# Benzothiazole compounds. XVII. 2-Alkyl- and 2-aralkylsulfonylbenzothiazoles and their antimicrobial activity

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By oxidation of 2-alkylthio-, 6-nitro-2-alkylthio-, and 2-aralkylthiobenzothiazoles the appropriate sulfones were prepared which showed good antibacterial, antifungal, and antimycobacterial activities. With some derivatives good activity was found also on *Mycobacterium fortuitum*. A correlation between the biological activity of the prepared compounds and their partition coefficients was proved in the system of octane–methanol.

Окислением 2-алкилтио-, 6-нитро-2-алкилтио- и 2-аралкилтиобензтиазолов были приготовлены соответствующие сульфоны и у них были отмечены хорошее антибактериальное, антифунгицидное а антимикобактериальное действия. Для некоторых производных было обнаружено также и воздействие на *Mycobacterium fortuitum*. Было доказано, что существует корреляция между биологической активностью приготовленных соединений и коэффициентами распределения в системе октан–метиловый спирт.

The results of the previous works [1—4] pointed at some relations between the structure and antimicrobial activity of the benzothiazole derivatives. The need to prepare some 2-alkyl-, 6-nitro-2-alkyl-, and 2-aralkylsulfonylbenzothiazoles was shown in further studies as the sulfone group in comparison with the sulfide group often increased the biological activity in several directions. Some comments marginally concerning the problem studied can be found in [5—12]. None of these works has paid attention to preparation of sulfones based on benzothiazole from the standpoint of antimicrobial activity. *Popoff* and coworkers [13] prepared a bactericidally and fungicidally active preparation containing an inert carrier and

an active compound 2-alkyl-5(6)-X-sulfonylbenzothiazole, where alkyl = $C_1$—$C_{12}$ nonbranched saturated chain or cycloalkyl, and X = halogen, $NO_2$, $NH_2$, NHR, $NR_2$, alkyl. *Agui* and coworkers [14] synthesized different 6-substituted 2-methylsulfonylbenzothiazoles which were found to show bactericidal and inhibitory activity.

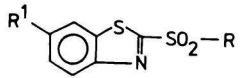
In this work 2-alkyl-, 6-nitro-2-alkyl-, and 2-aralkylsulfonylbenzothiazoles (Table 1) have been synthesized. These compounds have not been prepared and tested for antimicrobial activity as yet except the compounds *I*, *II*, *IV*—*VI* [13] which were tested for comparison with the other derivatives.

The starting 2-alkylthiobenzothiazoles were prepared by treatment of potassium salt of 2-mercaptobenzothiazole or 2-mercapto-6-nitrobenzothiazole with halogen derivatives [15, 3]. Oxidation to sulfones was carried out with 28% $H_2O_2$ in 99% acetic acid or with aqueous saturated solution of $KMnO_4$ in water–acetone medium. Under the conditions presented in Experimental the oxidation of all 6-nitro-2-alkylthiobenzothiazoles and 2-aralkylthiobenzothiazoles with $H_2O_2$ proceeded well but the oxidation of 2-alkylthiobenzothiazoles proceeded under decomposition or gave very low yields. Therefore, they were oxidized with $KMnO_4$. The prepared 2-alkylsulfonylbenzothiazoles, 6-nitro-2-alkylsulfonylbenzothiazoles, and 2-aralkylsulfonylbenzothiazoles were tested for antibacterial, antifungal, and antiprotozoal activities. It was found (Tables 2—4) that this group of compounds was antimicrobially active. The antibacterial, antifungal, antitrichomonal, and antitrypanosomal activities were proved to be good. A positive effect of $NO_2$ in the position 6 of the prepared compounds on antimicrobial activity was observed. For example, the activity of the compounds *I* and *II* on *Staphylococcus aureus:* $ED_{100}$ for $I = 98.0$ μg/ml $= 45 \times 10^{-5}$ mol/l and for $II = 6.5$ μg/ml $= 25 \times 10^{-6}$ mol/l, $ED_{50}$ for $I = 30.0$ μg/ml $= 14 \times 10^{-5}$ mol/l and for $II = 4.2$ μg/ml $= 16 \times 10^{-6}$ mol/l. The $ED_{100}$ and $ED_{50}$ values found with the other bacterial strains pointed to good antibacterial activity. The presence of the $NO_2$ group in the position 6 caused an increase in antimycobacterial and also in antifungal activity. The activity against *Mycobacterium fortuitum,* which is known to be very resistant against antibacterial preparations, can be positively estimated. The activity on *Tritrichomonas foetus* was interesting mainly with the 6-nitro derivatives when compared with that of the standard Metronidazol (1-(2-hydroxyethyl)-2-methyl-5-nitroimidazole) which is active on *Tritrichomonas foetus* at 2—5 μg/ml concentration. With this group of compounds the activity on epimastigotal forms of *Trypanosoma cruzi* can be highly evaluated. With some compounds we have found 100% lethal activity already at 0.8 μg/ml concentration at *in vitro* conditions.

