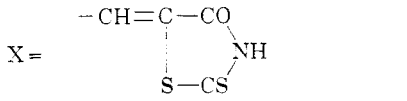
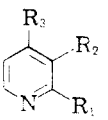
pyridine and quinoline aldehydes have been reported to possess antibacterial properties,[10–13] we have prepared substituted 5-methylene-rhodanines from the unsubstituted aldehydes of the pyridine series and two of the quinoline series for fungicidal and antibacterial evaluation.

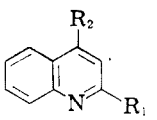


I



II

a. R_1 = CHO; R_2 = R_3 = H
b. R_2 = CHO; R_1 = R_3 = H
c. R_3 = CHO; R_1 = R_2 = H
d. R_1 = X; R_2 = R_3 = H
e. R_2 = X; R_1 = R_3 = H
f. R_3 = X; R_1 = R_2 = H



III

a. R_1 = CHO; R_2 = H
b. R_2 = CHO; R_1 = H
c. R_1 = X; R_2 = H
d. R_2 = X; R_1 = H

Condensation of rhodanine with pyridine-2-carboxaldehyde (IIa), pyridine-3-carboxaldehyde (IIb), pyridine-4-carboxaldehyde (IIc), quinoline-2-carboxaldehyde (IIIa), and quinoline-4-carboxaldehyde (IIIb) proceeds with great facility to yield the adducts (IId), (IIe), (IIf), (IIIc), and (IIId), respectively. The aldehyde-rhodanine derivatives were prepared using ammonia–ammonium chloride or acetic acid–sodium acetate as condensing agents.[14–17] These products, unlike other rhodanine-aldehyde condensation products, exhibit a characteristic insolubility in the common organic solvents, have high melting points (with decomposition) and can be crystallized from dimethylformamide. We ascribe these properties to the amphoteric nature of the adducts which permits intermolecular salt formation between the basic nitrogen of the pyridine ring and the acidic imino group of the rhodanine moiety. Substitution of the hydrogen atom of the imino group of the rhodanine ring in adducts (IIe) and (IIf) by a phenyl radical, to yield 3-phenyl-5(3-pyridylmethylene)- and 3-phenyl-5-(4-pyridylmethylene)rhodanine, with consequent blocking of possible intermolecular ionic bonding, restores the normal solubility pattern of rhodanine-aldehyde adducts, lowers the melting point and eliminates decomposition on melting.

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EXPERIMENTAL[18]

5-(2-Pyridylmethylene)rhodanine (IId). A solution of 2.0 g. (0.019 mole) of pyridine-2-carboxaldehyde and 2.6 g. (0.020 mole) of rhodanine in 15 ml. of ethanol and 13 ml. of concentrated ammonium hydroxide was heated on the steam bath. A solution of 13 g. of ammonium chloride in 20 ml. of hot water was added and heating continued for 30 min. The reaction mixture was allowed to stand overnight at 0° when crystals had separated. Recrystallization from ethanol gave 2.1 g. (yield 51%) of IId as bright yellow needles, m.p. 243–245° (dec.).

Anal. Calcd. for $C_9H_6N_2OS_2$: C, 48.62; H, 2.72; N, 12.6; S, 28.85. Found: C, 48.51; H, 2.70; N, 12.2; S, 28.7.

The following five compounds were similarly prepared.

5-(3-Pyridylmethylene)rhodanine (IIe), fine bright yellow needles (3.1 g., yield 75%) from dimethylformamide, m.p. 318–320° (dec.).

Anal. Calcd. for $C_9H_6N_2OS_2$: C, 48.62; H, 2.72; N, 12.6; S, 28.85. Found: C, 48.40; H, 2.80; N, 12.3; S, 28.50.

5-(4-Pyridylmethylene)rhodanine (IIf), fine yellow needles (2.9 g., yield 65%) from dimethylformamide, m.p. 320–322° (dec.).

Anal. Calcd. for $C_9H_6N_2OS_2$: C, 48.62; H, 2.72. Found: C, 48.41; H, 2.58.

5-(2-Quinolylmethylene)rhodanine (IIIc), bright yellow needles (560 mg., yield 69%) from aqueous acetone decomposing at 270°.

Anal. Calcd. for $C_{13}H_8N_2OS_2$: C, 57.31; H, 2.96; N, 10.29; S, 23.55. Found: C, 57.1; H, 2.8; N, 10.0; S, 23.2.

5-(4-Quinolylmethylene)rhodanine (IIId), yellow needles (500 mg., yield 59%) from dimethylformamide, m.p. 318–320° (dec.).

Anal. Calcd. for $C_{13}H_8N_2OS_2$: C, 57.31; H, 2.96. Found: C, 57.0; H, 2.8.

3-Phenyl-5-(3-pyridylmethylene)rhodanine. A mixture of 2.0 g. (0.019 mole) of pyridine-3-carboxaldehyde, 4.0 g. (0.019 mole) of 3-phenylrhodanine, and 4.0 g. of freshly fused sodium acetate in 15 ml. of acetic acid, to which 1 ml. of acetic anhydride had been added, was refluxed for 30 min. and allowed to cool. The yellow crystals which separated were recrystallized from ethanol to yield 1.5 g. (yield 27%) of *3-phenyl-5-(3-pyridylmethylene)rhodanine* as long yellow needles, m.p. 235–237°.

Anal. Calcd. for $C_{15}H_{10}N_2OS_2$: C, 60.37; H, 3.38. Found: C, 60.22; H, 3.2.

