Synthesis, Antibacterial and Antifungal Activity of 4-Substituted-5-Aryl-1,2,4-Triazoles

Katica Colanceska-Ragenovic¹, Vesna Dimova¹*, Vlado Kakurinov², Dora Gabor Molnar³ and Aleksandra Buzarovska¹

¹ Faculty of Technology and Metallurgy, The “Sv. Kiril & Metodij” University, R. Boskovic 16, 1000 Skopje, Macedonia.
² Faculty of Agriculture, Department of Microbiology, The “Sv. Kiril & Metodij” University, Bul. Aleksandar Makedonski, bb, 1000 Skopje, Macedonia.
³ Institute of Chemistry, Faculty of Sciences, University of Novi Sad, Trg Dositeja Obradovica 3, 21000 Novi Sad, Yugoslavia.

*Author to whom correspondence should be addressed; e-mail: vdimova@hotmail.com

Received: 8 February 2001; in revised form 24 September 2001 / Accepted: 26 September 2001 / Published: 30 September 2001

Abstract: A few 4-allyl/amino-5-aryl-1,2,4-triazoles were synthesized and tested for antibacterial and antifungal effects against Escherichia coli, Bacillus subtilis, Salmonella enteritidis, Staphylococcus aureus, Aspergillus niger and Candida albicans. 4-Allyl-5-aryl-1,2,4-triazoles were obtained by the oxidative cyclization of the appropriate 1-substituted-4-allylthiosemicarbazides and 4-amino-5-aryl-1,2,4-triazoles were obtained by cyclization of the potassium salts of appropriately substituted dithiocarbazinic acids with hydrazine hydrate. The new synthesized compounds were characterized using IR, ¹H-NMR, ¹³C-NMR and UV spectral data together with elemental analysis.

Key words: Substituted benzoyl/phenylcetyl-4-allylthiosemicarbazides, 1,2,4-triazoles, cyclization, inhibition zone.
Introduction

1,2,4-Triazole and its derivatives represent one of the most biologically active classes of compounds, possessing a wide spectrum of activities. The 1,2,4-triazole nucleus is associated with diverse pharmacological activities such as antibacterial, antifungal, hypoglycemic, antihypertensive and analgesic properties [1-5]. The scientific literature also states that the antiviral [6] and antibacterial [7,8] activities of thiourea derivatives are due to the presence of the \(-\text{NH-C(S)-NH-}\) function in the molecule and the changes in this activity depend on the nature of its substituents. These observations prompted us to synthesize some new triazoles and to investigate their antibacterial and antifungal activities.

Results and Discussion

The aim of this work was a synthesis of 4-substituted-5-aryl-1,2,4-triazoles (Scheme 1).
In order to achieve this aim it was necessary to first synthesize hydrazides 3a-f of some substituted benzoic (2-hydroxy-, 4-hydroxy-, 2-hydroxy-5chloro-and 4-ethoxy-) and substituted phenylacetic (4-hydroxy- and 4-ethoxy-) acids. Hydrazides 3a-f were prepared by reactions of corresponding methyl/ethyl esters and hydrazine hydrate. The next step was conversion of the derivatives 3 into the corresponding 4-allyl-5-aryl-1,2,4-triazoles (Route I) and 4-amino-5-aryl-1,2,4-triazoles (Route II).

When 2-hydroxy- (3a); 4-hydroxy- (3b); 2-hydroxy-5-chlorobenzhydrazide (3c) and 4-ethoxyphenylacetylhydrazide (3e) were refluxed with allylisothiocyanates in ethanolic solution, 1-substituted-4-allylthiosemicarbazides (4a-d) were obtained. The melting points, yields and elemental analyses of compounds (4a-d) are given in Table 1.