We attempted to express quantitatively the relationship between the structures of the prepared sulfones and their biological activity on the basis of partition coefficients [16]. The values of the partition coefficients varied in the range of

*Table 1*

Characterization of the synthesized 2-alkyl- and 2-aralkylsulfonylbenzothiazoles




| Compound | R | R¹ | Formula | *M* | Calculated/found % C | % H | % N | % S | Yield % | M.p., °C Solvent |
|---|---|---|---|---|---|---|---|---|---|---|
| *I* | $CH_3$ | H | $C_8H_7O_2NS_2$ | 213.3 | | | | | 48 | 90—92 Ethanol |
| *II* | $CH_3$ | $NO_2$ | $C_8H_6O_4N_2S_2$ | 258.3 | | | | | 59 | 192—193 Tetrahydrofuran–ethanol (1:1) |
| *III* | $CH_2Cl$ | H | $C_8H_6ClO_2NS_2$ | 247.7 | 38.74<br>38.60 | 2.43<br>2.48 | 5.64<br>5.88 | 26.25<br>26.36 | 26 | 125—127 Ethanol |
| *IV* | $C_2H_5$ | $NO_2$ | $C_9H_8O_4N_2S_2$ | 272.3 | | | | | 62 | 161—162 Ethanol |
| *V* | $C_3H_7$ | $NO_2$ | $C_{10}H_{10}O_4N_2S_2$ | 286.3 | | | | | 59 | 182—184 Ethanol |
| *VI* | i-$C_3H_7$ | H | $C_{10}H_{11}O_2NS_2$ | 241.3 | | | | | 31 | 84—86 Ethanol |
| *VII* | i-$C_3H_7$ | $NO_2$ | $C_{10}H_{10}O_4N_2S_2$ | 286.3 | 41.99<br>42.12 | 3.52<br>3.41 | 9.79<br>9.74 | 22.41<br>22.68 | 56 | 155—156 Ethanol |
| *VIII* | $CH_2C{\equiv}CH$ | H | $C_{10}H_8O_2NS_2$ | 238.3 | 50.46<br>50.24 | 3.38<br>3.24 | 5.88<br>6.08 | 26.94<br>27.10 | 34 | 114—116 Ethanol |
| *IX* | $CH_2CH(OH)CH_2Cl$ | H | $C_{10}H_{10}ClO_3NS_2$ | 291.8 | 41.13<br>41.07 | 3.41<br>3.30 | 4.81<br>4.79 | 22.03<br>22.08 | 42 | 145—146 Ethanol |
| *X* | $CH_2CH{=}CH_2$ | $NO_2$ | $C_{10}H_8O_4N_2S_2$ | 284.3 | 42.24<br>42.41 | 2.83<br>2.96 | 9.85<br>9.77 | 22.55<br>22.59 | 46 | 190—192 Tetrahydrofuran–ethanol (1:3) |
| *XI* | $CH_2CH(CH_3)_2$ | $NO_2$ | $C_{11}H_{12}O_4N_2S_2$ | 300.3 | 44.03<br>43.87 | 4.03<br>3.90 | 9.33<br>9.28 | 21.37<br>21.70 | 58 | 125—126 Ethanol |

