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# Synthesis and Antimicrobial Activity of 2-Arylsulfonamido-5-(Benzthiazol-2′-yl-Thiomethyl)-1,3,4-thiadiazoles

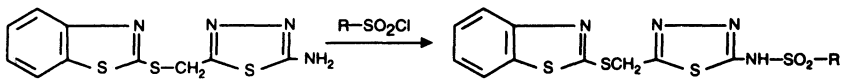
D.S. MEHTA, B.S. VASHI and V.H. SHAH*
*Department of Chemistry*
*Saurashtra University, Rojkot-360 005, India*

Certain new sulfonamide derivatives having benzthiazol moiety have been synthesised by the reaction of 2-amino-5-(benzthiazol-2′-yl-thiomethyl)-1,3,4-thiadiazole with different aromatic sulfonylchlorides in the presence of pyridine. These compounds have been characterised by spectral data and evaluated for antimicrobial activity. Some of them are found to be good active as compared with standard drugs.

## INTRODUCTION

Benzthiazole[1,2] derivatives possess a wide spectrum of biological activity. Thiadiazoles[3,4] exhibits anticonvulsant, antibacterial and antifungal activities. Recently interest has been developed in sulfonamide derivatives due to their biodynamic properties. In view of these findings, the present paper reports the combination of these three moieties and synthesised 2-aryl-sulfonamido-5-(benzthiazol-2′-yl-thiomethyl)-1,3,4-thiadiazoles of type (I).

2-Amino-5-(benzthiazol-2′-yl-thiomethyl)-1,3,4′-thiadiazole was synthesised by cyclocondensation of 2-carboxymethylthiobenzthiazole with thiosemicarbazide in the presence of phosphorus oxychloride. This was then condensed with different aromatic sulfonyl chlorides in dry pyridine to get 2-arylsulfonamido 5-(benzthiazol-2′-yl-thiomethyl)-1,3,4-thiadiazoles (I).




(I) R = Aryl

## EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. The structures of the compounds were established on the basis of their elemental analyses and spectral data. IR spectra (KBr) were recorded on a Shimadzu IR-435 spectrophotometer and PMR spectra were recorded in TFA on Hitachi R-1200 (60 MHz) using TMS as internal reference, chemical shifts are expressed in δ ppm.

*2-Carboxymethylthiobenzthiazole* (a): A mixture of 2-mercaptobenzthiazole (0.01 m), chloroacetic acid (0.01 M) and sodium hydroxide solution (32%., 5 mL) was heated for 8 h. The contents were cooled, diluted with water (50 mL) and neutralised with HCl (0.1 N). The product so obtained was filtered and recrystallised from methanol, m.p. 148°C, Yield 78%.

TABLE-1
ANTIMICROBIAL ACTIVITY OF 2-ARYLSULPHONAMIDO-5-(BENZTHIAZOL-2'-YL-THIOMETHYL)-1,3,4-THIADIAZOLES

| Compd. No. | R (m.f) | m.p. (°C) | N% Found (calc) | Antibacterial activity zone of inhibition in mm | | | Antifungal Activity zone of inhibition in mm | |
|---|---|---|---|---|---|---|---|---|
| | | | | *B. mega* | *B. subtilis* | *A. arogens* | *E. coli* | *A. awamory* |
| $I_a$ | Phenyl ($C_{16}H_{12}O_2N_4S_4$) | 182 | 13.29 (13.33) | 12 | 15 | 22 | 20 | 15 |
| $I_b$ | 4-Chlorophenyl ($C_{16}H_{11}O_2N_4S_4Cl$) | 235 | 12.25 (12.32) | 12 | 15 | 20 | 21 | 12 |
| $I_c$ | 4-Iodophenyl ($C_{16}H_{11}O_2N_4S_4I$) | 284 | 10.15 (10.22) | 12 | 14 | 24 | 22 | 13 |
| $I_d$ | 4-Anisyl ($C_{17}H_{14}O_3N_4S_4$) | 220 | 12.35 (12.44) | 17 | 17 | 21 | 22 | 14 |
| $I_e$ | 3-Carboxyphenyl ($C_{17}H_{12}O_4N_4S_4$) | 274 | 11.99 (12.06) | 11 | 12 | 24 | 23 | 12 |
| $I_f$ | 3-Carboxy-4-chlorophenyl ($C_{17}H_{11}O_4N_4S_4Cl$) | 289 | 11.15 (11.23) | 15 | 14 | 22 | 22 | 11 |
| $I_g$ | 3-Carboxy-6-chlorophenyl ($C_{17}H_{11}O_4S_4Cl$) | 300 | 11.18 (11.23) | 12 | 11 | 23 | 20 | 12 |
| $I_h$ | 3-Carboxy-4-methoxyphenyl ($C_{18}H_{14}O_5N_4S_4$) | 221 | 11.28 (11.33) | 12 | 12 | 22 | 19 | 16 |
| $I_i$ | 3-Carboxy-6-methoxyphenyl ($C_{18}H_{14}O_5N_4S_4$) | 177 | 11.30 (11.33) | 13 | 17 | 20 | 19 | 14 |
| $I_j$ | 3-Carboxy-4-hydroxyphenyl ($C_{17}H_{12}O_5N_4S_4$) | 205 | 11.60 (11.66) | 16 | 13 | 24 | 20 | 13 |
| $I_k$ | 3-Carboxy-4-methylphenyl ($C_{18}H_{14}O_4N_4S_4$) | 295 | 11.65 (11.72) | 12 | 15 | 19 | 18 | 15 |
| $I_l$ | 3-Carboxy-6-methylphenyl ($C_{18}H_{14}O_4N_4S_4$) | 300 | 11.67 (11.72) | 15 | 17 | 21 | 14 | 12 |
| $I_m$ | 3-Carboxy-4-bromophenyl ($C_{17}H_{11}O_4S_4Br$) | 262 | 10.23 (10.31) | 11 | 15 | 22 | 16 | 13 |
| $I_n$ | 4-(α'-Carboxy) styryl ($C_{19}H_{14}O_4S_4$) | 187 | 11.35 (11.42) | 14 | 15 | 22 | 20 | 14 |
| $I_o$ | 4-Tolyl ($C_{17}H_{14}O_2N_4S_4$) | 205 | 12.85 (12.90) | 11 | 18 | 23 | 21 | 15 |
| | Ampicillin | — | — | 23 | 18 | 23 | 21 | — |
| | Chloramphenicol | — | — | 24 | 19 | 25 | 26 | — |
| | Norfloxacin | — | — | 24 | 19 | 25 | 26 | — |
| | Griseofulvin | — | — | — | — | — | 26 | 23 |

