

## SYNTHESIS AND REACTIONS OF 3-(3'-THIONE)-1',2',4'-TRIAZOL-5'-YLCOUMARIN

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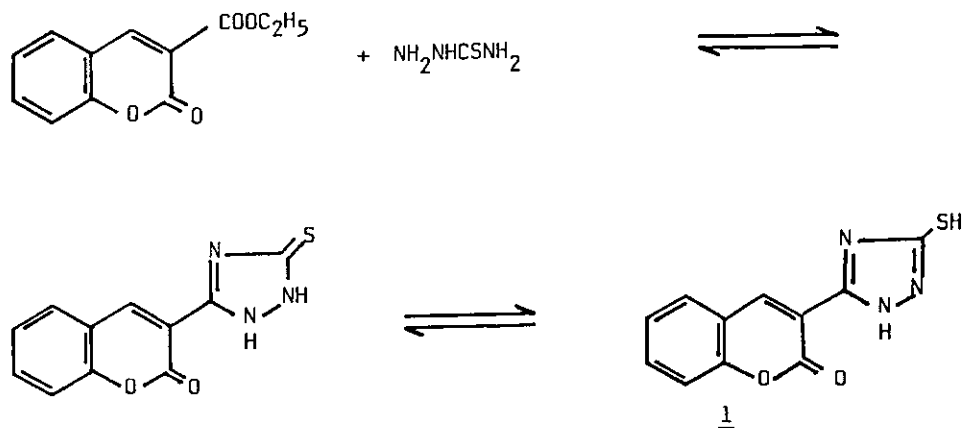
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**Abstract** — 3-(3'-Thione)-1',2',4'-triazol-5'-ylcoumarin (1) was prepared via condensation of 3-ethoxycarbonylcoumarin with thiosemicarbazide in boiling pyridine. The reaction of coumarin (1) with primary amines and hydrazines takes place by nucleophilic attack on the thione group to give 3-(3'-amino)-1',2',4'-triazol-5'-ylcoumarins (2a or 2b) and 3-(3'-hydrazinyl)-1',2',4'-triazol-5'-ylcoumarins (2c-d). Condensation of 2c with aromatic aldehydes gave the corresponding 3-(3'-arylidenehydrazonyl)-1',2',4'-triazol-5'-ylcoumarins (3a-g). Alkylation of coumarin (1) with methyl iodide and ethyl chloroacetate gave 3-(1'-methyl-3'-methylthio)-1',2',4'-triazol-5'-ylcoumarin (8) and 3-(3'-ethoxycarbonylmethylthio)-1',2',4'-triazol-5'-ylcoumarin (9) respectively. Addition of compound (1) to acrylonitrile or methyl vinyl ketone under Michael addition conditions afforded the 3-[3'-(2''-cyanoethylthio)]-1',2',4'-triazol-5'-ylcoumarin (11a) and 3[3'-(3-oxobutylthio)]-1',2',4'-triazol-5'-ylcoumarin (11b) and addition of (1) to Schiff bases afforded 3-[3'-( $\alpha$ -arylaminobenzylthio)]-1',2',4'-triazol-5'-ylcoumarins (12a-c). The antibacterial and antifungal activities of some compounds have been described.

**Introduction**

As extension of our studies on coumarin derivatives,<sup>1,4</sup> we intended to prepare 3-(3'-thione)-1',2',4'-triazol-5'-ylcoumarin in order to establish the reactivity of the carbonyl groups of the  $\alpha$ -pyrone and the thione group of the triazole rings toward some nitrogen nucleophiles, carbon nucleophiles and carbon electrophiles. The 3-(3'-thione)-1',2',4'-triazol-5'-ylcoumarin (1) was prepared by condensation of 3-ethoxycarbonylcoumarin with thiosemicarbazide in boiling pyridine. The formation of 1 may proceed by the initial nucleophilic attack of the amino group to the ester carbonyl without attack at the carbonyl

of the  $\alpha$ -pyrone ring followed by cyclization as shown in Scheme 1.