*Table 1* (Continued)

| Compound | R | R¹ | Formula | *M* | Calculated/found % C | % H | % N | % S | Yield % | M.p., °C Solvent |
|---|---|---|---|---|---|---|---|---|---|---|
| *XII* | $CH_2CH(C_2H_5)(CH_2)_3CH_3$ | $NO_2$ | $C_{15}H_{20}O_4N_2S_2$ | 356.4 | 50.60 | 5.66 | 7.86 | 18.01 | 61 | 92—92.5 |
| | | | | | 50.52 | 5.50 | 7.87 | 18.16 | | Ethanol |
| *XIII* | $CH_2C_6H_4Cl$-*p* | H | $C_{14}H_{10}ClO_2NS_2$ | 323.8 | 51.89 | 3.11 | 4.32 | 19.79 | 76 | 122—123 |
| | | | | | 51.93 | 3.06 | 4.22 | 19.54 | | Tetrahydrofuran–ethanol (1:3) |
| *XIV* | $CH_2C_6H_3(Cl)_2$-*m,p* | H | $C_{14}H_9Cl_2O_2NS_2$ | 359.2 | 47.10 | 2.50 | 3.89 | 17.86 | 73 | 154—156 |
| | | | | | 47.18 | 2.41 | 4.01 | 17.72 | | Tetrahydrofuran–ethanol (1:3) |
| *XV* | $CH_2C_6H_3(NO_2)_2$-*o,p* | H | $C_{14}H_9O_6N_3S_2$ | 380.3 | 44.50 | 2.37 | 11.05 | 16.84 | 70 | 210—212 |
| | | | | | 44.38 | 2.31 | 11.13 | 16.90 | | Tetrahydrofuran–ethanol (1:2) |
| *XVI* | $CH_2$-$\beta$-Naphthalene | H | $C_{18}H_{13}O_2NS_2$ | 339.3 | 63.76 | 3.86 | 4.12 | 18.91 | 82 | 116—118 |
| | | | | | 63.53 | 3.98 | 4.18 | 19.16 | | Ethanol |
| *XVII* | $CH_2SO_2$-2-Benzothiazole | H | $C_{15}H_{10}O_4N_2S_4$ | 410.5 | 43.94 | 2.45 | 6.83 | 31.28 | 52 | 199—201 |
| | | | | | 44.12 | 2.32 | 6.96 | 31.47 | | Ethanol |
| *XVIII* | $(CH_2)_2SO_2C_6H_4Cl$-*p* | H | $C_{15}H_{12}ClO_4NS_3$ | 401.9 | 44.81 | 3.00 | 3.48 | 23.93 | 57 | 178—179 |
| | | | | | 44.63 | 2.87 | 3.61 | 23.79 | | Tetrahydrofuran–ethanol (1:3) |
| *XIX* | $CH_2COOC_2H_5$ | $NO_2$ | $C_{11}H_{10}O_6N_2S_2$ | 330.5 | 39.99 | 3.05 | 8.47 | 19.41 | 59 | 141—142 |
| | | | | | 40.18 | 3.05 | 8.62 | 19.59 | | Ethanol–acetone (2:1) |
| *XX* | $CH_2COOCH_2CH_2Cl$ | H | $C_{11}H_{10}ClO_4NS_2$ | 287.7 | 45.91 | 3.50 | 4.86 | 22.28 | 32 | 97—98 |
| | | | | | 45.83 | 3.54 | 4.80 | 22.14 | | Ethanol |
| *XXI* | $CH_2COOCH_2CH_2Cl$ | $NO_2$ | $C_{11}H_9ClO_6N_2S_2$ | 364.8 | 36.19 | 2.48 | 7.67 | 17.56 | 73 | 98—100 |
| | | | | | 36.08 | 2.45 | 7.86 | 17.70 | | Ethanol |
| *XXII* | $CH_2COOCH_2CH{=}CH_2$ | $NO_2$ | $C_{12}H_{10}O_6N_2S_2$ | 342.3 | 42.14 | 2.84 | 8.18 | 18.74 | 68 | 107—108 |
| | | | | | 42.28 | 3.06 | 8.30 | 18.91 | | Ethanol |
| *XXIII* | $CH_2COOCH(CH_3)C_2H_5$ | $NO_2$ | $C_{13}H_{14}O_6N_2S_2$ | 358.4 | 43.61 | 3.94 | 7.82 | 17.91 | 76 | 96—98 |
| | | | | | 43.49 | 3.81 | 7.98 | 18.04 | | Ethanol |
| *XXIV* | $CH_2COOCH_2$-Furan | $NO_2$ | $C_{14}H_{10}O_7N_2S_2$ | 382.3 | 44.01 | 2.63 | 7.32 | 16.78 | 71 | 125—127 |
| | | | | | 43.89 | 2.70 | 7.35 | 16.81 | | Ethanol |

