base was converted into its hydrochloride, m.p. 227–228° dec. The yield was 5.85 g. (96%). Further crystallization from ethanol–isopropyl alcohol mixture raised the m.p. to 230–231° dec.

Anal. Calcd. for $C_{22}H_{23}ClN_2OS$: C, 66.20; H, 5.81; N, 7.05. Found: C, 66.36; H, 5.81; N, 6.93.

Table III lists two additional derivatives prepared in similar manner.

N-Alkylation of Benzo[a]phenothiazines. General Procedure.—The reactants were used in the following ratio: benzo[a]phenothiazine, 1.0 mole; sodium amide, 1.05 to 1.1 mole; dialkylaminoalkyl chloride, 1.1 to 1.4 mole.

Sodium amide, freshly prepared from an equivalent quantity of sodium and liquid ammonia in the presence of a catalytic amount of ferric nitrate, was suspended in dry toluene or xylene. The appropriate benzophenothiazine was added which caused the development of a deep red to purple color. The mixture was refluxed with stirring for 30 to 60 minutes and the dialkylaminoalkyl chloride, dissolved in an equal volume of toluene or xylene, was added dropwise during 60 to 90 minutes. After completion of addition, refluxing was continued for 3 to 5 hours. The mixture was cooled, decomposed with 5% aqueous acetic acid or 2% aqueous hydrochloric acid. The organic layer was separated and extracted twice more with dilute acid. The combined acid solution was washed once or twice with ether and then neutralized with sodium hydroxide solution. The liberated base was extracted with ether, washed with saline water, dried over sodium sulfate, the solvent evaporated and the residual oil was distilled under vacuum. The products were highly viscous oils, light yellow to orange-yellow in color with a greenish fluorescence.

The relevant data are summarized in Table V and the corresponding derivatives in Table VI.

KNOXVILLE, TENNESSEE

[CONTRIBUTION FROM THE ROHM AND HAAS CO.]

The Reaction of 5-Ethoxymethylenerhodanines with Amines

BY CHIEN-PEN LO

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A number of 5-aminomethylenerhodanines have been prepared by the reaction of 5-ethoxymethylenerhodanines with primary and secondary amines. Certain crystalline amine salts of rhodanine, 2,4-thiazolidinedione and their 5-substituted derivatives are also reported.

In a previous publication,[1] the synthesis of 5-alkoxymethylenerhodanines from rhodanines and alkyl orthoformates and their reaction with rhodanines were reported. At about the same time, Knott[2] published independently his work on the preparation of 5-1′-alkoxyalkylidenerhodanines by a similar method.[3] In his article the reaction of 3-allyl- and 3-carbethoxymethyl-5-1′-alkoxyalkylidenerhodanines with ammonia, primary and secondary amines also were described. The present paper reports our work on the reaction of amines with 5-ethoxymethylenerhodanines and the 3-substituted 5-ethoxymethylenerhodanines other than the two reported by Knott.

3-Substituted 5-ethoxymethylenerhodanines reacted with primary and/or secondary amines to give the corresponding 5-aminomethylenerhodanines as reported by Knott. The reaction of 5-ethoxymethylenerhodanine with amines was found to be dependent upon the nature of the latter. Most amines, primary or secondary, gave the amine salts of the corresponding 5-aminomethylenerhodanines, some of which were isolated as crystalline solids (Table I). These amine salts yielded the free 5-aminomethylenerhodanines when treated with acid. Aniline and diallylamine gave the corresponding 5-aminomethylenerhodanines directly. Dicyclohexylamine yielded the dicyclohexylamine salt of 5-ethoxymethylenerhodanine at room temperature, but at higher temperature the corresponding salt of 5-dicyclohexylaminomethylenerhodanine was formed. The details of these reactions are given in the Experimental part and the data on the 5-aminomethylenerhodanines thus prepared are given in Table II.

In connection with this and related work, we have found that rhodanine, 2,4-thiazolidinedione and their 5-alkylidene derivatives formed crystalline salts (Table III) with certain amines.[4] The amine salts of 2,4-thiazolidinediones appeared to be more stable than those of rhodanines which showed signs of decomposition on storage. As a rule, the amine salts of rhodanines melted with decomposition, whereas those of 2,4-thiazolidinediones melted without decomposition.

Experimental[5]

5-Ethoxymethylenerhodanines.—The 5-ethoxymethylenerhodanines were prepared by the reaction of rhodanines with ethyl orthoformate in acetic anhydride as reported previously.[1] The 5-ethoxymethylene-3-ethylrhodanine was similarly obtained in a 67% yield, m.p. 92–92.5°.

Anal. Calcd. for $C_8H_{11}NO_2S_2$: N, 6.5; S, 29.5. Found: N, 6.1; S, 29.6.

5-Anilinomethylenerhodanine (Method A).—Aniline (20 g.) was added to a solution of 5-ethoxymethylenerhodanine (20 g.) in acetone (100 ml.). The resulting solution was diluted with water (100 ml.). The yellow solid which separated was collected, washed with aqueous acetone (1:1) and air-dried. The product which decomposed at 215–217° weighed 17 g. After recrystallization from acetic acid, the 5-anilinomethylenerhodanine decomposed at 225–226°.