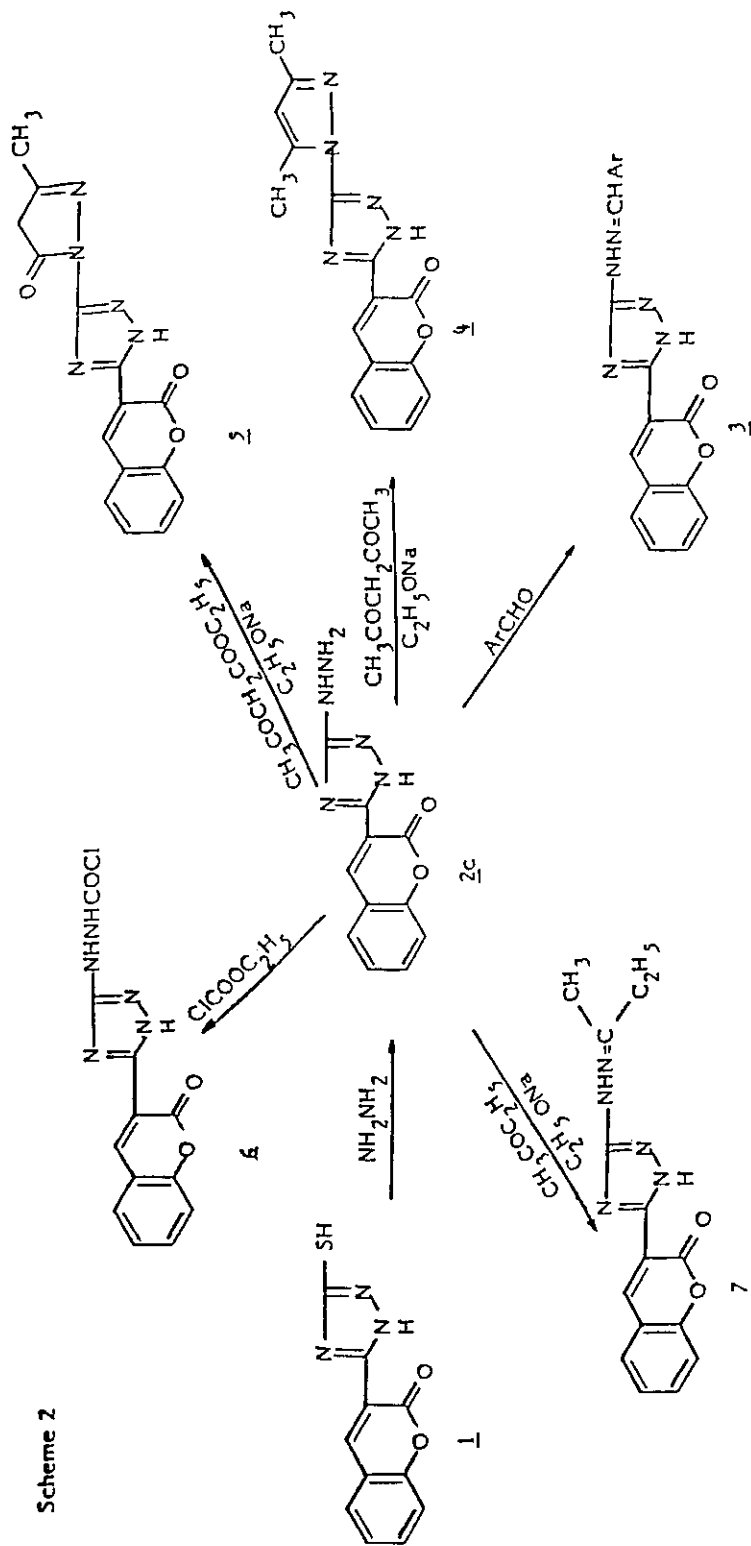


Scheme 1

It has been reported<sup>5,6</sup> that the  $\alpha,\beta$ -unsaturated  $\alpha$ -pyrone ring in coumarin derivatives had not been opened by primary amines, while the action of hydrazines caused the heterocyclic ring opening of coumarin.<sup>7</sup> The reaction of compound (1) with primary amine namely, benzylamine or 2,5-dimethylaniline in boiling ethanol gave the 3-(3'-amino)-1',2',4'-triazol-5'-ylcoumarins (2a or 2b). Also, the reaction of 1 with hydrazine hydrate or phenylhydrazine gave the corresponding 3-(3'-hydrazinyl)-1',2',4'-triazol-5'-ylcoumarins (2c-d). The formation of 2 proceeds by the nucleophilic attack at the thione group only. The condensation of 2c with aromatic aldehydes namely, benzaldehyde, anisaldehyde, *p*-chlorobenzaldehyde, *p*-nitrobenzaldehyde, *p*-hydroxybenzaldehyde, *m*-hydroxybenzaldehyde and *p*-*N,N*-dimethylaminobenzaldehyde yielded the corresponding 3-(3'-arylidenehydrazonyl)-1',2',4'-triazol-5'-ylcoumarins (3a-g).

The reaction of 2c with acetylacetone or ethyl acetoacetate in boiling ethanol gave 3-[3'-(3'',5''-dimethyl- or 3''-methyl-5''-oxopyrazol-5'-yl)]-1',2',4'-triazol-5'-ylcoumarin (4) or (5) respectively.

The behaviour of 2c as a nucleophile was further established by condensation with ethyl chloroformate or ethyl ketone in refluxing ethanol to afford the corresponding products (6), (7) respectively (cf. Scheme 2).