*Table 2*

Antibacterial activity of 2-alkyl- and 2-aralkylsulfonylbenzothiazoles

| Compound | *Staphylococcus aureus* | | | | *Bacillus subtilis* | | | | *Escherichia coli* | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $ED_{100}$ | | $ED_{50}$ | | $ED_{100}$ | | $ED_{50}$ | | $ED_{100}$ | | $ED_{50}$ | |
| | *a* | *b* | *a* | *b* | *a* | *b* | *a* | *b* | *a* | *b* | *a* | *b* |
| *I* | 98 | 45 −5 | 30.0 | 15 −5 | 90.0 | 42 −5 | 30.0 | 14 −5 | 91.0 | 42 −5 | 32.0 | 15 −5 |
| *II* | 6.5 | 25 −6 | 4.2 | 16 −6 | 6.0 | 23 −6 | 4.0 | 15 −6 | 5.0 | 19 −6 | 3.0 | 11 −6 |
| *III* | 120.0 | 48 −5 | 39.0 | 15 −5 | 110.0 | 44 −5 | 38.0 | 15 −5 | 110.0 | 44 −5 | 39.0 | 15 −5 |
| *IV* | 12.5 | 45 −6 | 6.0 | 22 −6 | 12.0 | 44 −6 | 5.8 | 21 −6 | 10.5 | 38 −6 | 4.5 | 16 −6 |
| *V* | 13.0 | 45 −6 | 6.2 | 21 −6 | 13.0 | 45 −6 | 6.2 | 21 −6 | 13.0 | 45 −6 | 6.2 | 21 −6 |
| *VI* | 200.0 | 82 −5 | 52.0 | 21 −5 | 200.0 | 82 −5 | 51.0 | 21 −5 | 200.0 | 82 −5 | 54.0 | 22 −5 |
| *VII* | 13.0 | 45 −6 | 6.2 | 21 −6 | 13.0 | 45 −6 | 6.2 | 21 −6 | 13.0 | 45 −6 | 6.2 | 21 −6 |
| *VIII* | 82.0 | 34 −5 | 26.0 | 10 −5 | 85.0 | 35 −5 | 25.0 | 10 −5 | 95.0 | 39 −5 | 28.0 | 11 −5 |
| *IX* | 200.0 | 68 −5 | 90.0 | 30 −5 | 200.0 | 68 −5 | 91.0 | 31 −5 | 200.0 | 68 −5 | 94.0 | 32 −5 |
| *X* | 6.2 | 27 −6 | 3.8 | 16 −6 | 6.2 | 27 −6 | 3.8 | 16 −6 | 5.4 | 23 −6 | 3.0 | 13 −6 |
| *XI* | 15.0 | 49 −6 | 6.5 | 21 −6 | 13.0 | 43 −6 | 6.5 | 21 −6 | 14.5 | 48 −6 | 6.5 | 21 −6 |
| *XII* | 55.0 | 15 −5 | 38.0 | 10 −5 | 55.0 | 15 −5 | 30.0 | 8 −5 | 60.0 | 16 −5 | 31.0 | 8 −5 |
| *XIII* | 200.0 | 61 −5 | 55.0 | 16 −5 | 200.0 | 61 −5 | 50.0 | 15 −5 | 160.0 | 49 −5 | 46.0 | 14 −5 |
| *XIV* | 220.0 | 61 −5 | 56.0 | 15 −5 | 200.0 | 55 −5 | 49.0 | 13 −5 | 180.0 | 50 −5 | 46.0 | 12 −5 |
| *XV* | 220.0 | 57 −5 | 54.0 | 14 −5 | 200.0 | 52 −5 | 51.0 | 13 −5 | 175.0 | 46 −5 | 45.0 | 11 −5 |
| *XIX* | 25.0 | 75 −6 | 7.2 | 21 −6 | 25.2 | 77 −6 | 7.4 | 22 −6 | | | | |
| *XXI* | 24.0 | 65 −6 | 6.8 | 17 −6 | 24.0 | 65 −6 | 6.5 | 17 −6 | 22.0 | 60 −6 | 7.0 | 19 −6 |
| *XXII* | 24.0 | 70 −6 | 6.5 | 18 −6 | 24.0 | 70 −6 | 6.5 | 18 −6 | 22.0 | 64 −6 | 7.0 | 20 −6 |
| *XXIII* | 90.0 | 25 −5 | 24.0 | 66 −6 | 90.0 | 25 −5 | 28.0 | 64 −6 | 83.0 | 23 −5 | 22.0 | 61 −6 |
| *XXIV* | 25.0 | 65 −6 | 7.0 | 18 −6 | 25.0 | 65 −6 | 7.0 | 18 −6 | 24.0 | 62 −6 | 7.0 | 18 −6 |
| *XXV* | 120.0 | 55 −5 | 35.0 | 16 −5 | 110.0 | 51 −5 | 30.0 | 13 −5 | 110.0 | 51 −5 | 30.0 | 13 −5 |

