THE CONDENSATION OF RHODANINE WITH AROMATIC DIALDEHYDES AND SOME RELATED COMPOUNDS¹

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ABSTRACT

The condensation of rhodanine and its 3-ethyl and 3-phenyl derivatives with terephthaldehyde, pyridine-2,6-dicarboxaldehyde, and phthaldehyde has been investigated. Twenty-nine 5-arylidene-rhodanines containing an electrophilic substituent in the aromatic ring have been prepared.

Rhodanine condenses readily with a variety of aliphatic (1, 2, 3, 4), aromatic (5, 6), and heterocyclic (7, 8) aldehydes. The analogous reaction with ketones has been less extensively investigated (9, 10). Very few examples of rhodanine-diketone interaction have been described (11, 12, 13, 14, 15, 16) and we have been unable to find in the literature any reference to the condensation of rhodanine with dialdehydes. Our interest in rhodanine-dialdehyde adducts was actuated by the fungicidal and mildew-proofing properties of the 5-substituted rhodanines (I) in general, and the 5-arylidene-rhodanines (II) in particular (5, 6). In spite of the many variants of R in (II) only two compounds in which R is electrophilic have been evaluated as fungicides (5). The location of the substituent diminished or increased the fungitoxicity of (II), suggesting evaluation of electron distribution as a rationale for structure and activity. With a view to preparing further examples of this type of compound for testing we have examined the condensation of some aromatic dialdehydes with rhodanine derivatives.



Termolecular reaction of rhodanine and the 3-ethyl and 3-phenyl derivatives (two molecular proportions) with terephthaldehyde (IIIa) or pyridine-2,6-dicarboxaldehyde (IVa) (one molecular proportion) proceeds with great facility to yield the diadducts (IIIb), (IIIc), (IIId), (IVb), (IVc), and (IVd) respectively, which separated from the reaction mixture in an almost pure state. The aldehyde-rhodanine derivatives were prepared using ammonia – ammonium chloride (17), acetic acid – sodium acetate (19), or acetic acid – acetic anhydride – sodium acetate (7) as condensing agents. No crystalline adducts were obtained from the reaction of phthaldehyde with either rhodanine, 3-ethyl-, or 3-phenyl-rhodanine using these reagents or with 3-ethylrhodanine under the conditions used to condense phthaldehyde with malonic ester (18). Condensation of equimolecular proportions of 3-ethyl- or 3-phenyl-rhodanine (but not rhodanine itself) with the dialdehydes (IIIa) and (IVa) gave readily separable mixtures of the appropriate diadducts

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b. с. d. е. f.

g. h. i. j. k.

11

 R_1



Xph

(111)

 $\begin{array}{l} R_1 = R_4 = CHO; \ R_2 = R_3 = H \\ R_1 = R_4 = X_{H}; \ R_2 = R_3 = H \\ R_1 = R_4 = X_{Et}; \ R_2 = R_3 = H \\ R_1 = R_4 = X_{Ph}; \ R_2 = R_3 = H \\ R_1 = CHO; \ R_2 = R_3 = H; \ R_4 = X_{Ph} \\ R_1 = CHO; \ R_2 = R_3 = H; \ R_4 = H \\ R_1 = CH:NOH; \ R_2 = R_3 = H; \ R_4 = H \\ R_1 = X_{Et}; \ R_2 = NO_2; \ R_3 = R_4 = H \\ R_1 = X_{Ph}; \ R_2 = NO_2; \ R_3 = R_4 = H \\ R_1 = X_{Ph}; \ R_2 = NO_2; \ R_3 = R_4 = H \\ R_1 = X_{Ph}; \ R_2 = NO_2; \ R_3 = R_4 = H \\ R_1 = X_{Ph}; \ R_2 = NO_2; \ R_3 = R_4 = H \\ R_1 = X_{Ph}; \ R_2 = NO_2; \ R_3 = R_4 = H \\ R_1 = X_{Ph}; \ R_3 = NO_2; \ R_2 = R_4 = H \\ \end{array}$