- a, Ar = C<sub>6</sub>H<sub>5</sub>
- b, Ar = C<sub>6</sub>H<sub>4</sub>-OCH<sub>3</sub>-4
- c, Ar = C<sub>6</sub>H<sub>4</sub>-Cl-4
- d, Ar = C<sub>6</sub>H<sub>4</sub>-NO<sub>2</sub>-4
- e, Ar = C<sub>6</sub>H<sub>4</sub>-OH-4
- f, Ar = C<sub>6</sub>H<sub>4</sub>-OH-3
- g, Ar = C<sub>6</sub>H<sub>4</sub>-N(CH<sub>3</sub>)<sub>2</sub>-4

Scheme 2

The alkylation of 1 with methyl iodide in ethanolic sodium hydroxide gave 3-(1'-methyl-3'-methylthio)-1',2',4'-triazol-5'-ylcoumarin (8), on the other hand, alkylation of 1 with ethyl chloroacetate and anhydrous potassium carbonate in dry acetone occurred at the thione group only and not at the NH group of the cyclic system to give 3-(3'-ethoxycarbonylmethylthio)-1',2',4'-triazol-5'-ylcoumarin (9). The structure of 9 was established from the condensation of 9 with aniline yielded (10) (Scheme 3).

The presence of thione-thiol equilibrium in compound (1) promoted us to study the behaviour of the active thiol group towards activated olefinic bond such as acrylonitrile or methyl vinyl ketone in the presence of anhydrous potassium carbonate under Michael reaction condition to give 3-[3'-(2''-cyanoethylthio)]-1',2',4'-triazol-5'-ylcoumarin (11a) and 3-[3'-(3-oxobutylthio)]-1',2',4'-triazol-5'-ylcoumarin (11b). Also, the addition of compound (1) to Schiff bases in the presence of sodium ethoxide gave the corresponding 3-[3'-( $\alpha$ -arylamino benzylthio)]-1',2',4'-triazol-5'-ylcoumarins (12a-c).

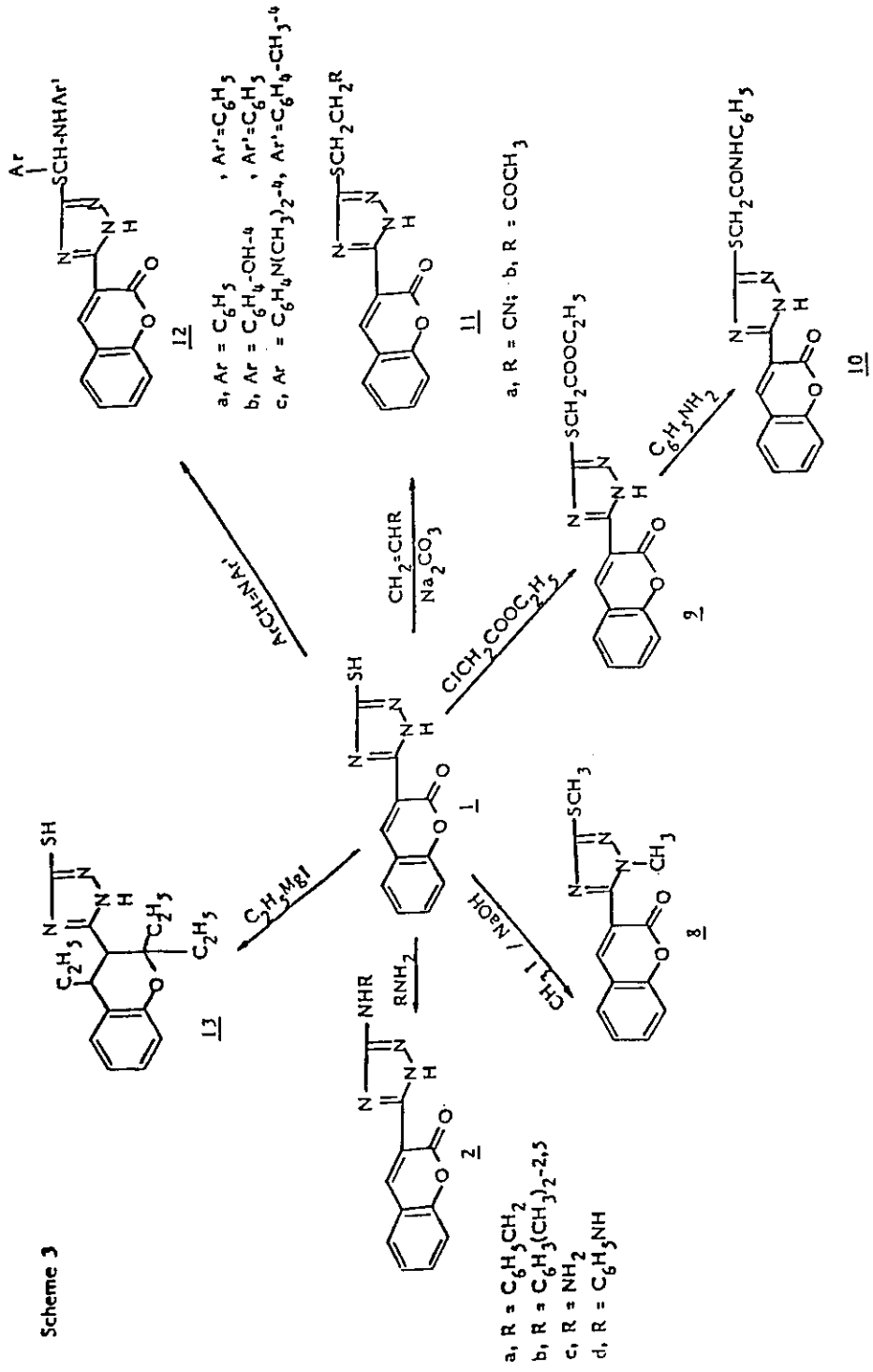
We also investigated<sup>7</sup> the behaviour of compound (1) toward ethylmagnesium iodide under Gerignard reaction conditions to give 3-(3'-thiol-1',2',4'-triazol-5'-yl)-2,2,4-triethylchroman (13) (cf. Scheme 3). Although the stereochemistry of compound (13) reveals four stereoisomers, but all chemical and physical methods for isolation of these isomers has been failed.