$a$ = μg/ml.

$b$ = mol × $10^{-n}$/l; the negative number means the value of the exponent $-n$.

0.15—0.30. This problem was worked up mathematically by correlation analysis where $\log(1/ED_{50})$ was expressed as a function of $P$ and $P^2$ ($P$ = partition coefficient) at tests on *Staphylococcus aureus, Bacillus subtilis,* and *Escherichia coli.* The derivatives of the series 1 (the compounds *I*, *III*, *VIII*, *IX*, *XIII—XV*) showed good correlations for *Staphylococcus aureus.* This relationship can be expressed by the equation: $\log 1/ED_{50} = 3.76 + 1.39P - 4.88P^2$. The derivatives of the series 2 (the compounds *IV*, *V*, *VII*, *X*, *XI*, *XII*, *XXI*, *XXIV*) showed statistical relationships for all strains of bacteria examined except the compounds *VIII* and *IX* which, regarding their structures, could have acted in the given

*Table 3*

Antifungal activity of 2-alkyl- and 2-aralkylsulfonylbenzothiazoles

| Compound | Nature of growth | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Microsporum gypseum* | | | *Trichophyton rubrum* | | | *Epidermophyton floccosum* | | | *Candida pseudotropicalis* | | |
| | 50 | 5 | 0.5 | 50 | 5 | 0.5 | 50 | 5 | 0.5 | 50 | 5 | 0.5 |
| *I* | A | B | C | A | B | C | A | B | C | A | B | C |
| *II* | A | A | B | A | A | B | A | A | B | A | A | B |
| *III* | A | B | C | A | B | C | A | B | C | A | C | C |
| *IV* | A | B | C | A | A | C | A | A | C | A | A | B |
| *V* | A | B | C | A | B | C | A | B | C | A | A | B |
| *VI* | B | C | C | A | C | C | A | C | C | B | C | C |
| *VII* | A | B | C | A | B | C | A | B | C | A | B | C |
| *VIII* | A | C | C | A | C | C | A | C | C | A | C | C |
| *IX* | C | C | C | C | C | C | C | C | C | C | C | C |
| *X* | A | B | C | A | B | C | A | A | B | A | A | B |
| *XI* | A | B | C | A | A | C | A | B | C | A | B | C |
| *XII* | B | C | C | A | C | C | A | C | C | B | C | C |