Table 1: Physical and analytical data of compounds 4a-d and 5a-h

| Comp. | Ar                        | Mol. formula (mol.wt) | Mp °C | Yield % | Elemental analysis calc./found |
|-------|---------------------------|-----------------------|-------|---------|--------------------------------|
|       |                           |                       |       |         | C   | H    | N    |
| 4a    | 2-OH-C6H4-                | C_{11}H_{13}N_{3}O_{2}S (251.311) | 198-9 | 84.39   | 52.57 | 52.40 | 52.51 | 16.72 | 16.69 |
| 4b    | 4-OH-C6H4-                | C_{11}H_{13}N_{3}O_{2}S (251.311) | 194-6 | 84.76   | 52.57 | 52.51 | 52.19 | 16.72 | 16.75 |
| 4c    | 2-OH-5-Cl-C6H3-           | C_{11}H_{12}N_{3}O_{2}ClS (285.755) | 188-90 | 92.53 | 45.92 | 45.99 | 5.07  | 14.71 | 14.64 |
| 4d    | 4-C2H5O-C6H4-CH2-        | C_{14}H_{19}N_{3}O_{2}S (293.389) | 180-2 | 82      | 57.31 | 57.41 | 6.49  | 14.32 | 14.44 |
| 5a*   | 2-OH-C6H4-                | C_{11}H_{11}N_{3}OS (233.293) | 203-5 | 85.59   | 56.63 | 56.03 | 4.75  | 18.01 | 17.95 |
| 5b    | 4-OH-C6H4-                | C_{11}H_{11}N_{3}OS (233.293) | 176-8 | 93.54   | 56.63 | 56.85 | 4.75  | 18.01 | 18.32 |
| 5c    | 2-OH-5-Cl-C6H4-           | C_{11}H_{10}N_{3}OCIS (267.738) | 142-4 | 67.62   | 49.35 | 49.27 | 3.57  | 15.69 | 15.58 |
| 5d    | 4-C2H5O-C6H4-CH2-        | C_{14}H_{17}N_{3}OS (275.374) | 125-7 | 90      | 61.06 | 61.12 | 6.22  | 15.26 | 15.31 |
| 5e**  | 2-OH-C6H4-                | C_{8}H_{8}N_{4}OS (208.17) | 202-3 | 71.6    | 46.14 | 45.96 | 3.89  | 26.90 | 26.39 |
| 5f    | 4-OH-C6H4-                | C_{8}H_{8}N_{4}OS (208.17) | 217   | 81.5    | 46.14 | 46.96 | 3.89  | 26.90 | 26.59 |
| 5g    | 4-OH-C6H4-CH2-            | C_{9}H_{10}N_{4}OS (222.18) | 203-4 | 13.87   | 48.63 | 49.14 | 5.02  | 25.20 | 24.84 |
| 5h    | 4-C2H5O-C6H4-CH2-        | C_{11}H_{14}N_{4}OS (250.22) | 101-3 | 64.9    | 52.98 | 52.91 | 5.87  | 22.29 | 21.99 |
The structures of compounds 4a-d were established by their IR, ¹H-NMR and ¹³C-NMR spectra. The IR absorptions due to the C=O and C=S functions appeared at 1660/1600 and 1280/1240 cm⁻¹, respectively. The absorption bands associated with other functional groups present all appeared in the expected regions. The ¹H-NMR spectra of compounds 4a-d (in DMSO-d₆) exhibited a multiplet in the aromatic region at 6.83-7.91 ppm corresponding to the Hₐrom protons. Three or four low fields singlets were observed at the 8.11-11.96 ppm region representing the protons of the OH group and the NH (thiosemicarbazide moiety), due to strong deshielding effect of the aromatic ring system and the thiocarbonyl group. The ¹H-NMR spectra of 4a-d also exhibited the CH₂- and –CH- signals of the allyl group as multiplets and doublets between 4.09 and 5.83 ppm. The ¹³C-NMR spectra of 4a-d exhibited C=S signals at 181.5 – 181 ppm.

When compounds 4a-d were refluxed in 2M NaOH solution for about 4 hours, they produced 4-allyl-5-aryl-1,2,4-triazoles 5a-d in good yields (Table 1). Oxidative cyclization reactions of thiosemicarbazides have been previously described [9-11]. Except for 5a, which had been previously reported in the literature [21], all the compounds 5 reported in the present work are novel, and were all obtained in the form of high melting solids. The spectral data are in good agreement with the proposed structures. While 1,2,4-triazoles may exist in thione-thiol tautomeric forms, our investigations showed that in this case the thione structures dominate in the solid state, as indicated by the IR and NMR data of compounds 5a-d. Thus, their IR spectra (KBr disks) showed no absorption bands around 2600-2550 cm⁻¹ indicative of the thiol form. The IR absorptions due to the C=S functions in 5a-d appeared at about 1320-1300 cm⁻¹[8,12]. The ¹H-NMR spectra of 5a-d (DMSO-d₆) exhibited the NH signals (NH function of the triazoline ring) as a singlet between 12.49 and 13.98 ppm which also supports the proposed thione structure [13,14]. The signals associated with other functional groups all appeared in the expected regions, such as CH₂- and –CH- signals of the allyl groups as multiplets and doublets between 4.49 and 5.80 ppm. The ¹³C-NMR spectra of 5a-d exhibited C=S signals at 166.7-167.4 ppm.