 $X_{\rm H}; R_3 = {
m NO}_2; R_2 = R_4 = {
m H}$

III	
	$l_{1} = R_{1} = X_{E_{1}}; R_{3} = NO_{2}; R_{2} = R_{4} = H$
	$m. R_1 = X_{Ph}; R_3 = NO_2; R_2 = R_4 = H$
	<i>n</i> . $R_1 = X_H$; $R_4 = NO_2$; $R_2 = R_3 = H$
	o. $R_1 = X_{E_4}; R_4 = NO_2; R_2 = R_3 = H$
	$p. R_1 = X_{Ph}; R_4 = NO_2; R_2 = R_3 = H$
	$q. R_1 = X_H; R_2 = CO_2H; R_3 = R_4 = H$
	$r. R_1 = X_{Et}; R_2 = CO_2H; R_3 = R_4 = E_4$
	s. $R_1 = X_{Ph}; R_2 = CO_2H; R_3 = R_4 = F_1$
	<i>i</i> . $K_1 = X_H; K_4 = CO_2 n; K_2 = K_3 = n$
	$u_1 R_1 = A_{Et}; R_4 = CO_2 H; R_2 = R_3 = H$
	$v_1 = x_{Ph}, x_4 = CO_{211}, x_2 = x_3 = 1$

(iv)



described above and the related monoadducts (IIIe), (IIIf), (IVe), and (IVf). The retention of a free formyl group under the conditions of condensation is evidenced by analysis and the formation of an oxime (IIIg).

Concurrently with this study we have prepared for fungicidal and antibacterial evaluation* fifteen 5-arylidene-rhodanines (II) containing an electrophilic substituent in the benzenoid moiety and comprising two groups. The first group consists of the adducts (IIIh) to (IIIp) inclusive, containing the toxiphoric nitro group, which were synthesized by the condensation of rhodanine, its 3-ethyl and 3-phenyl homologues with 2-, 3-, and 4-nitrobenzaldehyde. The second group of adducts, (IIIq) to (IIIv) inclusive, was derived from the condensation of rhodanine and its congeners with phthaldehydic and terephthaldehydic acid; analogous derivatives of which have recently received attention as bactericidal agents (20, 21).

EXPERIMENTAL[†]

1,4-Phenylene-di-(5-methylenerhodanine) (IIIb)

A solution of terephthaldehyde (1.34 g, 0.01 mole) and rhodanine (2.66 g, 0.02 mole) in ethanol (20 ml) and concentrated ammonium hydroxide (7 ml, d., 0.88) was heated on the steam bath. A solution of ammonium chloride (7 g) in hot water (10 ml) was added and heating continued for 1 hour when orange needles had separated. Recrystallization from dimethylformamide gave the diadduct IIIb as fine orange needles (2.8 g, yield 77%) which did not melt below 360°. Calc. for C14H8N2O2S4: C, 46.08; H, 2.2; N, 7.68; S, 35.25. Found: C, 45.81; H, 1.95; N, 7.31; S, 35.00%.

*Details of which we hope to publish later elsewhere. † Melting points have been corrected.