| *XIII* | B | C | C | A | C | C | A | C | C | B | C | C |
| *XIV* | B | C | C | A | C | C | B | C | C | B | C | C |
| *XV* | B | C | C | A | B | C | B | C | C | B | C | C |
| *XVI* | C | C | C | C | C | C | C | C | C | C | C | C |
| *XVII* | B | C | C | C | C | C | B | C | C | C | C | C |
| *XVIII* | C | C | C | C | C | C | C | C | C | C | C | C |
| *XIX* | A | C | C | A | B | C | A | B | C | A | C | C |
| *XX* | A | C | C | A | C | C | A | C | C | A | C | C |
| *XXI* | A | B | C | A | B | C | A | B | C | A | B | C |
| *XXII* | A | B | C | A | B | C | A | B | C | A | B | C |
| *XXIII* | A | C | C | A | C | C | A | C | C | A | C | C |
| *XXIV* | A | C | C | A | C | C | A | C | C | A | C | C |

A = 100% inhibition; B = 50% inhibition; C = without inhibition.

*Table 4*

Antimycobacterial and antiprotozoal activity of 2-alkyl- and 2-aralkylsulfonylbenzothiazoles (μg/ml)

| Compound | Bactericidal/bacteriostatical concentration | | Lethal concentration | |
|---|---|---|---|---|
| | *BCG* | *Mycobacterium fortuitum* | *Trypanosoma cruzi* | *Tritrichomonas foetus* |
| *I* | 50/12.5 | 200/50 | 50.0 | 12.5 |
| *II* | 3.1/3.1 | 12.5/3.1 | 0.8 | 0.8 |
| *III* | 50/12.5 | 200/50 | 50.0 | 12.5 |
| *IV* | 12.5/3.1 | 50/12.5 | 0.8 | 3.1 |
| *V* | 12.5/3.1 | 50/12.5 | 0.8 | 3.1 |
| *VI* | 200/50 | 400/200 | 200.0 | 50.0 |
| *VII* | 12.5/3.1 | 50/12.5 | 0.8 | 3.1 |
| *VIII* | 200/50 | 400/200 | 50.0 | 50.0 |
| *IX* | 200/50 | 400/200 | 200.0 | 200.0 |
| *X* | 3.1/3.1 | 12.5/3.1 | 0.8 | 0.8 |
| *XI* | 12.5/3.1 | 50/12.5 | 3.1 | 3.1 |
| *XII* | 50/12.5 | 200/50 | 3.1 | 12.5 |
| *XIII* | 200/50 | 400/200 | 200.0 | 200.0 |
| *XIV* | 200/50 | 400/200 | 200.0 | 200.0 |
| *XV* | 200/50 | 400/200 | 200.0 | 200.0 |
| *XIX* | 12.5/3.1 | 200/50 | 3.1 | |
| *XXI* | 12.5/3.1 | | 3.1 | 12.5 |
| *XXII* | 50/12.5 | 200/50 | 3.1 | 12.5 |
| *XXIII* | 50/12.5 | 200/50 | 12.5 | 12.5 |
| *XXIV* | 12.5/3.1 | 200/50 | 3.1 | 12.5 |