When 2-hydroxy- (3a); 4-hydroxybenzhydrazide (3b); 4-hydroxy- (3d) and 4-ethoxy-phenylacetylhydrazide (3e) were refluxed in ethanol with carbon disulfide and potassium hydroxide, the corresponding potassium salts of the substituted dithiocarbazinic acids 4e-h were formed. Further, the potassium salts upon reaction with hydrazine hydrate yielded the corresponding 4-amino-5-aryl-1,2,4-triazoles 5e-h. Of the 5e-h series, all the compounds prepared were novel, except for 5e [22, 23]. The melting points, yield and elemental analyses of these compounds are given in Table 1. The structures of 5e-h were established by their IR and UV spectra. Thus, the UV spectra of 5e-f showed two absorption maxima or shoulders at 252-256 and 288-298 nm. These data indicated that these compounds exist predominantly in the thione form in ethanolic solution [15,16]. The absorption at 288-298 nm indicated the presence of a chromophoric C=S group. In addition to the UV data, their IR spectra (KBr disks) also showed a band in the 1266-1249 cm⁻¹ region due to the C=S function, further supporting the predominance of the thione form in the solid state and in polar solvents [8,12].

The UV spectral data of compounds 5g-h showed that they exist predominantly in the thiol form in ethanolic solutions, as no absorption maxima or shoulders are observed in the 288-298 nm region which would be indicative of the thione form. The fact that the compounds exist in thione-thiol tautomeric equilibria is supported by the absence of characteristic (SH) absorption bands in the IR spectra. The IR
spectra of compounds 5e-h showed characteristic absorption bands around 3306-3152 cm\(^{-1}\) (OH and NH stretch); 3103-2955 cm\(^{-1}\) (C-H from Ar-H stretch); 2972-2788 cm\(^{-1}\) (C-H from CH\(_2\) stretch); 1626-1599 cm\(^{-1}\) (C=C); 1583-1514 cm\(^{-1}\) (C=N) and 1534-1480 cm\(^{-1}\) (N-H).

**Biological Testing**

A filter paper disc method [14] was employed for the *in vitro* study of antifungal and antibacterial effects against *Escherichia coli*, *Bacillus subtilis*, *Salmonella enteritidis*, *Staphylococcus aureus*, *Aspergillus niger* and *Candida albicans*. The inhibitory effects of compounds 4a-d and 5a-h against these organisms are given in Table 2.

The screening results indicate that not all compounds exhibited antibacterial and antifungal activities. It can be noted that compounds with free NH\(_2\) groups in the 4 position (5e-h) showed the greatest inhibitory effect against one or more types of bacteria compared to those with allyl groups in the same position (5a-d). Compounds 4a, 5a and 5d showed no inhibitory effects against any of the tested organisms. From the results, we can also see that the rest of compounds showed lower fungicidal effects compared with their bactericidal effects.

We can also compare the inhibitory effect of the thiosemicarbazides 4a-d with the similar effects of their cyclised products, the triazoles 5a-d. For example, after oxidative cyclization of 4b and 4c, the resulting 1,2,4-triazoles 5b and 5c showed the highest inhibitory effects against all the test organisms. But, this effect completely disappeared upon ring formation in the case of compound 4a. The 4-amino-5-(4-hydroxyphenyl)-1,2,4-triazole (5f) showed the highest inhibition zone diameter against *Staphylococcus aureus* (28 mm), compared with all the test organisms and all the tested compounds.