#### Antimicrobial Activity

Antibacterial activity was determined by the following agar-diffusion technique<sup>8</sup> against E. coli, P. aeruginosa and S. aureas. Compounds (1), (2c), (3b), (3c), (3q), (5), (8) and (12c) showed 80% activity at 500 ppm concentration level. Also, antifungal activity against A. niger, P. digitatum and T. viride using agar-plate diffusion technique<sup>9</sup> in 5% DMF and acetone has been screened. Most of the screened compounds showed about 65% inhibition at the concentration of 500 ppm. Compounds (1), (4), (6), (8), (11) and (13) showed more than 75% inhibition at lower concentration (250 ppm) see Table 2.

#### EXPERIMENTAL

Melting points are uncorrected. Ir spectra (KBr) were measured on a Perkin-Elmer infra-cord 137 spectrophotometer. The <sup>1</sup>H-nmr spectra were recorded of 60 MHz on a Varian EM-360-L spectrometer using TMS as internal standard.



### Formation of 3-(3'-thione)-1',2',4'-triazol-5'-ylcoumarin (1)

A mixture of 3-ethoxycarbonylcoumarin (2.17 g, 0.01 mol) and thiosemicarbazide (0.01 mol) in 30 ml of pyridine was refluxed for 5 h. The solution was poured into ice/10% HCl, then the solid separated was filtered, dried and recrystallized from acetic acid to give (1.6 g, 65%) of coumarin (1). Ir: 3180 - 3285 ( $\nu$ NH), 1690 ( $\nu$ C=O), 1630 ( $\nu$ C=N), 1620 ( $\nu$ C=C) and 1180  $\text{cm}^{-1}$  ( $\nu$ C=S).  $^1\text{H-Nmr}$  (DMSO- $d_6$ ):  $\delta$  6.8 - 8.8 (m, 5H, ArH + 1H olefinic), 9.6 (br, 1H of SH ratio 44.6) and 10.2, 11.4 (br, 2H of NH and NHC=S ratio 55.4, 44.6).

### Reaction of compound (1) with primary amines and hydrazines: Formation of 3-(3'-substituted) 1',2',4'-triazol-5'-ylcoumarins (2a-d)

A solution of compound (1) (2.46 g, 0.01 mol) and benzylamine, 2,5-dimethylaniline, hydrazine hydrate or phenylhydrazine (0.01 mol) in ethanol (50 ml) was refluxed for 5 h. The hot reaction mixture was filtered off then cooled. The solid separated was filtered, dried and recrystallized from ethanol to give (2a-d). Ir (2a-d) 1690 - 1695 ( $\nu$ CO), 1610 ~ 1615 ( $\nu$ C=N) and 3180 - 3370  $\text{cm}^{-1}$  ( $\nu$ NH).  $^1\text{H-Nmr}$  (2a) (DMSO- $d_6$ ):  $\delta$  3.2 (s, 2H,  $\text{CH}_2$ -Ph), 4.3 (s, 1H, NH), 7.2 - 8.6 (m, 10H, Ar-H and cyclic CH=C) and 10.6 (br, 1H, NH cyclic);  $^1\text{H-nmr}$  of 2b ( $\text{CDCl}_3$ ):  $\delta$  2.2, 2.4 (2xs, 6H, 2x $\text{CH}_3$ ), 4.7 (br, 1H, NH), 6.8 - 7.6 (m, 8H, ArH and cyclic CH=C) and 10.5 (br, 1H, cyclic NH);  $^1\text{H-nmr}$  of 2c ( $\text{CDCl}_3$ ):  $\delta$  4.2-5.0 (br, m, 3H,  $\text{NHNH}_2$ ), 6.6-7.5 (m, 5H, ArH and cyclic CH=C) and 10.6 (br, 1H, cyclic NH);  $^1\text{H-nmr}$  of 2d ( $\text{CDCl}_3$ ):  $\delta$  5.3 (br, 2H, NH-NH), 6.6 - 7.2 (m, 10H, ArH and cyclic CH=C) and 10.7 (br, 1H, cyclic NH).

