Benzothiazole compounds. IX. Synthesis and comparison of antibacterial activity of esters of (2-benzothiazolyl)acetic acid, (6-X-2-benzothiazolylthio)acetic acid, and of β-(6-X-2-benzothiazolylthio)propionic acid

[a]Ľ. OROSOVÁ, [b]V SUTORIS, [c]P. FOLTÍNOVÁ, and [d]Š. HAVIAROVÁ

[a]*Drug Research Institute, 801 00 Bratislava*

[b]*Department of Organic Chemistry, Faculty of Natural Sciences, Komenský University, 801 00 Bratislava*

[c]*Institute of Experimental Biology, Faculty of Natural Sciences, Komenský University, 886 04 Bratislava*

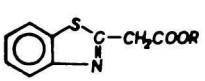
[d]*Drug Research Institute, 920 01 Hlohovec*

Received 21 April 1975

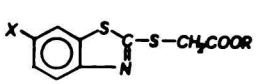
Alkyl (2-benzothiazolyl)acetates, aryl (6-X-2-benzothiazolylthio)acetates, and alkyl β-(6-X-2-benzothiazolylthio)propionates (X = H, NO_2, NH_2) were synthesized and tested on some microorganisms. *p*-Chlorophenyl (2-benzothiazolylthio)acetate (*X*) and *p*-nitrophenyl (6-nitro-2-benzothiazolylthio)acetate (*XIX*) were found to be the most active against nonspecific bacterial flora.

Синтезированные алкильные эфиры (2-бензтиазолил)уксусной кислоты, арильные эфиры (6-X-2-бензтиазолилтио) уксусной кислоты и алкильные эфиры β-(6-X-2-бензтиазолилтио)пропионовой кислоты (X = H, NO_2, NH_2) были испытаны на воздействие на некоторые микроорганизмы. Самое сильное действие на неспецифическую бактериальную флору обнаружено в случае *п*-хлорфенильного эфира (2-бензтиазолилтио)уксусной (*X*) и *п*-нитрофенильного эфира (6-нитро-2-бензтиазолилтио)уксусной (*XIX*) кислот.

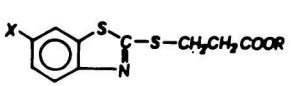
The synthesized derivatives of benzothiazole described in this paper enabled us to make partial conclusions on the relation of structure and antibacterial activity. The activity of alkyl (2-benzothiazolyl)acetates (formula *A*) was compared with that of the derivatives containing sulfur between the heterocycle and the ester residue of acetic acid (formula *B*; R = alkyl). Aryl (6-X-2-benzothiazolylthio)acetates (formula *B*; X = H, NO_2, NH_2) complete the series of investigated alkyl esters of this type. Alkyl β-(6-X-2-benzothiazolylthio)propionates (formula *C*) were prepared for the purpose to study the effect of the elongated carbon chain of the acid residue on antibacterial efficiency (Scheme 1).



A
I - VI



B
VII - XXIII

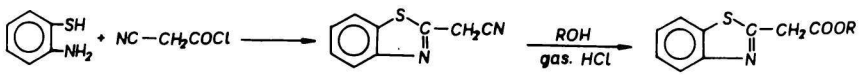


C
XXIV - XXIX

It is known from a rich experimental material that alkylation of 2-mercaptobenzothiazole is accomplished most frequently by the treatment of sodium or potassium salts of 2-mercaptobenzothiazole with alkyl halides in ethanol [1] or in an aqueous solution of alkali hydroxide [2]. In these cases only *S*-substituted mercaptobenzothiazole is formed as it is evident from the u.v. spectra [3, 4] and dipole moments [5]. Reactions with alkyl halides in xylene gave beside *S* derivative also small amounts of *N* derivative [6]. Synthesis of aryl (6-X-2-benzothiazolylthio)acetates and alkyl β-(6-X-2-benzothiazolylthio)propionates was carried out in the same way as in [1].

In previous works [7—9] synthesized compounds were evaluated as *S* derivatives. It was reasonable to assume that the compounds mentioned in this work will form *S* derivatives as well. The recorded i.r. spectra proved unambiguously that the prepared esters of (2-benzothiazolyl)acetic acid contained only one tautomer corresponding to the formula *A*.