**Table 2**: Inhibition zones (mm)

| Comp. | Concentration [mg/ml] | *Escherichia coli* | *Bacillus subtilis* | *Salmonella enteritidis* | *Staphylococcus aureus* | *Aspergillus niger* | *Candida albicans* |
|-------|------------------------|--------------------|---------------------|--------------------------|------------------------|--------------------|-------------------|
| 4a    | 1                      | -                  | -                   | -                        | -                      | -                  | -                 |
|       | 5                      | -                  | -                   | -                        | 5.5                    | -                  | 5.5               |
|       | 10                     | -                  | -                   | 6                        | 5.5                    | 5.5                | -                 |
| 4b    | 1                      | -                  | -                   | -                        | -                      | -                  | -                 |
|       | 5                      | -                  | -                   | -                        | -                      | -                  | -                 |
|       | 10                     | -                  | -                   | -                        | -                      | -                  | -                 |
| 4c    | 1                      | -                  | -                   | 6                        | 5.5                    | -                  | -                 |
|       | 5                      | -                  | -                   | 10                       | -                      | -                  | -                 |
|       | 10                     | -                  | -                   | 10                       | -                      | -                  | -                 |
|       | 1  | 5  | 10 |
|-------|----|----|----|
| 4d    | -  | -  | -  |
| 5a    | -  | -  | -  |
| 5b    | 10 | 6  | 8  |
| 5c    | -  | 9  | 12 |
| 6c    | -  | 8  | 12 |
| 5f    | -  | 10 | 12 |
| 5g    | -  | 6  | -  |
| 5h    | -  | 10 | 12 |

- : No inhibition zone
Experimental

General

The melting points of synthesized compounds were determined on a Büchi 510 melting point apparatus and are uncorrected. The IR spectra were recorded in the 4000-400 cm\(^{-1}\) range using KBr disks on a Perkin-Elmer 297 Spectrophotometer. The \(^1\)H- and \(^{13}\)C-NMR spectra were recorded on a Bruker AC 250E spectrometer in DMSO-d\(_6\) with TMS as an internal standard. UV spectra were recorded on a Varian Cary 219 spectrophotometer.

Synthesis of derivatives

Synthesis of methyl/ethyl esters of substituted benzoic/phenylacetic acids (2a-f)

These were synthesized by esterification of 2-hydroxy-; 4-hydroxy-; 2-hydroxy-5-chloro-and 4-ethoxybenzoic and 4-hydroxy- and 4-ethoxyphenylacetic acids, respectively, using excess methanol/ethanol in the presence of H\(_2\)SO\(_4\) [24].

Synthesis of hydrazides of substituted benzoic and phenylacetic acids (3a-f)

These were prepared by reaction of the corresponding methyl/ethyl esters 2a-f with hydrazine hydrate following literature methods [17,18,19].

Synthesis of 1-substituted benzoyl/phenacetyl-4-allylthiosemicarbazides (4a-d)

A mixture of the corresponding compound 3a-f (0.01 mol) and allylisothiocyanate (0.01 mol) in ethanol (120 mL) was heated under reflux for 2-3 hours. The excess of ethanol was distilled off under reduced pressure. The white precipitate thus formed was washed with ethanol and recrystallised from ethanol.

4a: IR (cm\(^{-1}\)): 1630 (C=O), 1260 (C=S); \(^1\)H-NMR: 6.89-6.96 (2H, d, arom), 7.45 (1H, dd, J=1.5 and 7.0 Hz, arom), 7.86 (1H, dd, J=1.2 and 7.9 Hz, arom), 8.38, 9.53 and 10.60-11.96 (4H, s, OH and 3NH), 4.10 (2H, m, CH\(_2\)=CH-CH\(_2\)-), 5.05 and 5.14 (2H, dd, J=1.5 and 10.1 Hz, CH\(_2\)=CH-CH\(_2\)-), 5.83 (1H, m, CH\(_2\)=CH-CH\(_2\)-); \(^{13}\)C-NMR: 46.0 (CH\(_2\)), 115.3, 117.2, 118.8, 128.6, 134.1, 134.9, 150.7 (Cq, C-O), 159.5 (C=O), 181.6 (C=S).