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						Carbon, %		Hydrogen, %	
Compound*	Structure	Crystalline form†	M.p., °C	Yield %	Formula	Calc.	Found	Calc.	Found
1,4-Phenylene-di-(3-phenyl-5-methylenerhodanine)	IIId	Fine orange needles ^a	>360	86	C20H16N2O2S4	60.39	60.34	3.12	3.27
2,6-(1-Azaphenylene)-di-(3-ethyl-5-methylenerhodanine)§§	IVc	Fine yellow needles ^b	228 - 229	93	C17H15N1O2S4	48.39	48.52	3.58	3.68
2.6-(1-Azaphenylene)-di-(3-phenyl-5-methylenerhodanine)	IVd	Fine orange needles ^a	335-336 (decomp.)	87	C25H15N3O2S4	57.97	57.63	2.92	3.01
5-(2-Nitrobenzylidene)rhodanine‡	IIIk	Yellow needles ^c	204 - 205	71	C10H0N2O3S2	45.09	45.31	2.27	2.13
3-Ethyl-5-(2-nitrobenzylidene)rhodanine	IIIi	Orange plates ^d	157-158	85	C12H10N2O3S2	48.96	48.73	3.42	3.21
3-Phenyl-5-(2-nitrobenzylidene)rhodanine§	IIIj	Orange plates ^e	245 - 246	45	C16H10N2O3S2	56.12	55.98	2.94	3.05
5-(3-Nitrobenzylidene)rhodanine	IIIk	Bright yellow needles ^e	264 - 265	60	C10H6N2O3S2	45.09	44.85	2.27	2.01
3-Ethyl-5-(3-nitrobenzylidene)rhodanine¶	1111	Golden-yellow blades ^c	194 - 195	58	C12H10N2O3S2	48.96	48.67	3.42	3.28
3-Phenyl-5-(3-nitrobenzylidene)rhodanine**	IIIm	Orange platelets ^e	245 - 246	48	C16H10N2O3S2	56.12	56.41	2.94	2.72
5-(4-Nitrobenzylidene)rhodanine††	111n	Orange-yellow needles ^d	273 - 274	90	C10H6N2O3S2	45.09	44.76	2.27	2.41
3-Ethyl-5-(4-nitrobenzylidene)rhodanine	IIIo	Orange-yellow prismatic needles ^d	232-233	85	C12H10N2O3S2	48.96	48.88	3.42	3.19
3-Phenyl-5-(4-nitrobenzylidene)rhodanine‡‡	III⊅	Yellow needles ^e	273-274	96	C16H10N2O3S2	56.12	55.88	2.94	2.69
3-Ethyl-5-(2-carboxybenzylidene)rhodanine	IIIr	Golden-yellow rectangular plates ^c	185-187	52	C13H11NO3S2	53.22	52.96	3.78	3.82
3-Phenyl-5-(2-carboxybenzylidene)rhodanine	IIIs	Yellow-orange felted needles ^d	225-226	70	C17H11NO3S2	59.80	59.67	3.25	3.17
5-(4-Carboxybenzylidene)rhodanine	1111	Yellow-orange prismatic needles ^b	307-308 (decomp.)	80	C11H7NO3S2	49.79	49.61	2.65	2.53
3-Ethyl-5-(4-carboxybenzylidene)rhodanine	III11	Golden-yellow needles ^b	290-291	79	C13H11NO3S2	53.22	52.99	3.78	3.52
3-Phenyl-5-(4-carboxybenzylidene)rhodanine	IIIv	Orange-yellow prisms ^a	307-308	85	$C_{17}H_{11}NO_3S_2$	59.80	59.63	3.25	3,31

*The 17 compounds appearing in this table were similarly prepared.

†Crystallization solvents: "dimethylformamide, bacetic acid, "methanol, dacetone-methanol, "benzene-methanol.

Bondzynski (22) gives m.p. 188-189° for this compound prepared by the condensation of 2-nitrobenzaldehyde with rhodanine in ethanol containing sulphuric acid. §Andreasch and Zipser (23) give m.p. 238° for this compound prepared by the same method.

||Bargellini (24) gives m.p. 245-255° for this compound prepared by the condensation of 3-nitrobenzaldehyde with rhodanine in ethanol containing sulphuric acid.

¶Andreasch and Zipser (25) give m.p. 188° for this compound prepared by the same method.

**Andreash and Zipser (25) give m.p. 240° for this compound prepared by the same method.

^{††}Bondzynski (22) gives m.p. 250–252° (decomp.) for this compound prepared by the condensation of 4-nitrobenzaldehyde with rhodanine in ethanol containing sulphuric acid. ^{‡‡}Andreasch and Zipser (25) give m.p. 240° (decomp.) for this compound prepared by the same method.

§§Nitrogen analysis: Calc., 9.96; found, 9.71%.

|| ||Nitrogen analysis: Calc., 8.11; found, 7.93%.

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2,6-(1-Azaphenylene)-di-(5-methylenerhodanine) (IVb)*

2,6-(1-Azaphenylene)-di-(5-methylenerhodanine) (IVb), fine bright yellow needles (100 mg, yield 52%), from dimethylformamide, which did not melt below 360°. Calc. for C₁₃H₇N₃O₂S₄: C, 42.82; H, 1.94; N, 11.53. Found: C, 43.14; H, 1.94; N, 11.63\%.