### Condensation of compound (2c) with aromatic aldehydes: Formation of 3-(3'-N-arylidenehydrazonyl)-1',2',4'-triazol-5'-ylcoumarins (3a-g)

A mixture of 2c (2.43 g, 0.01 mol) and benzaldehyde, anisaldehyde, *p*-chlorobenzaldehyde, *p*-nitrobenzaldehyde, *p*-hydroxybenzaldehyde, *m*-hydroxybenzaldehyde or *p*-*N,N*-dimethylamino-benzaldehyde (0.01 mol) in ethanol (30 ml) was refluxed for 5 h. The hot reaction mixture was filtered off and then cooled in an ice-bath. The solid separated was filtered off, dried and crystallized from ethanol to give 3a-g. Ir (3a-g) 3300 - 3250 ( $\nu$ NH), 1695-1685 ( $\nu$ CO), 1625 - 1615  $\text{cm}^{-1}$  ( $\nu$ C=N).  $^1\text{H-Nmr}$  of 3a (DMSO- $d_6$ ):  $\delta$  6.4 - 8.8 (m, 11H, ArH and 2H, C=CH) and 10.7 (br, 1H, NH cyclic);  $^1\text{H-nmr}$  of 3b ( $\text{CDCl}_3$ ):  $\delta$  3.6 (s, 3H,  $\text{OCH}_3$ ), 6.4 - 8.3 (m, 11H, ArH, 2xCH= and NH) and 10.7 (br, 1H, cyclic NH);  $^1\text{H-nmr}$  of 3c ( $\text{CDCl}_3$ ):

$\delta$  6,5 - 8.2 (m, 11H, ArH, 2CH= and NH) and 10.7 (br, s, 1H, cyclic NH);  $^1\text{H-nmr}$  of 3d ( $\text{CDCl}_3$ ) :  $\delta$  7.1 - 8.9 (m, 11H, ArH, 2xCH= and NH) and 10.7 (br, s, 1H, cyclic NH);  $^1\text{H-nmr}$  of 3e ( $\text{CDCl}_3$ ) :  $\delta$  4.3 (s, 1H, OH), 6.6 - 8.4 (m, 11H, ArH, 2xCH= and NH) and 10.7 (br, s, 1H, NH cyclic);  $^1\text{H-nmr}$  of 3f ( $\text{CDCl}_3$ ) :  $\delta$  4.3 (s, 1H, OH), 6.4 - 8.2 (m, 11H, ArH, 2H, CH= and 1H, NH) and 10.7 (br, s, 1H, cyclic NH);  $^1\text{H-nmr}$  of 3g ( $\text{CDCl}_3$ ) :  $\delta$  3.2 - 3.4 [2xs, 6H,  $\text{N}(\text{CH}_3)_2$ ], 6.3 - 8.3 (m, 11H, ArH, 2xCH= and NH) and 10.6 (br, s, 1H, cyclic NH).

**Condensation of compound (2c) with acetylacetone, ethyl acetoacetate, ethyl chloroformate and ethyl methyl ketone : Formation of 4, 5, 6 and 7**

A solution of compound (2c) (2.43 g, 0.01 mol) and acetylacetone, ethyl acetoacetate, ethyl chloroformate or ethyl methyl ketone (0.01 mol) in ethanol (30 ml) was heated under reflux 5 h. The hot reaction mixture was filtered, then cooled. The solid separated was filtered, dried and recrystallized from ethanol. 4 : Ir : 1620 ( $\nu\text{C=N}$ ), 1640 ( $\nu\text{CO}$ ) and 3200  $\text{cm}^{-1}$  ( $\nu\text{NH}$ ).  $^1\text{H-Nmr}$  ( $\text{CDCl}_3$ ) :  $\delta$  2.3 - 2.5 (2xs, 6H,  $2\text{CH}_3$ ), 6.7 - 8.1 (m, 6H, ArH, C=CH) and 10.8 (br, 1H, NH). 5 : Ir : 1650 ( $\nu\text{CO}$ ) and 1630  $\text{cm}^{-1}$  ( $\nu\text{C=N}$ ).  $^1\text{H-Nmr}$  ( $\text{CDCl}_3$ ) :  $\delta$  2.3 (s, 3H,  $\text{CH}_3$ ), 6.8 - 8.3 (m, 5H, ArH and C=CH) and 10.7 (br, 1H, cyclic NH). Ir (6 and 7) 1690 ( $\nu\text{CO}$ ), 1625 ( $\nu\text{C=N}$ ) and 3250 - 3300  $\text{cm}^{-1}$  ( $\nu\text{NH}$ ).  $^1\text{H-Nmr}$  of 6 ( $\text{CDCl}_3$ ) :  $\delta$  5.4 (br, 2H, NH-NH), 6.7 - 8.1 (m, 5H, ArH and C=CH) and 10.6 (br, 1H, cyclic NH);  $^1\text{H-nmr}$  of 7 ( $\text{CDCl}_3$ ) :  $\delta$  1.2 (t,  $J=7$  Hz, 3H,  $\text{CH}_2\text{-CH}_3$ ), 1.7 (s, 3H,  $\text{CH}_3$ ), 2.0 (q,  $J=7$  Hz,  $\text{CH}_2\text{CH}_3$ ), 6.6 - 8.1 (m, 5H, ArH, CH=C) and 10.4 (br, 1H, cyclic NH).