process by different mechanism. This group of compounds can be described by the following equations: for *Staphylococcus aureus* $\log 1/ED_{50} = -8.67 + 135.19P - 338.16P^2$, for *Bacillus subtilis* $\log 1/ED_{50} = -24.25 + 292.56P - 732.00P^2$, and for *Escherichia coli* $\log 1/ED_{50} = -26.32 + 312.38P - 779.87P^2$. The correlation coefficients varied in all cases in the range of 0.9—0.95, the errors in individual cases were lower than 12%. The analytical expression of individual functions can be utilized in investigation of antimicrobial activity for the known values of partition coefficients in the system of octane–methanol. However, it is to be considered that the results can be partly influenced by lesser number of the experimental points available for the analysis.

## Experimental

The melting points were determined on a Kofler block. Solvents for crystallization and analytical data of the synthesized compounds are presented in Table 1. The activity on

*Staphylococcus aureus, Bacillus subtilis,* and *Escherichia coli* was followed in liquid cultivation media. The activity was evaluated by a spectrophotometric method on a SPEKOL-ZV spectrophotometer at 37°C and 460 nm by following the growth of the individual strains under the action of different concentrations of the compounds investigated. The found values of optical density served to construct the curves from which the $ED_{100}$ and $ED_{50}$ values were graphically evaluated. These values represent the degree of antibacterial activity; the results are presented in Table 2.

The antifungal activity against *Microsporum gypseum, Trichophyton rubrum, Epidermophyton floccosum,* and *Candida pseudotropicalis* was followed by the dilution test tube method in Sabouraud agar. The compounds after dissolution in DMSO were added into the tempered agar so that the resulting concentrations were 500, 50, 5, and 0.5 μg/ml. The results are presented in Table 3. All sulfones tested acted fungicidally at 500 μg/ml and therefore, this concentration is not presented in Table 3.

The activity on mycobacterial strains was followed by the dilution method in a serum liquid Šula medium. The activity on *Mycobacterium fortuitum* was evaluated after 7 days cultivation at 37°C and on *BCG* after 21 days cultivation. The results are presented in Table 4.

The activity on *Tritrichomonas foetus* was followed in a liquid Diamond medium and was evaluated after 36 h cultivation at 37°C. The number of individuals in the control was compared with that in the test tubes containing the individual compounds at different concentrations. The activity on *Trypanosoma cruzi* strain *Z* was followed in a liquid LIT medium. In time intervals the number of motile individuals was followed and simultaneously, by inoculation into fresh LIT medium, the degree of trypanocidal activity was observed. More detailed procedures of tests can be found in [17, 18]. Partition coefficients were studied by shaking $10^{-3}$ M solutions with octane–methanol (1 : 1). The concentrations of compounds in the individual phases were determined spectrophotometrically on a Perkin—Elmer 450 apparatus at 23°C and 360—280 nm.

## *2-R-Sulfonylbenzothiazoles (I, III, VI, VIII, IX, XX)*

To 2-R-thiobenzothiazole (0.03 mol) dissolved in acetone (100 ml), water (20 ml), and acetic acid (10 ml), a saturated aqueous solution of potassium permanganate (4.74 g; 0.03 mol) was added portionwise under stirring. The reaction mixture was heated at 50—55°C for 4 h. Manganese dioxide was filtered off on heating and washed with acetone. After cooling the solid product was filtered off and purified by crystallization.

## *6-R$^1$-2-R-Sulfonylbenzothiazoles (II, IV, V, VII, X—XIX, XXI—XXIV)*

6-R$^1$-2-R-Thiobenzothiazole (0.03 mol) was dissolved in 98—99% acetic acid (150 ml). 28% Hydrogen peroxide (21.7 g; 0.18 mol) was added at 40—45°C under continuous stirring for 30 min. The reaction mixture heated to 55—65°C was stirred for further 3—4 h. After cooling it was poured onto crushed ice (400—600 g). The solid portion was filtered and purified by crystallization.

## References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