

A Comparative Study of Synthesis, Characterisation and Applications of 5-(Salicylidene) Rhodanine and 5-(2-Hydroxy naphthalidene) Rhodanine

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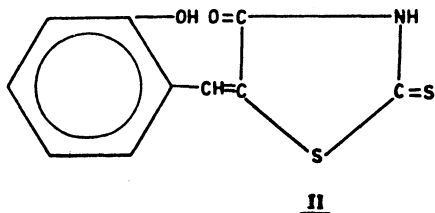
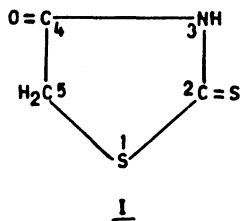
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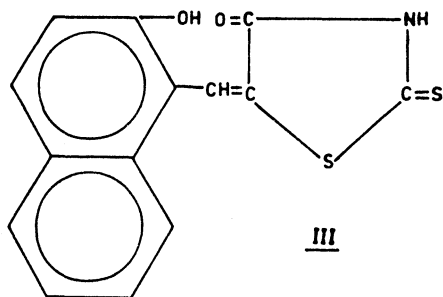
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Rhodanine (I) has been refluxed separately with salicylaldehyde and 2-hydroxy naphthaldehyde to get 5-substituted rhodanine derivatives (II-III). Their characterisation has been done by chemical and spectral data. The derivatives (II-III) have shown distinctive antibacterial, antifungal and anti-tubercular activity; and are able to act as specific spot-test and chromatographic spray reagents. Their insecticidal activity has been determined with respect to mortality of mosquito larvae, anopheles and culex sp.

INTRODUCTION

5-Substitued rhodanine derivatives are known¹ for their multiplex analytical and pharmaceutical properties such as fungicides, herbicides, bactericides, aldose reductase, anti-viral, anti-inflammatory and anti-cancerous. Inspired with these findings a systematic study of synthesis, characterisation and applications of some 5-substitued rhodanine derivatives of the type II-III has been undertaken. The III seems to have not been explored.





EXPERIMENTAL

All chemicals used were of AR grade. The rhodanine (I) was prepared as per reported literature². m.pts. were determined on Gallen Kamp apparatus and are uncorrected. Elemental analysis (C, H, N) was carried out on a Heraeus Carlo Erba 1108 elemental analyser. Sulphur was estimated by Messenger's method and molecular weights were determined by Rast method. The IR (KBr), electronic (DMF + DMSO) and ¹H NMR (CDCl₃ + DMSO-d₆/TMS) spectra were recorded on Perkin-Elmer 1800 (FTIR), Shimadzu UV-160-PC-controlled and Varian EM-360L spectrophotometers respectively.

5-(Salicylidene) rhodanine (II): A mixture of salicylaldehyde (1.3 mL) and rhodanine (1.33 g) in glacial acetic acid (15 mL) was refluxed on a water bath for 4.5 h, then cooled. The resulting dark yellow solid was crystallised from glacial acetic acid to obtain orange-yellow crystals; yield: (1.5 g, 55.5%); m.pt. 210°C; [Found: C, 50.12; H, 3.08; N, 6.02; S, 26.67%. Calcd.: C, 50.63; H, 2.95; N, 5.90; S, 27.0%]; [Mol. wt.: found, 236; required, 237]; ν_{\max} : 4000–3640, 1420, 1240 (OH); 3040, 1340, 1280 (NH); 1700 (C=O); 1480 (mercaptamide); 1175, 780 (C=S); and 1100, 1080, 1020, 900, 880, 820 (Ar) cm⁻¹; λ_{\max} : 269, 302, 393 nm; δ : 2.85 (OH), 6.80–7.80 (Ar, H, C=CH), 7.95 (NH); R_f: Ag⁺, 0.16 (reddish); Pb²⁺, 0.079 (yellow); Cu²⁺, 0.21 (brown) and Cd²⁺, 0.73 (orange).

5-(2-Hydroxy naphthalidene) rhodanine (III): The procedure adopted for its preparation was similar to that of II with the difference that 2-hydroxy naphthaldehyde (1.72 g) was used and the refluxing time required was 4 h to get reddish yellow crystals; yield: (1.8 g, 59.01%); m.pt. 185°C; [Found: C, 58.10; H, 2.80; N, 5.00; S, 22.29%; Calcd.: C, 58.53; H, 3.13; N, 4.87; S, 22.08%]; [Mol. wt.: found, 286; required, 287]; ν_{\max} : 4000–3480, 1425, 1250 (OH); 3040, 1340 (NH); 1740 (C=O); 1480 (mercaptamide); 1180, 780 (C=S); and 1100, 1020, 880, 820 (Ar) cm⁻¹; λ_{\max} : 302, 462, 564 nm; δ : 1.89 (OH), 5.80 (naphthyl), 7.0–7.70 (Ar, H, C=CH), 7.95 (NH); R_f: 0.15 (black); Pb²⁺, 0.08 (yellow); Cu²⁺, 0.20 (light green) and Cd²⁺, 0.74 (yellow).