% Yield varied from 60 to 78.

*2-Amino-5-(benzthiazol-2'}-yl-thiomethyl)-1,3,4-thiadiazole* (b): A mixture of (a) (0.01 M), thiosemicarbazide (0.015 M) and phosphorous oxychloride (7 mL) was refluxed on oilbath for 12 h. The contents were poured on crushed ice and neutralised with 1% $NaHCO_3$ solution. The isolated product was filtered and recrystallised from 1,4-dioxane : methanol (3 : 1). m.p. 238°C, yield 61%. IR: $\nu_{max}$ $cm^{-1}$: 3390 (—NH str), 1680 (C=O str), 1570 (—C=N str), 710 (C—S—C str). PMR(TFA) δ: 4.6 (s, 2H, S—$CH_2$), 7.5–8.1 (m, 4H, AR–*H*).

*2-(5'-Carboxy-2'-methoxysulfonamidophenyl)-5-(benzthiazol-2''-yl-thiomethyl)-1,3,4-thiadiazole* ($I_g$): A mixture of (b) (0.01 M) and 3-chlorosulfonyl-4-methoxybenzoic acid in dry pyridine (5 mL) was refluxed on oil bath for 5 h. The contents were cooled and poured on crushed ice, acidified by diluted HCl and resulting solid was filtered, dried and recrystallised from DMF, m.p. 188°C, yield 65%. IR $\nu_{max}$ $cm^{-1}$: 3400 (—NH str), 1670 (—C=O str), 1570 (—C=N str), 1360 and 1155 (—$SO_2$·NH str), 710 (C—S—C str). PMR (TFA) δ: 4.1 (s, 3H, —O$CH_3$), 4.66 (s, 2H, S—$CH_2$). 7.8–8.15 (m, 8H, AR–*H*).

Similarly other sulfonamides were prepared and physical constants are recorded in Table-1.

**Antimicrobial Activity:** All the compounds were screened for their antibacterial activity against gram positive *B. mega, B. subtilis* and gram negative *E. coli, A. arogens* and antifungal activity against *A. awamory*. The zone of inhibition was measured in mm and recorded in Table-1. The activity was compared with known chosen standard drugs viz., ampicillin, chloramphenicol, norfloxacin and griseofulvin at the same concentration i.e., 50 μg.

In case of antibacterial activity from experimental data it has been observed that sulphonamide derivatives of type $I_{a-o}$ were found to possess moderate activity against *B. mega* and *B. subtilis*, However, compounds such as $I_j$, $I_m$, $I_n$, $I_o$, exhibited comparable activity with standard drugs *viz.*, chloramphenicol and norfloxacin; compounds $I_{a-o}$ showed good activity against *A. arogens* and *E. coli* but less than the standard drugs.

However compounds such as $I_c$, $I_f$, $I_h$, $I_k$ showed comparable activity with known standard drugs, *viz.* chloramphenicol, ampicillin and norfloxacin. In case of antifungal activity compounds $I_{a-o}$ exhibited moderate activity against *A. awamory* but less than the standard drugs *viz.* griseofulvin.

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## REFERENCES

1. B.H. Trivedi and V.H. Shah, *Indian Drugs*, **29**, 262 (1992).
2. J. Patrick, J. Leblevee and Nemecek, Eur. Pat. Appl. EP., 409, 692; *Chem. Abstr.*, **114**, 228902d (1991).
3. P.M. Parashariya and A.R. Parikh, *J. Inst. Chem. (India)*, **63**, 196 (1991).
4. P.M. Parasharyia, V.H. Shah and A.R. Parikh, *J. Inst. Chem. (India)*, **65**, 106 (1993).
5. B.H. Trivedi and V.H. Shah, *Asian J. Chem.*, **7**, 563 (1995).

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