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

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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, ^{1}H- NMR, ^{13}C-NMR and UV spectral data together with elemental analysis.

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

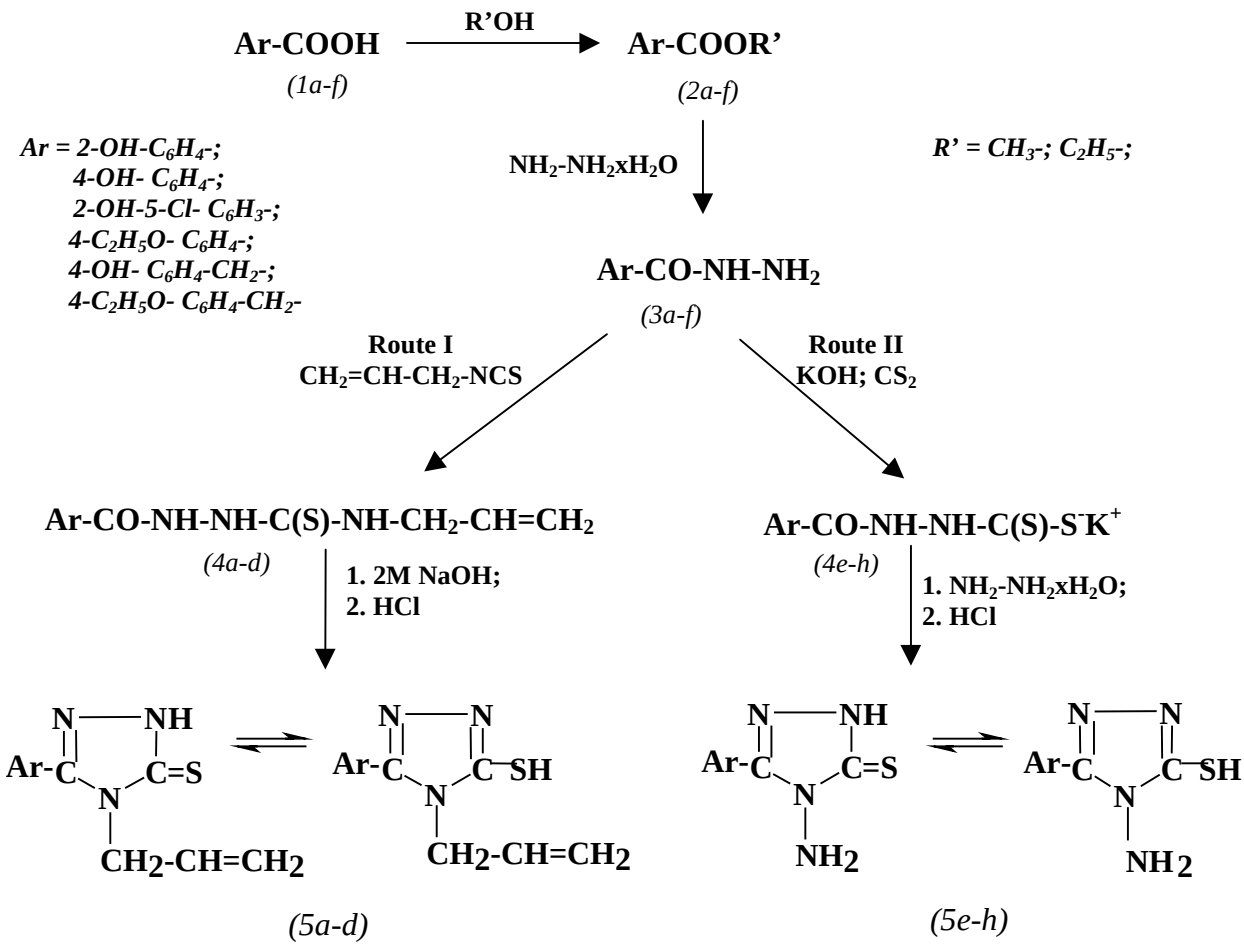
Introduction

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 **-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).

