobacter* families, etc. Compounds **XIII** and **XIV** showed a strong growth-stimulating effect on *Candida* fodder yeasts; their addition at a concentration of 10^{-4} to 10^{-8} wt % increased the biomass yield by 3–8% and the productivity by 10–15%. These compounds accelerated the synthesis of main cell metabolites by a factor of 2 to 4; therefore, a 10–15% gain in the efficiency of the microbiological synthesis can be obtained without change of the equipment. In addition, the use of compounds **XIII** and **XIV** as growth stimulators reduces consumption of initial materials and increases protein concentration in the final product.

Compounds **V**, **XI**, and **XIV** at a concentration of 10^{-4} to 10^{-8} wt % positively affected the growth of *Aspergillus niger* fungus that produces citric acid. As a result, the yield of edible citric acid increased by 9–26%, and its output, by 17–27%. Presumably, the mechanism of action of growth stimulators is related to change of permeability of cell membranes, which leads to enhanced metabolism and reduces expenditures for growth and breathing of fungus.

We were the first to reveal the ability of tris(2-hydroxyethyl)ammonium arylsulfanyl- and arylsulfonylacetates **II**, **VIII**, and **XII** to effectively stimulate growth of bifidobacteria that are very important for humans. Stimulating effect was observed upon cultivation over nutrient media and preparation of therapeutic–prophylactic cultured milk product Bifidumbacterin: it was reflected in increased number of viable cells per unit volume, enhanced acid-forming activity, higher rate of growth of bacteria, and increased biological and nutritional value. Addition of the stimulator at a concentration of 10^{-2} to 10^{-6} wt % accelerated the gain in the biomass yield by a factor of 3–4, and the concentration of bifidobacteria reached 10^{12}–10^{14} cells per ml, i.e., it was higher by 4–6 orders of magnitude than that attained in reference sample over a longer

time [28, 29]. Cultivation of bifidobacteria in the presence of new stimulators increased the concentration of vitamins in the product.

At present, methods for cell therapy of various diseases are extensively studied. For this purpose, embryonic fibroblasts or low-molecular peptides are isolated from embryo cells of mammalians and humans. An important problem is search for methods of stimulating growth of embryo cells with a view to increase their number in a culture applied to a wound, burn surface, or surgical field. Such methods should make cell preparations and medical agents based thereon accessible. Our study on fibroblast growth stimulators performed in collaboration with the Sechenov Moscow Medical Academy revealed for the first time growth-stimulating effect of compounds of the 2-hydroxyethylammonium organylheteroacetate series at low concentrations. In the first step of this study we examined quantitative effect of Trekrezan on the growth of fibroblasts and estimated its possible cytotoxicity. The results showed that Trekrezan at a concentration of 10^{-4} to 10^{-6} wt % considerably (by a factor of 2–2.5 relative to control) and reliably increases growth of human embryo cells in M27 culture. Here, no signs of cell degeneration were observed [30]. Taking these data into account, a number of 2-hydroxyalkylammonium salts of sulfur-containing alkanoic acids that showed growth-stimulating effect in bacteria, yeasts, and higher plant cells were selected for further testing. Insofar as compounds **I**–**XX** exhibit strong immunomodulatory, membrane stabilizing, antioxidant, and antiaggregation activity, their use as growth-stimulators of embryo cells seems to be promising.

Compounds **VI**, **VII**, **XII**, and **XVI**–**XIX** at a concentration of 6×10^{-4} to 6×10^{-8} wt % stimulate germination of barley grains in the preparation of light malt which is an important starting material for the preparation of medical agents, drinks, and vitamins. Sulfacetamine at a concentration of 50–60 mg per ton of grain accelerates the malting process, shortening it from 7 to 5 days and increasing the yield of malt by 3% as compared to the standard process. The use of new stimulators makes it possible to discontinue the use of expensive and difficultly accessible gibberellin. The consumption of the new stimulators is lower by a factor of 5, and their cost is lower by a factor of 30, as compared to gibberellin. Such an important parameter of malt as the concentration of amine nitrogen reaches its maximal value in 5–6 days, and accumulation of maltose reaches its maximum in 5.5 days, i.e., by 1.5–2 days more rapidly than in control experiment. Qualitative parameters of malt were also improved: the amylolytic activity increased by 19.5%, the activity of catalase increased by 20.7%, and the degree of dissolution of green malt, the number of mealy grains, and the extractivity of light malt also increased as compared to the standard malting procedure [31–34].

The new stimulators can also find application in such field of agriculture as sericulture. Some 2-hydroxyethylammonium salts of sulfur-containing alkanoic acids, e.g., **XX**, increased the weight of the silk shell of silk moth chrysalises by 35–43% after spraying of food leaves with a 0.02–004% aqueous solution of the stimulator. It is especially important that the stimulator affected mainly just the silk production, while the effect on the weight of chrysalises was insignificant [35].

We can conclude that hydroxyalkylammonium salts of organylsulfanyl(sulfonyl)acetic acids are new effective and nontoxic stimulators of microbiological processes, ensuring their high selectivity. This is very important from the viewpoint of development of new wasteless technologies for the preparation of valuable fodder and food products, raw materials for manufacture of drugs, etc.

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