5-(2-Carboxybenzylidene)rhodanine (IIIq)*

5-(2-Carboxybenzylidene) rhodanine (IIIq), clusters of bright yellow needles (1.1 g, yield 42%) from aqueous ethanol, m.p. 268–270° with decomp. Calc. for $C_{11}H_7NO_3S_2$: C, 49.79; H, 2.65. Found: C, 49.58; H, 2.78%. Dijksman and Newbold (19) give m.p. 265–266° for this compound prepared by the condensation of phthaldehydic acid with rhodanine in acetic acid containing sodium acetate.

1,4-Phenylene-di-(3-ethyl-5-methylenerhodanine) (IIIc)

A mixture of terephthaldehyde (0.67 g, 0.005 mole), 3-ethylrhodanine (1.62 g, 0.01 mole), and freshly fused sodium acetate (3 g) in acetic acid (50 ml), to which acetic anhydride (1 ml) had been added, was refluxed for 1 hour during which time orange needles separated. The mixture was allowed to cool and the product collected. Recrystallization from acetic acid gave the diadduct IIIc as long prismatic orange needles (1.5 g, yield 71%) m.p. 295–296°. Calc. for $C_{18}H_{16}N_2O_2S_4$: C, 51.35; H, 3.83. Found: C, 51.42; H, 3.94%.

3-Ethyl-5-(4-formylbenzylidene)rhodanine (IIIe)

A mixture of terephthaldehyde (1.34 g, 0.01 mole), 3-ethylrhodanine (1.62 g, 0.01 mole), and freshly fused sodium acetate (3 g) in acetic acid (50 ml), to which acetic anhydride (1 ml) had been added, was refluxed for 1 hour when crystals had separated. The hot reaction mixture was filtered and the diadduct (IIIc) (1.25 g) removed. The filtrate was diluted with water (100 ml) and the yellow precipitate collected and washed with hot water. Crystallization from acetone-methanol gave 3-ethyl-5-(4-formylben-zylidene)rhodanine (550 mg, yield 20%) as orange-yellow plates, m.p. 171–172°. Calc. for $C_{13}H_{11}NO_2S_2$: C, 56.29; H, 4.0. Found: C, 56.48; H, 4.06%.

3-Phenyl-5-(4-formylbenzylidene)rhodanine (IIIf)†

3-Phenyl-5-(4-formylbenzylidene)rhodanine (IIIf), yellow needles (1.71 g, yield 53%) from benzene-ethanol, m.p. 233-234°. Calc. for $C_{17}H_{11}NO_2S_2$: C, 62.82; H, 3.41. Found: C, 62.71; H, 3.45%. The related *oxime* (IIIg) was prepared in pyridine-ethanol solution (26) and crystallized from benzene-ethanol as yellow needles, m.p. 276-278°. Calc. for $C_{17}H_{12}N_2O_2S_2$: C, 59.96; H, 3.55. Found: C, 59.77; H, 3.69%.

3-Ethyl-5-[2-(6-formyl)pyridylmethylene]rhodanine (IVe)†

3-Ethyl-5-[2-(6-formyl)pyridylmethylene]rhodanine (IVe), yellow prismatic needles (500 mg, yield 18%) from aqueous methanol, m.p. 191–192°. Calc. for $C_{12}H_{10}N_2O_2S_2$: C, 51.78; H, 3.62. Found: C, 51.53; H, 3.45%.

3-Phenyl-5-[2-(6-formyl)pyridylmethylene]rhodanine (IVf) \dagger

3-Phenyl-5-[2-(6-formyl)pyridylmethylene]rhodanine (IVf), clusters of yellow prismatic needles (1.98 g, yield 60%) from methanol, m.p. 248-250°. Calc. for $C_{16}H_{10}N_2O_2S_2$: C, 58.88; H, 3.09. Found: C, 58.52; H, 3.01%.

*The compounds designated by * were similarly prepared.

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