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 ^{0}C	Yield %	Elemental analysis calc./found C	H	N
4a	2-OH-C_6H_4-	$C_{11}H_{13}N_3O_2S$ (251.311)	198-9	84.39	52.57 52.40	5.21 5.25	16.72 16.69
4b	4-OH-C_6H_4-	$C_{11}H_{13}N_3O_2S$ (251.311)	194-6	84.76	52.57 52.51	5.21 5.19	16.72 16.75
4c	2-OH-5-Cl-C_6H_3-	$C_{11}H_{12}N_3O_2ClS$ (285.755)	188-90	92.53	45.92 45.99	4.59 5.06	14.71 14.64
4d	4-C_2H_5O-C_6H_4-CH_2-	$C_{14}H_{19}N_3O_2S$ (293.389)	180-2	82	57.31 57.41	6.53 6.49	14.32 14.44
5a*	2-OH-C_6H_4-	$C_{11}H_{11}N_3OS$ (233.293)	203-5	89.59	56.63 56.03	4.75 4.90	18.01 17.95
5b	4-OH-C_6H_4-	$C_{11}H_{11}N_3OS$ (233.293)	176-8	93.54	56.63 56.85	4.75 4.98	18.01 18.32
5c	2-OH-5-Cl-C_6H_4-	$C_{11}H_{10}N_3OClS$ (267.738)	142 - 4	67.62	49.35 49.27	3.76 3.55	15.69 15.58
5d	4-C_2H_5O-C_6H_4-CH_2-	$C_{14}H_{17}N_3OS$ (275.374)	125 - 7	90	61.06 61.12	6.22 6.10	15.26 15.31
5e**	2-OH-C_6H_4-	$C_8H_8N_4OS$ 208.17	202-3	71.6	46.14 45.96	3.89 4.29	26.90 26.39
5f	4-OH-C_6H_4-	$C_8H_8N_4OS$ 208.17	217	81.5	46.14 46.96	3.89 4.09	26.90 26.59
5g	4-OH-C_6H_4-CH_2-	$C_9H_{10}N_4OS$ 222.18	203-4	13.87	48.63 49.14	4.35 5.02	25.20 24.84
5h	4-C_2H_5O-C_6H_4-CH_2-	$C_{11}H_{14}N_4OS$ 250.22	101-3	64.9	52.98 52.91	5.61 5.87	22.29 21.99

The structures of compounds **4a-d** were established by their IR, ^{1}H-NMR and ^{13}C-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 ^{1}H-NMR spectra of compounds **4a-d** (in DMSO-d$_6$) exhibited a multiplet in the aromatic region at 6.83-7.91 ppm corresponding to the H_{arom} 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 ^{1}H-NMR spectra of **4a-d** also exhibited the CH_2- and –CH- signals of the allyl group as multiplets and doublets between 4.09 and 5.83 ppm. The ^{13}C-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 ^{1}H-NMR spectra of **5a-d** (DMSO-d$_6$) 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 CH_2- and –CH- signals of the allyl groups as multiplets and doublets between 4.49 and 5.80 ppm. The ^{13}C-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 3306-3152cm^{-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*, *Salmonela 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*	*Staphilococcus aureus*	*Aspergillus niger*	*Candida albicans*
4a	***1***	**-**	**-**	**-**	**-**	**-**	**-**
	5	**5.5**	**-**	**-**	**5.5**	**-**	**5.5**
	10	**6**	**-**	**-**	**6**	**5.5**	**5.5**
4b	***1***	**-**	**-**	**-**	**-**	**-**	**-**
	5	**-**	**-**	**-**	**-**	**-**	**-**
	10	**-**	**-**	**-**	**-**	**-**	**-**
4c	***1***	**6**	**-**	**-**	**5.5**	**-**	**-**
	5	**6**	**-**	**-**	**10**	**-**	**-**
	10	**9**	**-**	**-**	**10**	**-**	**-**

4d	***1***	**-**	**-**	**-**	**-**	**-**	**-**
	5	**-**	**-**	**-**	**-**	**-**	**-**
	10	**-**	**-**	**-**	**-**	**-**	**-**
5a	***1***	**-**	**-**	**-**	**-**	**-**	**-**
	5	**-**	**-**	**-**	**-**	**-**	**-**
	10	**-**	**-**	**-**	**-**	**-**	**-**
5b	***1***	**6**	**-**	**-**	**-**	**-**	**-**
	5	**6**	**5.5**	**-**	**7**	**-**	**-**
	10	**6**	**8**	**-**	**8**	**-**	**5.5**
5c	***1***	**-**	**5.5**	**-**	**-**	**-**	**5.5**
	5	**-**	**6**	**-**	**6**	**-**	**5.5**
	10	**-**	**9**	**-**	**12**	**5.5**	**5.5**
5d	***1***	**-**	**-**	**-**	**-**	**-**	**-**
	5	**-**	**-**	**-**	**-**	**-**	**-**
	10	**-**	**-**	**-**	**-**	**-**	**-**
5e	***1***	**6**	**6**	**8**	**8**	**-**	**-**
	5	**6**	**7**	**10**	**10**	**-**	**-**
	10	**6.5**	**10**	**12**	**23**	**-**	**-**
5f	***1***	**8**	**7**	**10**	**12**	**-**	**-**
	5	**8**	**10**	**12**	**25**	**-**	**-**
	10	**10**	**11**	**14**	**28**	**-**	**-**
5g	***1***	**6**	**6**	**-**	**6**	**-**	**-**
	5	**7**	**6**	**-**	**12**	**-**	**-**
	10	**8**	**7**	**-**	**12**	**-**	**-**
5h	***1***	**10**	**6**	**8**	**12**	**-**	**-**
	5	**10**	**6**	**9**	**16**	**-**	**-**
	10	**10**	**7**	**9**	**22**	**-**	**7**