Condensation of *o*-aminothiophenol with cyanoacetyl chloride resulted in 2-benzothiazolylacetonitrile which gave directly alkyl (2-benzothiazolyl)acetates (*I—IV*; Scheme 2) on acid hydrolysis in appropriate alcohol. The elaborated method of preparation of alkyl (2-benzothiazolyl)acetates is rapid and the yields depend on the purity of *o*-aminothiophenol.



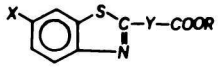
The purity of some aryl (6-X-2-benzothiazolylthio)acetates was controlled by gas chromatography. The measurement proved that the substances were pure and the effect of the substituent on retention times could be established. This effect was evident in the case of esters containing unsubstituted phenyl. There was a big difference between t_R of *VII* (X = H) and *XV* (X = 6-NO_2) ($\Delta \sim 14$) and these compounds could be distinguished. On the other hand, this difference was small with the substituted aryl esters (*e.g.* $\Delta \sim 0.21$ between *XIII* and *XXI*) which could not be distinguished by gas chromatography.

Alkyl β-(6-X-2-benzothiazolylthio)propionates (*XXIV—XXIX*, X = H, NO_2, NH_2) were synthesized with purpose to compare their activity with that of alkyl (6-X-2-benzothiazolylthio)acetates. Allyl and propargyl esters which were the most active in the series of (6-X-2-benzothiazolylthio)acetates were prepared (Table 1).

The basic screening for antimicrobial activity was carried out with all compounds. The obtained results are given in Table 2. *p*-Chlorophenyl (2-benzothiazolylthio)acetate (*X*) and *p*-nitrophenyl (6-nitro-2-benzothiazolylthio)acetate (*XIX*) were most active against nonspecific bacterial flora G^+ (*Staphylococcus pyogenes aureus*, *Bacillus subtilis*, and *Streptococcus faecolis* V 130). The compound *XIX* was found to be fairly active also against *Pseudomonas aeruginosa* which was relatively resistant towards antimicrobially effective preparations. The other esters tested did not inhibit the nonspecific strains of bacterial flora even at the highest concentration (200 μg/ml). The higher resistivity of the fast growing strain *Mycobacterium fortuitum* towards antimycobacterially active preparations as compared with *Mycobacterium bovis* BCG was reconfirmed. Also the activity of allyl (2-benzothiazolylthio)propionate (*XXIV*) and allyl β-(6-amino-2-benzothiazolylthio)propionate (*XXVI*) against *Aspergillus niger* is worth mentioning. The tests of some structurally similar compounds (Table 3) on microorganisms showed that allyl (2-benzothiazolylthio)acetate (*XXXI*) was the most active compound. The absence of sulfur (allyl (2-benzothiazolyl)acetate (*V*)) and to a lesser extent also of methylene group (allyl (2-benzothiazolylthio)formate

Table 1

Analytical data of the synthesized esters of (2-benzothiazolyl)acetic acid, (6-X-2-benzothiazolylthio)acetic acid, and of (6-X-2-benzothiazolylthio)propionic acid



No.	R	Y	X	Formula	*M*	Calculated/found				Yield %	M.p. °C
						% C	% H	% N	% S		
I	CH_3	CH_2	H	$C_{10}H_9O_2NS$	207.2	57.96 57.79	5.21 5.26	6.75 6.80	15.47 15.35	90	Highly viscous liquid
II	C_2H_5	CH_2	H	$C_{11}H_{11}O_2NS$	221.3	59.69 59.78	5.01 4.92	6.33 6.51	14.44 14.62	90	Highly viscous liquid
III	C_3H_7	CH_2	H	$C_{12}H_{13}O_2NS$	235.3	61.24 61.16	5.56 5.70	5.96 6.03	13.63 13.78	70	60
IV	C_3H_7-i	CH_2	H	$C_{12}H_{13}O_2NS$	235.3	61.24 61.38	5.56 5.43	5.96 6.12	13.63 13.74	73	67
V	$CH_2CH{=}CH_2$	CH_2	H	$C_{12}H_{11}O_2NS$	233.3	61.77 61.53	4.75 4.89	6.04 6.16	13.74 13.72	65	Highly viscous liquid
VI	$CH_2C{\equiv}CH$	CH_2	H	$C_{12}H_9O_2NS$	231.2	62.33 62.18	3.92 3.80	6.06 6.06	13.86 13.69	62	Highly viscous liquid
VII	C_6H_5	SCH_2	H	$C_{15}H_{11}O_2NS_2$	301.4	59.77 59.74	3.67 3.59	4.65 4.84	21.27 21.28	60	75
VIII	*o*-Cl—C_6H_4	SCH_2	H	$C_{15}H_{10}O_2NS_2Cl$	335.7	53.66 53.75	3.00 2.91	4.17 3.98	19.13 19.02	70	Highly viscous liquid