**Alkylation of compound (1) with methyl iodide : Formation of 8**

A mixture of compound (1) (2.46 g, 0.01 mol) and methyl iodide (1.42 g, 0.01 mol) in ethanol (10 ml) was refluxed for 15 h together with aqueous NaOH (10 ml, 20%). The reaction mixture was cooled, neutralized with ice/10% HCl and extracted with ether. The solid produced after evaporation of ether was crystallized from ethanol to give 8. Ir : 1630 ( $\nu\text{C=N}$ ) and 1730  $\text{cm}^{-1}$  ( $\nu\text{C=O}$ ).  $^1\text{H-Nmr}$  ( $\text{CDCl}_3$ ) :  $\delta$  3.0 (s, 3H, S- $\text{CH}_3$ ), 6.4 - 8.2 (m, 5H, ArH and C=CH) and 10.4 (br, 1H, cyclic NH).

**Alkylation of compound (1) with ethyl chloroacetate : Formation of 9**

A mixture of compound (1) (2.46 g, 0.01 mol), ethyl chloroacetate (1.23 g, 0.01 mol) and potassium carbonate (5.52 g, 0.04 mol) in dry acetone (30 ml) was heated under reflux for 15 h. After evaporation of excess solvent, the reaction product was poured into

ice/10% HCl, filtered, dried and crystallized from ethanol to give 9. Ir : broad 1710-1740 ( $\nu\text{CO}$ ), 1620 ( $\nu\text{C=N}$ ) and broad 3160 - 3300  $\text{cm}^{-1}$  ( $\nu\text{NH}$ ).  $^1\text{H-Nmr}$  ( $\text{CDCl}_3$ ) :  $\delta$  2.2 (s, 2H,  $\text{CH}_2\text{COO}$ ), 3.5 (t,  $J=7$  Hz, 3H,  $\text{CH}_2\text{CH}_3$ ), 4.1 (q,  $J=7$  Hz, 2H,  $\text{CH}_2\text{CH}_3$ ), 6.6 - 8.3 (m, 5H, ArH and C=CH) and 10.2 (br, 1H, cyclic NH).

**Condensation of compound (9) with aniline : Formation of compound (10)**

A mixture of compound (9) (3.31 g, 0.01 mol) and aniline (0.93 g, 0.01 mol) was dissolved in ethanol (30 ml). The mixture was heated for 5 h, cooled, poured into ice/10% HCl and the solid separated was crystallized from ethanol to give (1.5 g, 50%) of 10.  $^1\text{H-Nmr}$  ( $\text{DMSO-d}_6$ ) :  $\delta$  2.7 (s, 2H,  $\text{CH}_2\text{-S}$ ), 6.8 - 8.0 (m, 10H, ArH and cyclic CH=C), 9.2 (br, 1H, NH-Ph) and 10.8 (br, 1H, cyclic NH).

**Reaction of compound (1) with acrylonitrile or methyl vinyl ketone : Formation of 11a, b**

A mixture of compound (1) (2.46 g, 0.01 mol) and acrylonitrile or methyl vinyl ketone (0.01 mol) dissolved in ethanol (30 ml) and anhydrous sodium carbonate (2.12 g, 0.02 mol) was heated for 5 h. The reaction mixture was poured into ice/10% HCl mixture and the solid products were filtered off, dried and crystallized from ethanol to give 11a, b. 11a : Ir : 1620 ( $\nu\text{C=N}$ ), 1690 ( $\nu\text{CO}$ ), 2200 ( $\nu\text{C=N}$ ) and 3180  $\text{cm}^{-1}$  (br,  $\nu\text{NH}$ ).  $^1\text{H-Nmr}$  ( $\text{DMSO-d}_6$ ) :  $\delta$  3.2 and 4.5 (2xt,  $J=7$  Hz, 4H,  $\text{CH}_2\text{CH}_2$ ), 6.9 - 8.3 (m, 5H, ArH and cyclic CH=C) and 10.1 (s, 1H, NH). 11b : Ir : 1690, 1700 ( $\nu\text{CO}$ ) and 3220  $\text{cm}^{-1}$  ( $\nu\text{NH}$ ).  $^1\text{H-Nmr}$  ( $\text{DMSO-d}_6$ ) :  $\delta$  2.5 (s, 3H,  $\text{CH}_3$ ), 3.0, 3.6 (2xt,  $J=6$  Hz, 4H,  $\text{CH}_2\text{CH}_2$ ), 7.0 - 7.9 (m, 5H, ArH + CH=C cyclic), 10.3 (s, 1H, cyclic NH).