- : 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_2SO_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-$\underline{CH_2}$-), 5.05 and 5.14 (2H, dd, J=1.5 and 10.1 Hz, $\underline{CH_2}$=CH-CH_2-), 5.83 (1H, m, CH_2=$\underline{CH}$-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-$\underline{CH_2}$-), 5.03 and 5.13 (2H, dd, J=1.6 and 10.3 Hz, $\underline{CH_2}$=CH-CH_2-), 5.82 (1H, m, CH_2=$\underline{CH}$-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); ^{1}H-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, CH_2=CH-$\underline{CH_2}$-), 5.06 and 5.10 (1H, dd, J=1.8 and 10.3 Hz, $\underline{CH_2}$=CH-CH_2-), 5.83 (1H, m, CH_2=$\underline{CH}$-CH_2-); ^{13}C-NMR 46.0 (CH_2), 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); ^{1}H-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, CH_2=CH-$\underline{CH_2}$-), 5.05 and 5.10 (1H, dd, J=1.5 and 10.3 Hz, $\underline{CH_2}$=CH-CH_2-), 5.82 (1H, m, CH_2=$\underline{CH}$-CH_2), 1.31 (3H, t, J=7.0 Hz, -$OCH_2\underline{CH_3}$), 3.98 (2H, q, J=7.0 Hz, -O$\underline{CH_2}CH_3$), 3.39 (2H, s, -CH_2-); ^{13}C-NMR: 14.7 (CH_3), 39.4 (CH_2), 45.8 (CH_2), 62.9 (CH_2), 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); ^{1}H-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, CH_2=CH-$\underline{CH_2}$-), 4.70 (1H, dd, J=1.5 and 17.1 Hz, $\underline{CH_2}$=CH-CH_2-), 4.95 (1H, dd, J=1.5 and 10.1 Hz, $\underline{CH_2}$=CH-CH_2-), 5.65 (1H, m, CH_2=$\underline{CH}$-CH_2-); ^{13}C-NMR: 45.6 (CH_2), 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); ^{1}H-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, CH_2=CH-$\underline{CH_2}$-), 4.82 (1H, d, J=17.1 Hz, $\underline{CH_2}$=CH-CH_2-), 5.09 (1H, d, J=10.4, $\underline{CH_2}$=CH-CH_2-), 5.80 (1H, m, CH_2=$\underline{CH}$-CH_2-); ^{13}C-NMR 46.2 (CH_2), 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); ^{1}H-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, CH_2=CH-$\underline{CH_2}$-), 4.75 (1H, dd, J= 1.2 and 17.1 Hz, $\underline{CH_2}$=CH-CH_2), 4.98 (1H, dd, J=1.2 and 10.38 Hz, $\underline{CH_2}$=CH-CH_2-), 5.67 (1H, m, CH_2=$\underline{CH}$-CH_2-); ^{13}C-NMR 45.8 (CH_2), 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); ^{1}H-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, CH_2=CH-$\underline{CH_2}$-), 5.06 (1H, d, J=17.09 Hz,

$\underline{CH_2}$=CH-CH_2-), 5.22 (1H, dd, J=0.6 and 10.4 Hz, $\underline{CH_2}$=CH-CH_2-), 5.76 (1H, m, CH_2=$\underline{CH}$-CH_2-), 1.36 (3H, t, J=7.0 Hz, -$OCH_2\underline{CH_3}$), 4.00 (2H, q, J=7.0 Hz, -$O\underline{CH_2}CH_3$), 3.96 (2H, s, -CH_2-); ^{13}C-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.

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Sample Availability: Available from the authors.