Table 1 (Continued)

No.	R	Y	X	Formula	*M*	Calculated/found				Yield %	M.p. °C
						% C	% H	% N	% S		
IX	*m*-Cl—C_6H_4	SCH_2	H	$C_{15}H_{10}O_2NS_2Cl$	335.7	53.66 53.52	3.00 3.12	4.17 4.13	19.13 18.96	69	Highly viscous liquid
X	*p*-Cl—C_6H_4	SCH_2	H	$C_{15}H_{10}O_2NS_2Cl$	335.7	53.66 53.59	3.00 3.06	4.17 4.31	19.13 19.30	89	69
XI	*p*-NO_2—C_6H_4	SCH_2	H	$C_{15}H_{10}O_4N_2S_2$	346.4	52.00 51.87	2.90 2.98	8.08 8.26	18.51 18.78	30	Highly viscous liquid
XII	3,5-diCH_3—C_6H_3	SCH_2	H	$C_{17}H_{15}O_2NS_2$	328.4	62.17 62.30	4.60 4.51	4.26 4.33	19.52 19.37	71	54
XIII	2,4-diCH_3—C_6H_3	SCH_2	H	$C_{17}H_{15}O_2NS_2$	328.4	62.17 62.22	4.60 4.49	4.26 4.40	19.52 19.41	69	72
XIV	4-Cl-2,6-diCH_3—C_6H_2	SCH_2	H	$C_{17}H_{14}O_2NS_2Cl$	363.9	56.10 56.28	3.87 3.77	3.84 5.01	17.62 17.49	60	148
XV	C_6H_5	SCH_2	NO_2	$C_{15}H_{14}O_4N_2S_2$	346.4	52.00 51.84	4.07 4.16	8.08 8.23	18.51 18.45	76	120
XVI	*o*-Cl—C_6H_4	SCH_2	NO_2	$C_{15}H_9O_4N_2S_2Cl$	380.8	47.30 47.11	2.38 2.23	7.56 7.40	16.83 16.88	86	105
XVII	*m*-Cl—C_6H_4	SCH_2	NO_2	$C_{15}H_9O_4N_2S_2Cl$	380.8	47.30 47.17	2.38 2.50	7.56 7.72	16.83 17.04	89	117
XVIII	*p*-Cl—C_6H_4	SCH_2	NO_2	$C_{15}H_9O_4N_2S_2Cl$	380.8	47.30 47.36	2.38 2.30	7.56 7.35	16.83 16.93	67	137
XIX	*p*-NO_2—C_6H_4	SCH_2	NO_2	$C_{15}H_9O_6N_3S_2$	391.2	46.05 46.22	2.31 2.19	10.73 10.51	16.38 16.12	50	92
XX	3,5-di$CH_3C_6H_3$	SCH_2	NO_2	$C_{17}H_{14}O_4N_2S_2$	373.4	54.67 54.50	3.77 3.69	7.50 7.59	17.17 16.94	74	119

Table 1 (Continued)