Spot-tests: A drop of rhodanine derivative's (II-III) solution (0.01%, DMF) was added to few drops of alcoholic solutions (0.01 M) of the respective metal salts (Cl⁻, NO₃⁻) on a spot plate. The colours so developed have been recorded in Table-1. Then two drops of NH₄OH (aq 5%) were added to the respective reaction mixtures present in the spot-plate cavity and the incurred changes have also been noted in Table-1.

TABLE-I
SPOT-TESTS OF CATIONS BY RHODANINE DERIVATIVES (II-III)

Cations	(II)		(III)	
	(a)	(b)	(a)	(b)
Ag ⁺	Red	Reddish-brown + ppt	Black	Black + ppt
Mn ²⁺	Orange	Pinkish-orange	Orange	Pinkish-orange
Ni ²⁺	Brownish-green	Reddish-brown	Brownish-gray	Reddish-brown
Cu ²⁺	Pinkish-brown	Reddish-brown + ppt	Brownish-green	Reddish-brown + ppt
Zn ²⁺	Orange	Orange + ppt	Orange	Orange + ppt
Cd ²⁺	Orange	Yellowish-orange	Yellow	Brown
Hg ²⁺	Orange	Brown + ppt	Orange	Orange + ppt
Pb ²⁺	Yellow	Orange	Orange-yellow	Orange
Cr ³⁺	Green	Reddish-green	Green	Reddish-brown
Fe ³⁺	Orange-brown	Reddish-brown + ppt	Orange-brown	Reddish-brown + ppt
Co ³⁺	Reddish-yellow	Orange	Reddish-yellow	Orange
Ti ³⁺	Yellow	Orange	Yellow	Orange

(a) = Reagent alone and (b) = Reaction mixture + NH₄OH

Paper chromatographic separation: It was executed on chromatographic filter paper (30 × 2.5 cm) number one. The *n*-butyl alcohol mixed with glacial acetic acid (5%, v/v) and the same alcohol saturated with 3 N HCl were used as developing solvent for Ag⁺, Pb²⁺ and Cu²⁺, Cd²⁺ separations respectively. The separation time required *ca.* 12 h in case of former and *ca.* 16 h for subsequent metal-ion pair. The spray reagents used was the 0.1% solution of rhodanine derivatives (II-III) in DMF. The determined R_f values and the colour of spots have been recorded.

Biological screening: The anti-microbial activity of II-III was evaluated *in vitro* by using some selected bacterial and fungal species. The inhibitory zone by "Agar Diffusion Method", Laben (1950), was used to determine the potentiality of II-III. To inhibit the growth of selected test organisms the solutions (DMF) of II-III were employed at 30, 50 and 100 μg mL⁻¹ concentrations. For bacterial species the incubation period demanded 24 h (37°C) but for fungal species it required 8 days (27°C). All the experiments were repeated in triplicate and the average results are being recorded in Table-2.

Insecticidal activity: Mosquito (anopheles and culex sp.) eggs were collected, identified and kept separately in proper environment for hatching. The ethanolic-DMF (5 : 1) solutions (10 mL), with different concentrations (10–90 μg mL⁻¹), of rhodanine derivatives (II-III) were tested for insecticidal activity against twenty mosquito larvae, at subsequent developing stages, in water (100 mL). The results have been recorded in Table-3.

TABLE-2
ANTI-MICROBIAL ACTIVITY OF RHODANINE DERIVATIVES (II-III)

Test species	DP	(II)		(III)	
		Z	Res	Z	Res
<i>Bacterial</i>					
<i>E. Aeruginosa</i>	30	09		10	
	50	12	S	15	S
	100	15		18	
<i>P. Putida</i>	30	—		02	
	50	08	PS	10	PS
	100	10		12	
<i>Rhz. sp.</i>	30	07		09	
	50	10	S	13	S
	100	16		18	
<i>S. Faecalis</i>	30	18		20	
	50	22	VS	28	VS
	100	27		36	
<i>S. Aureus</i>	30	20		23	
	50	24	VS	29	VS
	100	30		37	
<i>Fungal</i>					
<i>S. Schenckii</i>	30	05		08	
	50	16	S	20	S
	100	20		22	
<i>A. Fumigates</i>	30	12		14	
	50	18	VS	25	VS
	100	28		32	

DP = Disc potency (μg), Z = Zone of inhibition (mm), Res = Result, S = Sensitive, PS = Partially sensitive and VS = Very sensitive.

TABLE-3
INSECTICIDAL ACTIVITY OF RHODANINE DERIVATIVES (II-III)

Larva in subsequent stages	Required time (min) for 100% mortality (25°C)								Control
	(II)				(III)				
	(a)	(b)	(c)	(d)	(a)	(b)	(c)	(d)	
<i>Anopheles sp.</i>									
Wrigglers	24.0	20.0	18.0	15.0	14.0	13.0	11.0	9.5	80.0
3-days old	26.0	23.0	20.5	19.0	15.0	14.5	12.5	10.5	95.0
6-days old	29.0	25.5	24.0	21.5	16.0	15.5	13.5	12.5	110.0
Full grown	30.0	28.0	27.0	25.0	17.0	16.5	16.0	15.0	125.0
<i>Culex sp.</i>									
Wrigglers	23.5	19.5	17.5	14.5	14.0	13.0	10.8	9.2	79.0
3-days old	25.5	22.5	19.5	18.5	15.2	14.0	12.3	10.3	98.5
6-days old	28.5	25.0	23.5	22.0	16.0	15.3	13.6	12.4	110.0
Full grown	29.5	27.0	26.5	24.8	16.9	16.4	15.8	14.8	124.8

Concentrations: (a), (b), (c) and (d) represent *ca.* 10, 20, 40 and 90 $\mu\text{g mL}^{-1}$ respectively.