**Reaction of compound (1) with Schiff bases : Formation of compound (12a-c)**

A mixture of 1 (2.46 g, 0.01 mol) and the respective Schiff base (0.01 mol) was dissolved in sodium ethoxide solution [formed from 0.7 g (0.03 mol) of metallic sodium in ethanol (30 ml)] was heated for 3 h. The solid that separated after cooling was crystallized from ethanol to give 12a-c. 12a-c : Ir : 1210 ( $\nu\text{C-S}$ ), 1620 - 1630 ( $\nu\text{C=N}$ ), 1680 - 1715 ( $\nu\text{CO}$ ) and 3150 - 3420  $\text{cm}^{-1}$  ( $\nu\text{NH}$  and OH). 12a :  $^1\text{H-Nmr}$  ( $\text{CDCl}_3$ ) :  $\delta$  2.9 (s, 1H, SCHAR), 6.0 (br, 1H, NHCH), 6.6 - 8.4 (m, 15H, ArH and cyclic CH=C) and 10.3 (br, 1H, cyclic NH). 12b :  $^1\text{H-Nmr}$  ( $\text{CDCl}_3$ ) :  $\delta$  3 (s, 1H, SCHAR), 4.3 (s, 1H, OH), 6.1 (br, 1H, NHCH), 6.6 - 8.2 (m, 14H, ArH, cyclic CH=C) and 10.6 (br, s, 1H, cyclic NH). 12c :  $^1\text{H-Nmr}$  ( $\text{CDCl}_3$ ) 2.3 (s, 3H,  $\text{CH}_3$ ), 2.9 (s, 1H, SCHAR), 3.2 - 3.4 [s, 6H,  $\text{N}(\text{CH}_3)_2$ ], 6.5 - 8.3 (m, 13H, ArH and cyclic C=CH) and 10.5 (br, 1H, cyclic NH).



Reaction of Grignard reagent with compound (1) : Formation of 13

To the Grignard reagent prepared from magnesium (0.96 g, 0.04 mol) and ethyl iodide (6.24 g, 0.04 mol) in ether (100 ml) was added a suspension of 1 (2.46 g, 0.01 mol) in ether (50 ml). The reaction mixture was heated for 2 h, decomposed with sat. aqueous ammonium chloride solution and the aqueous layer was extracted with ether which was evaporated. The residue was washed with light petroleum (bp 40/60°C) and crystallized from ethanol to give 13 (1.7 g, 53%). IR : 1630  $\text{cm}^{-1}$  ( $\nu_{\text{C=N}}$ );  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) :  $\delta$  0.9 (t, J=7 Hz, 9H,  $\text{CH}_3\text{-CH}_2\text{-}$ ), 1.3 (q, J=7 Hz, 6H,  $\text{-CH}_2\text{-CH}_3$ ), 1.5 (m, 1H, cyclic  $\text{C}_4$ ), 1.7 (d, J=7 Hz, 1H, cyclic  $\text{C}_3$ ), 6.6 - 8.4 (m, 4H, ArH), 9.6 (br, 1H, SH ratio 44.6) and 10.2, 11.4 (br, 2H, NH and NHC=S, ratio 55.4:44.6).

Table 1 : Physical and Analytical Data of Compounds (1-13)