No.	R	Y	X	Formula	*M*	Calculated/found				Yield %	M.p. °C
						% C	% H	% N	% S		
XXI	2,4-di$CH_3C_6H_3$	SCH_2	NO_2	$C_{17}H_{14}O_4N_2S_2$	373.4	54.67 54.68	3.77 3.82	7.50 7.71	17.17 16.91	78	85
XXII	4-Cl-2,6-di$CH_3C_6H_2$	SCH_2	NO_2	$C_{17}H_{13}O_4N_2S_2Cl$	408.9	49.93 49.74	3.20 3.31	6.85 7.00	15.68 15.52	86	180
XXIII	4-Cl-2,6-di$CH_3C_6H_2$	SCH_2	NH_2	$C_{17}H_{15}O_2N_2S_2Cl$	378.9	53.88 53.60	3.99 4.08	7.36 7.15	16.93 16.94	61	169
XXIV	$CH_2CH{=}CH_2$	SCH_2CH_2	H	$C_{13}H_{13}O_2NS_2$	297.4	52.49 52.32	4.40 4.26	5.01 5.22	22.95 22.79	64	Highly viscous liquid
XXV	$CH_2CH{=}CH_2$	SCH_2CH_2	NO_2	$C_{13}H_{12}O_4N_2S_2$	324.4	48.12 48.00	3.72 3.60	8.63 8.59	19.77 19.89	70	86
XXVI	$CH_2CH{=}CH_2$	SCH_2CH_2	NH_2	$C_{13}H_{15}O_2N_2S_2$	294.4	53.03 53.31	4.79 4.91	9.53 9.40	21.78 21.65	60	Highly viscous liquid
XXVII	$CH_2C{\equiv}CH$	SCH_2CH_2	H	$C_{13}H_{11}O_2NS_2$	277.4	56.28 56.12	3.99 3.72	5.04 5.15	23.12 23.03	65	Highly viscous liquid
XXVIII	$CH_2C{\equiv}CH$	SCH_2CH_2	NO_2	$C_{13}H_{10}O_4N_2S_2$	322.4	48.42 48.24	3.12 3.30	8.68 8.81	19.89 20.05	69	110
XXIX	$CH_2C{\equiv}CH$	SCH_2CH_2	NH_2	$C_{13}H_{12}O_2N_2S_2$	292.4	53.39 53.45	4.13 4.07	9.58 9.39	21.93 21.77	62	Highly viscous liquid

Table 2

Antimicrobial activity of esters of (2-benzothiazolyl)acetic acid, (6-X-2-benzothiazolylthio)acetic acid, and of (6-X-2-benzothiazolylthio)propionic acid

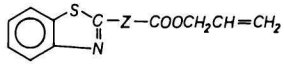
No.	*Staphylococcus aureus*	*Bacillus subtilis*	*Streptococcus faecolis*	*Escherichia coli*	*Proteus hauseri*	*Pseudomonas aeruginosa*	Bactericidal/bacteriostatical conc.		MIC		Lethal conc.			
							BCG	*Mycobacterium fortuitum*	*Candida pseudotropicalis*	*Aspergillus niger*	*Tetrahimena piriforis*	*Trichomonas foetus*	*Euglena gracilis*	*Trypanosoma cruzi*
I	>200	>200		>200	>200	>200	>100/100	800/400	>200		>800	>500	800	400
II	>200	>200		>200	>200	>200	>100/100	800/400	>200		>800	>500	800	400
III	>200	>200		>200	>200	>200	>100/100	800/600	>200		>800	>500	800	>400
IV	>200	>200		>200	>200	>200	>100/100	800/600	>200		>800	>500	800	>400
V	>200	>200		>200	>200	>200	>100/100	800/400	>200		>800	>500	400	400
VI	>200	>200		>200	>200	>200	>100/100	800/400	>200		>800	>500	400	400
VII	>200	>200	>200	>200	>200	>200	100/>50	>500/500	>200	>200	>800	>500		
VIII	>200	>200	>200	>200	>200	>200	>100/100	>500/500	>200	>200	>800	>500		
IX	>200	>200	>200	>200	>200	>200	100/10	500/100	>200	>200	800	>500		
X	50	12.5	>200	50	>200	>200	>100/100	500/>100	50	>200	800	>500		
XI	>200	200	>200	200	>200	>200	100/10	500/100	>200	>200	200	>500		
XII	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	>800	>500		
XIII	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	>800	>500		
XIV	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	>800	>500		
XV	>200	>200	>200	>200	>200	>200	>100/100	>500/>500	>200	>200	>800	>500		
XVI	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	800	>500		
XVII	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	>800	>500		
XVIII	>200	>200	>200	>200	>200	>200	100/10	500/>100	>200	>200	>800	>500		
XIX	50	50	>200	12.5	>200	50	100/10	500/100	50	>200	800	>500		
XX	>200	>200	>200	>200	>200	>200	>100/100	>500/>500	>200	>200	800	>500		
XXI	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	800	>500		
XXII	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	>800	>500		
XXIII	>200	>200	>200	>200	>200	>200	>100/>100	>500/>500	>200	>200	>800	>500		
XXIV	>200	>200	>200	>200	>200	>200	—	500/100	>200	12.5	800	>500		
XXV	>200	>200	>200	>200	>200	>200	100/>10	500/100	>200	>200	>800	>500		
XXVI	>200	>200	>200	>200	>200	>200	100/>10	>500/500	>200	12.5	>800	>500		