4b: IR (cm\(^{-1}\)): 1600 (C=O), 1240 (C=S); \(^1\)H-NMR: 6.83 (2H, d, J=8.7 Hz, arom), 7.81 (2H, d, J=8.7 Hz, arom), 8.24, 9.30 and 10.03-10.13 (4H, OH and 3NH), 4.11 (2H, m, CH\(_2\)=CH-CH\(_2\)-), 5.03 and 5.13 (2H, dd, J=1.6 and 10.3 Hz, CH\(_2\)=CH-CH\(_2\)-), 5.82 (1H, m, CH\(_2\)=CH-CH\(_2\)-); \(^{13}\)C-NMR: 46.0 (CH\(_2\)), 115.0 (2 x C), 115.3, 123.3, 130.1 (2 x C), 135.2, 160.2, 160.9, 165.9.
**4c:** IR (cm⁻¹): 1650 (C=O), 1280 (C=S); ¹H-NMR: 6.96 (1H, d, J=8.8 Hz, arom), 7.49 (1H, dd, J=2.6 and 8.8 Hz, arom), 7.91 (1H, d, J=2.6 Hz, arom), 8.36, 9.55, 10.65 and 11.89 (4H, s, OH and 3NH), 4.09 (2H, m, CH₂=CH-CH₂-), 5.06 and 5.10 (1H, dd, J=1.8 and 10.3 Hz, CH₂=CH-CH₂-), 5.83 (1H, m, CH₂=CH-CH₂-); ¹³C-NMR 46.0 (CH₂), 115.4, 116.5, 119.1, 126.8, 128.1, 133.6, 138.4, 158.0 (qC, C=O), 181.5 (C=S).

**4d:** IR (cm⁻¹): 1660 (C=O), 1260 (C=S); ¹H-NMR 6.84 (2H, d, J=8.5 Hz, arom), 7.18 (2H, d, J=8.5 Hz, arom), 8.11, 9.27 and 9.92 (3H, s, NH), 4.10 (2H, m, CH₂=CH-CH₂-), 5.05 and 5.10 (1H, dd, J=1.5 and 10.3 Hz, CH₂=CH-CH₂-), 3.39 (2H, s, -CH₂-); ¹³C-NMR: 14.7 (CH₃), 39.4 (CH₂), 45.8 (CH₂), 62.9 (CH₂), 114.1 (2 x C), 115.2, 127.2, 130.3 (2 x C), 134.9, 157.2, 170.2 (C=O), 181.8 (C=S).

**Synthesis of 4-allyl-5-aryl-1,2,4-triazoles (5a-d)**

1-Substituted benzoyl/phenylacetyl-4-allylthiosemicarbazides (4a-d) (0.005 mol) were dissolved in 2M NaOH (15 mL) and the reaction mixture refluxed for 4 hours. After cooling, the solution was dissolved in ice-cold water and acidified with hydrochloric acid to pH 5-6. The solid was filtered, washed with cold water (to neutral pH), dried and recrystallised from the appropriate solvent.

**5a:** IR (cm⁻¹): 1485 (s, C=N), 1300 (s, C=S); ¹H-NMR: 6.90 (1H, td, J=7.3 Hz, arom), 6.99 (1H, dd, J=8.2 Hz, arom), 7.26 (1H, dd, J=1.8 and 8.2 Hz, arom), 7.38 (1H, td, J=1.8 and 7.3 Hz, arom), 10.38 (1H, s, OH), 13.91 (1H, s, NH), 4.54 (2H, d, J=5.2 Hz, CH₂=CH-CH₂-), 4.70 (1H, dd, J=1.5 and 17.1 Hz, CH₂=CH-CH₂-), 4.95 (1H, dd, J=1.5 and 10.1 Hz, CH₂=CH-CH₂-), 5.65 (1H, m, CH₂=CH-CH₂-); ¹³C-NMR: 45.6 (CH₂), 113.3, 116.0, 117.1, 119.3, 131.5, 132.5, 150.1, 155.7, 166.7 (C=S).

**5b:** IR (cm⁻¹): 1500 (s, C=N), 1320 (s, C=S); ¹H-NMR 6.87 (2H, d, J=8.5 Hz, arom), 7.44 (2H, d, J=8.5 Hz, arom), 10.13 (1H, s, OH), 13.81 (1H, s, NH), 4.62 (2H, d, J=3.4 Hz, CH₂=CH-CH₂-), 4.82 (1H, d, J=17.1 Hz, CH₂=CH-CH₂-), 5.09 (1H, d, J=10.4, CH₂=CH-CH₂-), 5.80 (1H, m, CH₂=CH-CH₂-); ¹³C-NMR 46.2 (CH₂), 116.0 (2 x C), 116.7, 117.4, 130.2 (2 x C), 132.1, 151.9, 160.7 (Cq, C=O), 167.4 (C=S).