Since Dains and Davis[6] had prepared 5-anilinomethylenerhodanine by the reaction of diphenylformamidine with rhodanine and reported its m.p. as 248°, this compound was made according to the procedure of Dains and Davis. The crude product (m.p. 215° dec., 74% yield) after one recrys-

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[1] C. P. Lo and W. J. Croxall, THIS JOURNAL, **76**, 4166 (1954).

[2] E. B. Knott, *J. Chem. Soc.*, 1482 (1954).

[3] It is interesting to note that among the six 5-alkoxymethylenerhodanines reported by us and the four by Knott prepared independently by the same method, only one compound, namely, 5-ethoxymethylene-3-phenylrhodanine, is described in both places. There is a good agreement in the m.p. and yield of this compound from the two sources.

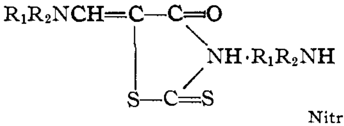
[4] 3-Substituted 5-alkylidene- and 5-aminomethylenerhodanines did not react with amines under the experimental conditions, indicating that the amines do not add to the double bond conjugated to the carbonyl group under these conditions.

[5] All melting points are uncorrected.

[6] F. B. Dains and S. I. Davis, *Kansas Univ. Sci. Bull.*, **15**, 265 (1924).

TABLE I

AMINE SALTS OF 5-AMINOMETHYLENERHODANINES



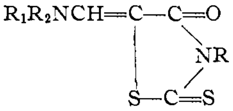
$R_1R_2NCH{=}C{-}C{=}O$ (ring: C–S–C(=S)–NH·R_1R_2NH)

R_1	R_2	Yield, %	M.p., °C.	Empirical formula	Nitrogen, % Calcd.	Nitrogen, % Found
H	t-C_8H_{17}[a]	14[b]	108–110	$C_{20}H_{39}N_3OS_2$	10.5	10.4
C_2H_5	C_2H_5	78	209–211	$C_{12}H_{23}N_3OS_2$	14.5	14.3
C_6H_{11}[c]	C_6H_{11}[c]	87[d]	170–172	$C_{28}H_{47}N_3OS_2$	8.3[e]	8.3[e]
$-CH_2CH_2CH_2CH_2CH_2-$[f]		92[d]	141–143[g]	$C_{14}H_{23}N_3OS_2$	13.4	13.6
$-CH_2CH_2OCH_2CH_2-$[h]		79	236–237[g]	$C_{12}H_{19}N_3O_3S_2$	13.2	13.0

[a] 1,1,3,3-Tetramethylbutyl. [b] The low yield of this product evidently was due to its solubility in acetone; for the isolation of the free rhodanine from a similar reaction mixture in good yield, see Table II. [c] Cyclohexyl. [d] Described in the text. [e] Calcd.: S, 12.7. Found: S, 12.7. [f] From piperidine. [g] With decomposition. [h] From morpholine.

TABLE II

5-AMINOMETHYLENERHODANINES



$R_1R_2NCH{=}C{-}C{=}O$ (ring: C–S–C(=S)–NR)