Table 2 (Continued)

No.	*Staphylococcus aureus*	*Bacillus subtilis*	*Streptococcus faecolis*	*Escherichia coli*	*Proteus hauseri*	*Pseudomonas aeruginosa*	Bactericidal/bacteriostatical conc.		MIC		Lethal conc.			
							BCG	*Mycobacterium fortuitum*	*Candida pseudotropicalis*	*Aspergillus niger*	*Tetrahimena piriforis*	*Trichomonas foetus*	*Euglena gracilis*	*Trypanosoma cruzi*
XXVII	>200	>200	>200	>200	>200	>200	—	500/100	>200	>200	200	>500		
XXVIII	>200	>200	>200	>200	>200	>200	100/>10	>500/>500	>200	>200	>800	>500		
XXIX	50	>200	>200	>200	>200	>200	100>10	>500/>500	>200	>200	>800	>500		

Table 3

Comparison of antimicrobial activity of some benzothiazole derivatives



No.	Z	MIC		BCG		MIC	*Euglena gracilis*		*Trypanosoma cruzi*		Ref.
		Bacillus subtilis	*Escherichia coli*	Bacteriostatical conc.	Bactericidal conc.	*Candida pseudotropicalis*	Lethal conc.	Statical conc.	Lethal conc.	Statical conc.	
V	CH_2	200	200	100	100	200	400	200	400	400	
XXX	S	50	100	50	100	100	250	125	100	50	[9]
XXXI	SCH_2	10	50	10	50	100	100	100	50	10	[12]
XXXII	$SCH(CH_3)$	50	50	50	100	>100	500	250	>100	100	[10]
XXXIII	$SCH(C_2H_5)$	50	50	50	100	>100	>500	500	>100	100	[10]
XXXIV	SCH_2CH_2	200	200	200	200	200	500	500	400	400	

(*XXX*)) caused a significant decrease of antibacterial activity. Alkylation of the methylene group in the compound *XXXI* (allyl 2-(2-benzothiazolylthio)propionate (*XXXII*) and allyl 2-(2-benzothiazolylthio)butyrate (*XXXIII*)) resulted in a decrease of activity to the level of allyl (2-benzothiazolylthio)formate (*XXX*) and elongation of the carbon chain of the acid residue in compound *XXXI* (allyl (2-benzothiazolylthio)propionate (*XXIV*)) had approximately the same negative effect as the absence of sulfur in the compound *V* The microbiological activity of aryl (6-X-2-benzothiazolylthio)acetates (*VII—XXIII*) in comparison with alkyl (6-X-2-benzothiazolylthio)acetates (X = H, NO_2, NH_2) [8—10] decreased so much that these derivatives became uninteresting from this point of view.

Experimental

Melting points (Kofler) and analytical data of the synthesized compounds are presented in Table 1. Gas chromatography was performed on a Hewlett—Packard 7620 A apparatus with a column of VCW-98 on Diatoport (80—100 mesh), $t = 120°C$, $t_{det.+inj.} = 170°C$, flow rate of $N_2 = 0.245$ MPa, $H_2 = 0.098$ MPa, sensitivity 10^4, integration 1 mV/min. The measurements were evaluated quantitatively using a H—P integrator.

Tests for antimicrobial activity were carried out according to the solubility of individual compounds and specific conditions of cultivation of test-organisms [11, 12].

2-Benzothiazolylacetonitrile

To the solution of *o*-aminothiophenol (12.5 g; 0.1 mole) in chloroform (60 ml) cyanoacetyl chloride was added dropwise under stirring and ice-cooling at such a rate so that the temperature did not rise above 0°C. The mixture was then heated to 50—60°C for 30 min. Chloroform was distilled off under reduced pressure and the residue was neutralized with 20% sodium carbonate and extracted with ether. After drying with sodium sulfate the ether solution was evaporated and upon cooling a yellow crystalline substance precipitated. Yield 67%, m.p. 89°C from ethanol.

For $C_9H_6N_2S$ (174.2) calculated: 62.05% C, 3.47% H, 16.09% N, 18.71% S; found: 61.97% C, 3.51% H, 15.86% N, 18.51% S.