**5c:** IR (cm⁻¹): 1500 (s, C=N), 1320 (s, C=S); ¹H-NMR 7.01 (1H, d, J=8.9 Hz, arom), 7.36 (1H, d, J=2.5 Hz, arom), 7.43 (1H, dd, J=2.5 and 8.6 Hz, arom), 10.72 (1H, s, OH), 13.98 (1H, s, NH), 4.55 (2H, d, J=5.2 Hz, CH₂=CH-CH₂-), 4.75 (1H, dd, J=1.2 and 17.1 Hz, CH₂=CH-CH₂-), 4.98 (1H, dd, J=1.2 and 10.38 Hz, CH₂=CH-CH₂-), 5.67 (1H, m, CH₂=CH-CH₂-); ¹³C-NMR 45.8 (CH₂), 114.9, 117.2, 117.8, 122.7, 130.7, 131.52, 132.2, 148.7, 154.9, 166.9 (C=S).

**5d:** IR (cm⁻¹): 1500 (s, C=N), 1310 (s, C=S); ¹H-NMR: 6.84 (2H, d, J=8.5 Hz, arom), 7.08 (2H, d, J=8.5 Hz, arom) 12.49 (1H, s, NH), 4.49 (2H, d, J=5.2 Hz, CH₂=CH-CH₂-), 5.06 (1H, d, J=17.09 Hz,
Molecules 2001, 6

\[ \text{CH}_2=\text{CH-CH}_2\), 5.22 (1H, dd, J=0.6 and 10.4 Hz, \text{CH}_2=\text{CH-CH}_2\), 5.76 (1H, m, \text{CH}_2=\text{CH-CH}_2\), 1.36 (3H, t, J=7.0 Hz, -OCH_2CH_3), 4.00 (2H, q, J=7.0 Hz, -OCH_2CH_3), 3.96 (2H, s, -CH_2-); \]^13C-NMR 14.7 (CH_3), 31.0 (CH_2), 45.7 (CH_2), 63.4 (CH_2), 114.9 (2 x C), 118.4, 125.0, 129.5 (2 x C), 130.2, 151.6, 158.3, 167.4 (C=S).

**Synthesis of potassium salts of substituted dithiocarbazinic acids (4e-f)**

A mixture of 3a-d (0.01 mol), CS\(_2\) (0.15 mol) and KOH (0.15 mol) in absolute ethanol (350 mL) was heated under the reflux for 10 hours, cooled to room temperature and diluted with dry ether (200 mL). The precipitate that appeared was filtered, washed with 2 x 50mL of ether and vacuum dried at 65°C.

**Synthesis of 4-amino-5-aryl-1,2,4-triazoles (5e-h)**

To a suspension of 4e-h (0.002 mol), hydrazine hydrate (0.04 mol) and water (4 mL) were added and the mixture was refluxed with stirring for several hours, until the evolution of hydrogen sulfide had ceased. After dilution with water (100 mL) and acidification with HCl, the precipitates were filtered, washed with 2 x 30 mL of water and recrystallised from ethanol-water.

5e: IR (cm\(^{-1}\)): 3271-3172 (O-H) and (s, NH), 3028 (s, C-H, Ar-H), 1618(s, C-C, Ar-H), 1583 (s, C=N), 1534 (δ, N-H), 1249 (C=S) cm\(^{-1}\); UV 218, 252, 290 nm

5f: IR (cm\(^{-1}\)): 3306-3173 (O-H) and (s, NH), 3025-2955 (s, C-H, Ar-H), 1615 (s, C-C, Ar-H), 1514 (s, C=N), 1480 (δ, N-H), 1266 (C=S) cm\(^{-1}\); UV: 216-218, 252, 288-298 nm;

5g: IR (cm\(^{-1}\)): 3287-3152 (O-H) and (s, NH), 3103-3046 (s, C-H, Ar-H), 2938(s, C-H, CH_2-), 1626-1599 (s, C-C, Ar-H), 1569 (s, C=N), 1497(δ, N-H), 1228 (C=S) cm\(^{-1}\); UV 228, 254 nm.