3-Phenyl-5-(4-pyridylmethylene)rhodanine was prepared in a similar manner and was recrystallized from ethanol as golden yellow needles (3.2 g., yield 54%), m.p. 245–246°.

Anal. Calcd. for $C_{15}H_{10}N_2OS_2$: C, 60.37; H, 3.38; N, 9.39; S, 21.5. Found: C, 60.22; H, 3.2; N, 9.05; S, 21.2.

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(18) Melting points are uncorrected.

Reaction of Nitroacetamide with Hypobromite

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When nitroacetamide is heated in an aqueous solution of sodium hypobromite, dibromonitro-

methane is obtained. It has been reported that the product was a mixture of the di- and tribromo compounds.[1] This conclusion came solely from the fact that the elemental analysis of the crude reaction product was between the values for di- and tribromonitromethane, and could easily be misleading.

An intermediate may be isolated if the reaction mixture is cooled and acidified after ten minutes' heating. This intermediate, whose empirical formula is $C_2H_2Br_2N_2O_3$, was thought to be α,α-dibromo-α-nitroacetamide.[1] The infrared spectrum of this compound has intense absorption at 2.93, 3.17, 5.90, and 6.35 microns which is characteristic of secondary amides.[2] Therefore, it is most likely N,α-dibromonitroacetamide. When this compound is refluxed in water, dibromonitromethane is obtained and the aqueous solution is acidic and contains ammonia and bromide ion.

The reaction occurs in two steps:

$$O_2N{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}NH_2 + 2OBr^- \longrightarrow O_2NCHBr{-}\overset{\overset{O}{\|}}{C}{-}NHBr + 2OH^- \quad (I)$$

$$O_2NCHBr{-}\overset{\overset{O}{\|}}{C}{-}NHBr + H_2O \longrightarrow O_2NCHBr_2 + CO_2 + NH_3 \quad (II)$$

Step II is a further example of the rearrangement observed when α-haloamides are treated with hypobromite.[3] Since the reaction will occur in water initially free of bromide ion it is an indication that the rearrangement of the N-bromoamide is intramolecular as postulated by Haszeldine.[4]

The reaction was tried in acidic, neutral, and basic solution, both at room temperature and 100° but under none of these conditions could nitroacetamide be converted to nitromethylamine.

EXPERIMENTAL

Ethyl nitroacetate. This compound was prepared by the method of Rodionov and its physical constants agreed with those reported.[5]

Ammonium ethyl acinitroacetate. Into 6 g. of ethyl nitroacetate in 50 ml. of anhydrous ether, cooled in Dry Ice, was bubbled anhydrous ammonia. A pasty precipitate formed immediately. It was recrystallized from 95% ethanol to give 3.2 g. (57%) of ammonium ethyl acinitroacetate with m.p. 86–88° with decomposition.

Anal. Calcd. for $C_4H_{10}N_2O_4$: C, 32.00; H, 6.67; N, 18.68. Found: C, 31.76; H, 6.51; N, 18.61.

An aqueous solution of the compound gives a red color with ferric chloride solution, but no precipitate with silver nitrate solution, as had been reported.[1]

Ammonium acinitroacetamide. A solution of 3 g. of ammonium ethyl acinitroacetate in 45 ml. of absolute ethanol saturated with ammonia was heated in a sealed tube at 100° for 1.25 hr. The solid initially present quickly dissolved, and soon after glistening plates began to precipitate from the solution. The tube was cooled and the crystals collected to yield 1.5 g. (70%) of ammonium acinitroacetamide with m.p. 117–119° with decomposition.

Anal. Calcd. for $C_2H_7N_3O_3$: C, 19.81; H, 5.79; N, 34.75. Found: C, 19.87; H, 5.63; N, 34.58.

The compound gives a red color with ferric chloride solution and no precipitate with silver nitrate solution. Although the properties are different from those previously reported;[6] m.p. 152°, precipitate with silver nitrate solution; the present assignment is probably correct since nitroacetamide, m.p. 99–100°, is obtained upon acidification and extraction with ether.[7]

N,α-dibromonitroacetamide. To an aqueous solution of 2.42 g. (0.02 mole) of ammonium acinitroacetamide was added 0.80 g. (0.02 mole) of sodium hydroxide and the solution warmed to expel ammonia. After addition of 0.04 mole of hypobromite solution the mixture was warmed for 10 min., cooled, acidified, filtered, and the precipitate recrystallized from chloroform to give 2.9 g. (55%) of N,α-dibromonitroacetamide with m.p. 113–114°.

Anal. Calcd. for $C_2H_2Br_2N_2O_3$: C, 9.17; H, 0.77; N, 10.70; Br, 61.03. Found: C, 9.42; H, 0.87; N, 10.82; Br, 61.00.

Dibromonitromethane. 5.2 g. of N,α-dibromonitroacetamide was refluxed in 30 ml. of water for 2 hr. The organic layer was separated, dried over calcium chloride, and vacuum distilled to give 2.6 g. (61%) of dibromonitromethane, b.p. 44–45° (0.7 mm.) and n_D^{25} 1.5757.

Anal. Calcd. for $CHBr_2NO_2$: C, 5.49; H, 0.46; N, 6.40; Br. 73.06. Found: C, 5.46; H, 0.50; N, 6.15; Br, 73.27.

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Investigations in Heterocycles. II. Unsymmetrical Ureas, Thioureas and Related Thiazolines

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In the past few years several papers[1–3] have appeared on the use of thioureas as effective chematherapeutic agents for the treatment of tubercular infections in experimental animals. Our recent work[4,5] on cycloalkeno[*d*]thiazolin-2-ones suggested

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