Esters of (2-benzothiazolyl)acetic acid (I—VI)

2-Benzothiazolylacetonitrile (5.5 g) was dissolved in proper alcohol (60 ml) and dry hydrogen chloride was passed through the solution for 3 hrs. Then the reaction mixture was heated at 50 °C for 1 hr, poured into glacial water (250 ml), extracted with ether, and dried with sodium sulfate. Ether was distilled off and the product was purified chromatographically on a column of Al_2O_3 using benzene as elution agent.

Substituted phenyl (6-X-2-benzothiazolylthio)acetates (VII—XXIII)

6-X-2-Mercaptobenzothiazole (0.1 mole) and potassium hydroxide (5.6 g; 0.1 mole) were dissolved in ethanol (300 ml) at 40—50°C. After cooling to the ambient temperature, the solution of the appropriate phenyl chloroacetate (0.1 mole) in ethanol (50—100 ml) was added dropwise. The reaction mixture was stirred for 1 hr and for additional 3—5 hrs at 60°C and poured into glacial water (1000 ml). The solid products were filtered off and crystallized from ethanol; the liquid esters were extracted from water solution with ether and purified chromatographically on a column of silica gel using benzene as eluent.

Allyl β-chloropropionate

β-Chloropropionic acid (31.6 g; 0.3 mole), allyl alcohol (26.1 g; 0.45 mole), benzene (150 ml), and sulfuric acid (1 ml) were refluxed through an esterification column under withdrawal of reaction water. After the calculated amount of water was removed, benzene was distilled off and allyl β-chloropropionate was redistilled *in vacuo*. Yield 77 %, b.p. 80—85 °C/3.3 kPa.

For $C_6H_9O_2Cl$ (148.5) calculated: 48.68% C, 6.08% H, 23.95% Cl; found: 48.58% C, 6.08% H, 23.78% Cl.

Propargyl β-chloropropionate was prepared similarly. Yield 73%, b.p. 101°C/2.8 kPa.

For $C_6H_7O_2Cl$ (146.5) calculated: 49.35% C, 4.79% H, 24.34% Cl; found: 49.22% C, 4.9% H, 24.29% Cl.

Allyl β-(6-X-2-benzothiazolylthio)propionate (XXIV—XXVI) (X = H, NO_2, NH_2)

The procedure of preparation was the same as with aryl (6-X-2-benzothiazolylthio)acetates except that the reaction time was 2 hrs. Liquid products (*XXIV* and *XXVI*) were purified on a column of silica gel with benzene as eluent and the solid product (*XXV*) was crystallized from ethanol.

The compounds *XXVII—XXIX* were prepared by the same method.

References

1. Kuznetsova, E. A., Zhuravlev, S. V., Stoyanova, T. N., Solovyev, N. V., and Zueva, V. S., *Khim. Farm. Zh.* **1**, 7 (1967).
2. Rogachevskaya, T. A., *Prisadkam Mineral. Maslan* **1968**, 118; *Chem. Abstr.* **71**, 13044*h* (1969).
3. Hason, C. and Hunter, R. F., *J. Chem. Soc.* **1936**, 1972.
4. Morton, R. A. and Stob, A. L., *J. Chem. Soc.* **1939**, 1312.
5. Vesper, P. F., *J. Amer. Chem. Soc.* **64**, 1130 (1942).
6. Lizumova, L. M. and Rozhkova, N. K., *Uzb. Khim. Zh.* **1969**, 13 (6), 24; *Chem. Abstr.* **73**, 35246*y* (1970).
7. Mikulášek, S., Sutoris, V., Foltí ová, P., Konečný, V., and Blöckinger, G., *Chem. Zvesti* **28**, 686 (1974).
8. Sutoris, V. Blöckinger, G., Foltí ová, P., and Perjéssy, A., *Acta Facult. Rer. Natur. Univ. Comenianae (Chimia)*, in press.
9. Sutoris, V. Blöckinger, G., Foltínová, P., and Perjéssy, A., *Chem. Zvesti* **27**, 703 (1973).
10. Sutoris, V. Foltínová, P., and Blöckinger, G., *Chem. Zvesti* **27**, 698 (1973).
11. Foltínová, P., Blöckinger, G., Sutoris, V. and Ebringer, L., *Acta Facult. Rer. Natur. Univ. Comenianae (Microbiologia)* **2**, 79 (1972).
12. Raška, K., *Mikrobiologické vyšetřovací methody.* (Microbiological Examination Methods.) P. 152. Státní zdravotnické nakladatelství. (State Publishing House of Health.) Prague, 1958.

Translated by A. Kardošová