5h: IR (cm\(^{-1}\)): 3282-3171 (O-H) and (s, NH), 3048(s, C-H, Ar-H), 2972-2788 (s, C-H, CH_2-), 1619 (s, C-C, Ar-H), 1514 (s, C=N), 1260 (C=S) cm\(^{-1}\); UV 228, 256 nm.

**Microbiology**

The filter paper disc method [14,20] was performed using Sabouraud dextrose broth and Mueller Hinton broth. These agar media were inoculated with 0.5 mL of the 24 h liquid cultures containing 10\(^7\) microorganisms/mL. Filter paper discs (5 mm diameter) saturated with solutions of each compound (concentrations: 1mg/mL; 5mg/mL and 10mg/mL DMSO) were placed on the indicated agar mediums. The incubation time was 24h at 37°C for bacterial and 48h at 30°C for Candida species. Discs with only DMSO were used as control. Inhibitory activity was measured (in mm) as the diameter of the observed inhibition zones. The tests were repeated to confirm the findings and the average of the readings was taken into consideration.
References

1. Jones, D.H.; Slack, R.; Squires, S.; Woolridge, K.R.H.; J. Med. Chem., 1965, 8, 676.
2. Goswami, B.N.; Kataky, J.C.S.; Baruah, J.N.; J. Heterocyclic Chem., 1984, 21, 225.
3. Holla, B.S.; Kalluraya, B.; Sridhar, K.R.; Curr. Sci., 1987, 56, 236.
4. Abdon, N.A.; Amin, F.M.; Mansoura, A. J. Pharm. Sci., 1990, 6, 25.
5. Mishra, R.K.; Tewari, R.K.; Srivastava, S.K.; Bahel, S.C.; J. Indian Chem. Soc., 1991, 68, 110.
6. Galabov, A.S.; Galabov, B.S.; Neykova, N.A.; J. Med. Chem., 1980, 23, 1048.
7. Hazzaa, A.A.B.; Labouta, I.M.; Kassem, M.G.; Arch. Pharm. Chem. Sci. Ed., 1983, 11, 43.
8. Rollas, S.; Büyüktimkin, S.; Çevikbas, A.; Arch. Pharm. (Weinheim), 1991, 324, 189.
9. Hoggart, E.; J. Chem. Soc., 1949, 1163.
10. Parmar, S.; Gupta, A.K.; Singh, H.H.; Gupta, T.K.; J. Med. Chem., 1972, 15, 999.
11. Coburn, R.A.; Bhooshan, B.; Gellennon, R.A.; J. Org. Chem., 1973, 38, 3947.
12. Mohsen, A.; Omar, M.E.; Osman, S.A.; Pharmazie, 1973, 28, 30.
13. Ergeuc, N.; Ilhan, E.; Ötük, G.; Pharmazie, 1992, 47, 59.
14. Rollas, S.; Kalyoncuoglu, N.; Sür-Altiner, D.; Yegenoglu, Y.; Pharmazie, 1993, 48, 308.
15. Kubata, S.; Uda, M.; Chem. Pharm. Bull., 1972, 20, 2096.
16. Kubata, S.; Uda, M.; Chem. Pharm. Bull., 1973, 21, 1342.
17. Smith, P.A.S., Org. Reactions, 1966, 3, 366.
18. Browne, E.J; Polya, J.B., J. Chem. Soc., 1962, 5149.
19. Nicolaides, E.D., J. Org. Chem., 1967, 32, 1251.
20. Bauer, A.W.; Kirby, W.W.M.; Sherris, J. C.; Turck, M., Am. J. Clin. Pathol., 1966, 45, 493.
21. Strzembecka, L. Pol. J. Chem., 1983, 57, 567.
22. Sengupta, S.K.; Sahni, S.K.; Kapoor, R.N.; J. Indian Chem. Sect. A, 1980, 19,7, 703.
23. Sengupta, S.K.; Sahni, S.K.; Kapoor, R.N.; J. Indian Chem. Sect. A, 1981, 20, 692.
24. Vogel, A.I.; A Textbook of Practical Organic Chemistry, 3rd Edition, Longmans: London, 1956, 1000.

Sample Availability: Available from the authors.

© 2001 by MDPI (http://www.mdpi.org). Reproduction is permitted for noncommercial purposes.