Sample	mp °C	yield %	Mol. Formula	Analysis Found / Calcd			
				C	H	N	S
<u>1</u>	240	65	$\text{C}_{11}\text{H}_7\text{N}_3\text{O}_2\text{S}$	53.62	2.61	17.52	13.22
				53.88	2.86	17.40	13.00
<u>2a</u>	127	61	$\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_2$	67.73	4.52	17.32	
				67.92	4.40	17.61	
<u>2b</u>	114	65	$\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_2$	68.48	4.93	16.68	
				68.67	4.82	16.87	
<u>2c</u>	122	69	$\text{C}_{11}\text{H}_9\text{N}_5\text{O}_2$	54.46	3.53	28.66	
				54.32	3.70	28.80	
<u>2d</u>	81	74	$\text{C}_{17}\text{H}_{13}\text{N}_5\text{O}_2$	63.78	3.89	21.72	
				63.95	4.08	21.94	
<u>3a</u>	77	60	$\text{C}_{18}\text{H}_{13}\text{N}_5\text{O}_2$	65.00	3.79	20.98	
				65.26	3.93	21.15	
<u>3b</u>	162	53	$\text{C}_{19}\text{H}_{15}\text{N}_5\text{O}_3$	63.52	4.38	19.02	
				63.16	4.16	19.39	
<u>3c</u>	202	66	$\text{C}_{18}\text{H}_{12}\text{N}_5\text{O}_2\text{Cl}$	58.79	3.14	19.00	
				59.10	3.28	19.15	
<u>3d</u>	154	58	$\text{C}_{18}\text{H}_{12}\text{N}_6\text{O}_4$	57.31	3.14	22.09	
				57.45	3.19	22.34	

Table 1 : Continued

Sample	mp °C	yield %	Mol. formula	Analysis Found / Calcd			
				C	H	N	S
<u>3e</u>	202	72	C <sub>18</sub> H <sub>13</sub> N <sub>5</sub> O <sub>3</sub>	62.11	4.02	20.20	
				62.25	3.75	20.17	
<u>3f</u>	181	60	C <sub>18</sub> H <sub>13</sub> N <sub>5</sub> O <sub>3</sub>	61.98	3.94	19.88	
				62.25	3.75	20.17	
<u>3g</u>	204	62	C <sub>20</sub> H <sub>18</sub> N <sub>6</sub> O <sub>2</sub>	64.57	4.50	22.86	
				64.17	4.80	22.46	
<u>4</u>	186	57	C <sub>16</sub> H <sub>13</sub> N <sub>5</sub> O <sub>2</sub>	62.91	4.32	21.97	
				62.54	4.23	22.80	
<u>5</u>	203	61	C <sub>15</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>	58.21	3.62	23.42	
				58.43	3.75	23.89	
<u>6</u>	205	69	C <sub>12</sub> H <sub>8</sub> N <sub>5</sub> O <sub>3</sub> Cl	47.79	2.41	22.59	
				47.14	2.62	22.91	
<u>7</u>	197	66	C <sub>15</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub>	60.23	5.12	23.72	
				60.60	5.05	23.65	
<u>8</u>	135	57	C <sub>13</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S	57.00	4.32	15.66	11.61
				57.14	4.02	15.38	11.72
<u>9</u>	187	48	C <sub>15</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> S	54.70	3.87	12.85	9.60
				54.38	3.93	12.69	9.66
<u>10</u>	222	50	C <sub>19</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S	60.62	3.59	15.08	8.50
				60.32	3.70	14.81	8.46
<u>11a</u>	294	48	C <sub>14</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S	56.89	3.11	18.61	10.98
				56.38	3.36	18.79	10.74
<u>11b</u>	227	67	C <sub>15</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S	57.48	4.08	13.21	10.08
				57.14	4.13	13.33	10.16
<u>12a</u>	262	64	C <sub>24</sub> H <sub>18</sub> N <sub>4</sub> O <sub>2</sub> S	67.51	4.35	13.42	7.12
				67.61	4.23	13.15	7.15
<u>12b</u>	170	60	C <sub>24</sub> H <sub>18</sub> N <sub>4</sub> O <sub>3</sub> S	65.19	4.18	12.31	7.20
				65.16	4.07	12.67	7.24
<u>12c</u>	347	73	C <sub>27</sub> H <sub>25</sub> N <sub>5</sub> O <sub>2</sub> S	67.01	5.11	14.09	6.55
				67.21	5.18	14.49	6.63
<u>13</u>	283	53	C <sub>17</sub> H <sub>23</sub> N <sub>3</sub> O S	64.68	7.32	13.41	10.25
				64.35	7.25	13.25	10.09

Table 2 : Antimicrobial Activity

Comp.	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>A. niger</i>	<i>P. digitatum</i>	<i>T. virid</i>
<u>1</u>	+	+	+++	++	+	++
<u>2a</u>	-	-	-	-	-	+
<u>2b</u>	+	-	-	+	-	-
<u>2c</u>	+++	++	+	-	-	-
<u>3b</u>	++	+	++	+	-	-
<u>3c</u>	-	++	+++	-	-	-
<u>3g</u>	+	+	++	+	+	-
<u>4</u>	-	-	-	++	-	+++
<u>5</u>	++	+	+	-	+	-
<u>6</u>	-	-	-	++	+	++
<u>7</u>	-	-	-	+	-	-
<u>8</u>	++	+	+++	+	++	+++
<u>11</u>	-	-	-	+++	-	+
<u>12c</u>	++	++	++	-	+	-
<u>13</u>	-	-	-	+++	++	++

- No antibacterial activity.

+ Mild activity.

++ Moderate activity.

+++ Marked activity.

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