RESULTS AND DISCUSSION

The recorded analytical and physical data support the proposed structures of the synthesised rhodanine derivatives (**II-III**). The IR spectra³ of **II-III** showed no indication of a —SH band in the region 2600–2500 cm^{-1} but exhibited a strong absorption at 1480 cm^{-1} pertaining to mixed vibration of mercaptomide band. Along with frequent absorptions of aromatic rings the **II-III** showed bands at 4000–3480, 1425–1420 and 1250–1240; 3040, 1340 and 1280; 1740–1700, 1180–1175 and 780 cm^{-1} corresponding to $\nu(\text{OH})$, $\nu(\text{NH})$, $\nu(\text{C}=\text{O})$ and $\nu(\text{C}=\text{S})$ respectively. Thus, the association of rhodanine moiety with respective aldehydes is evident in **II-III**.

The electronic spectra³ of **II-III** exhibited characteristic maxima for $\pi-\pi^*$ transitions, corresponding to conjugated aromatic rings containing a thio-keto structure, in the range 269–302 nm. The other absorption bands observed at 393 (**II**) and 462 (**III**) nm may be ascribed to $\pi-\pi^*$ transitions related to thio-keto structure and lengthening of conjugated system. An additional band at 564 nm found in **III** may however be attributed to existence of a naphthyl system.

The ¹H NMR spectra³ of **II-III** have shown sharp to medium bands at δ 1.89, 2.85, 5.80 (**II**), 6.80–7.80, and 7.95 corresponding to the resonated —OH protons, aromatic and C=CH protons and —NH protons respectively. In **III** the —OH proton has shown a medium intensity band at δ 1.89 in comparison to sharp band at δ 2.85 in **II**, and the —CH proton has exhibited an additional broad sharp band at δ 5.80. These differences may be attributed to different electronic environment due to presence of a hydroxy naphthyl system in **III**.

The perusal of results, Table-1, suggests that the rhodanine derivatives (**II-III**) on interaction with metal ions generate specific colours and so they may be used as spot-test reagents. Rhodanine derivatives are known to function as good complex forming ligands. Thus, with their available donor sites the **II-III** must have interacted with respective metal ions to form either a coloured lake or a soluble metal chelate. For this the coordination is very likely through potential thio-carbonyl and nitrogen part of the rhodanine entity of the studied derivatives (**II-III**). This expectation gets support from the study of IR spectra of respective Cu(II) complexes, where the absence of bands at 3040, 1340 and 1280 ($\nu(\text{NH})$), 1180–1175 and 780 ($\nu(\text{C}=\text{S})$) cm^{-1} and the slight lengthening of bands pertaining to $\nu(\text{C}=\text{O})$ and $\nu(\text{OH})$ has been confirmed.

On adding two drops of dil.NH₄OH to the coloured solutions resulting due to interactions of respective metal ions with **II-III**, it was noticed that either the colour intensity has increased or the colour has changed. This type of indications may also be useful in the detection of metal ions by spot-test method. In case of Ag⁺, Cu²⁺, Zn²⁺, Hg²⁺ and Fe³⁺ the precipitation (traces) has also been noticed. This finding may therefore be employed for gravimetric estimations of the aforesaid metal ions.

On the basis of spot-test results, Table-1, the **II-III** have successfully been deployed as spray reagents in the paper chromatographic separations of pair of some metal ions (Ag⁺, Pb²⁺; Cu²⁺, Cd²⁺). The recorded R_f values are in good agreement with the standard results and the colours of the spots are distinctive.

In biological screening, Table-2, it was found that the solutions of **II-III** are very sensitive against *S. faecalis*, *S. aureus* and *A. fumigates*; sensitive against *S. aeruginosa*, *Rhz. sp.* and *S. Schenekii*; and partially sensitive against *P. putida*. It is also apparent from the results, Table-2, that the sensitivity of **III** is distinctly greater than of **II** against all test species.

Anti-tubercular activity of the rhodanine derivatives (**II-III**) was tested against *Mycobacterium tuberculosis* H₃₇Ra and it was found that the minimum inhibitory concentration required is 100 and 98 µg mL⁻¹ for **II** and **III** respectively.

Insecticidal activity results, Table-3, clearly indicate that the toxicity effect for 100% mortality of mosquito (anopheles and culex sp.) larvae is maximum at 90 µg mL⁻¹ concentration with respect to control. It is also evident that **III** is more effective than **II** in respect of both species and **II-III** are slightly more efficacious for culex sp.

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