R_1	R_2	R	Method	Yield, %	Color	M.p., °C.	Empirical formula	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
t-C_8H_{17}[a]	H	H	C[b]	81	Yellow	175–176	$C_{12}H_{20}N_2OS_2$	10.3	10.1	23.5	23.8
C_6H_{11}[c]	H	H	A	47	Yellow	184–185	$C_{10}H_{14}N_2OS_2$	11.6	11.5	26.4	26.7
C_6H_5	H	H	A[b]	100	Yellow[d]	225–226[e]	$C_{10}H_8N_2OS_2$	11.9	11.5	27.1	27.0
C_2H_5	C_2H_5	H	B	85[f]	Orange[d]	212–213	$C_8H_{12}N_2OS_2$	13.0	12.9	29.6	29.6
n-C_4H_9	n-C_4H_9	H	D[b]	83.5	Yellow[g]	140–141	$C_{12}H_{20}N_2OS_2$	10.3	10.0	23.5	23.9
C_3H_5	C_3H_5	H	A	49	Orange[d]	157–157.5	$C_{10}H_{12}N_2OS_2$	11.7	11.5	26.6	27.2
$HOCH_2CH_2$	$OHCH_2CH_2$	H	D	91	Yellow	182–185[h]	$C_8H_{12}N_2O_3S_2$	11.3	10.9	25.8	25.6
C_6H_{11}[c]	C_6H_{11}[c]	H	B	92.5[f]	Yellow	236–236.5	$C_{16}H_{24}N_2OS_2$	8.7	8.6	19.8	19.6
$CH_2CH_2CH_2CH_2CH_2$[i]		H	B[b]	86[f]	Yellow[d]	253[h]	$C_9H_{12}N_2OS_2$	12.3	12.0	28.1	28.4
$CH_2CH_2OCH_2CH_2$[j]		H	B	95[f]	Orange[d]	265–266[h]	$C_8H_{10}N_2O_2S_2$	12.2	12.2	27.8	28.1
H	H	H	E[b]	50	Green	174–175	$C_5H_6N_2OS_2$	16.1	15.9	36.8	36.6
t-C_8H_{17}[a]	H	CH_3	F[k]	42.5	Green	144–145	$C_{13}H_{22}N_2OS_2$	9.8	9.8	22.4	22.7
n-C_4H_9	n-C_4H_9	CH_3	F[l]	92.5	Yellow[g]	87–88	$C_{13}H_{22}N_2OS_2$	9.8	9.9	22.4	22.4
CH_3	$HOCH_2CH_2$	CH_3	F[k]	52.5	Green	131–131.5	$C_8H_{12}N_2O_2S_2$	12.1	11.9	27.6	27.6
$HOCH_2CH_2$	$HOCH_2CH_2$	CH_3	F[k]	49	Gray	118–120	$C_9H_{14}N_2O_3S_2$	10.7	10.4	24.4	24.2
$CH_2CH_2CH_2CH_2CH_2$[i]		CH_3	F[k]	84	Yellow	170–172	$C_{10}H_{14}N_2OS_2$	11.6	11.3	26.5	25.9
i-C_9H_{19}[o]	$^1/_2(CH_2CH_2)$[o]	CH_3[o]	F[k]	65	Yellow	167–168[h]	$C_{20}H_{50}N_4O_2S_4$	9.0	8.8	20.5	20.9
C_6H_5	H	C_2H_5	F[m]	98	Yellow	182–184[n]	$C_{12}H_{12}N_2OS_2$	10.6	10.3	24.2	23.9
$CH_2CH_2CH_2CH_2CH_2$[i]		C_2H_5	F[k]	70	Yellow	150–151[p]	$C_{11}H_{16}N_2OS_2$	11.0	10.9	25.0	25.0
C_6H_5	H	C_6H_5	G[b]	73	Yellow	246–247[q]	$C_{16}H_{12}N_2OS_2$	9.0	8.9	20.5	20.5
C_7H_4NS[r]	H	C_6H_5	G[s]	40	Yellow	258–260[h]	$C_{17}H_{11}N_3OS_3$	11.4	11.3	26.0	26.0

[a] 1,1,3,3-Tetramethylbutyl. [b] Described in the text. [c] Cyclohexyl. [d] Recrystallized from acetic acid. [e] Dains and Davis[6] reported 248°. [f] Based on the amine salt of 5-aminomethylenerhodanine used. [g] Recrystallized from acetone and water. [h] With decomposition. [i] From piperidine. [j] From morpholine. [k] Acetone as reaction medium. [l] Petroleum ether as reaction medium. [m] Ethanol as reaction medium. [n] L. G. S. Brooker, G. H. Keyes, R. H. VanDyke, E. VanLare, G. VanZandt, F. L. White, H. W. J. Cressman and S. G. Dent, THIS JOURNAL, **73**, 5349 (1951), reported 184–186°. [o] This compound is N,N'-di-(2,2,4,4-tetramethylpentyl)-5,5'-ethylenebis-(aminomethylene-3-methylrhodanine). [p] G. H. Keyes, U. S. Patent 2,186,608 (1940), reported 150.5–152.5°. [q] Dains and Davis[6] reported 247°. [r] 2-Benzothiazolyl. [s] Ten minutes in boiling methyl isobutyl ketone. There was no reaction in boiling acetone.

tallization from ethanol decomposed at 224–225°. Further recrystallization from ethanol or acetic acid did not raise the m.p. A mixture of this and the above product gave no depression in m.p.

5-Acetanilidomethylenerhodanine.—The 5-anilinomethylenerhodanine obtained above (method A) (7 g.) was heated with acetic anhydride (60 ml.) and triethylamine (3 g.) on a steam-bath for ten minutes. The mixture was treated with water to decompose the excess of acetic anhydride. The yellow solid which separated was collected and recrystallized from ethanol. The 5-acetanilidomethylenerhodanine weighed 8 g. (97%) and decomposed at 248–249°.

A sample of 5-acetanilidomethylenerhodanine was prepared directly from the reaction of rhodanine, diphenylformamidine and acetic anhydride by the method of Sytnik.[7] The product decomposed at 248–249°.[8] A mixture of the two products decomposed at the same temperature.

Amine Salts of 5-Aminomethylenerhodanine.—Some amines react with 5-ethoxymethylenerhodanine to give solid amine salts of the corresponding 5-aminomethylenerhodanine. This is illustrated by the following example.

Piperidine Salt of 5-Piperidinomethylenerhodanine.—To a suspension of 5-ethoxymethylenerhodanine (19 g.) in acetone (60 ml.) was added piperidine (25 ml.). Heat was evolved and a clear solution was obtained. The crystals which separated upon cooling were collected, washed with acetone and air-dried. The piperidine salt of 5-piperidinomethylenerhodanine thus obtained was a yellow solid (29 g.) and melted at 141–143° dec.

The five solid amine salts of 5-aminomethylenerhodanines thus isolated are listed in Table I.

5-Piperidinomethylenerhodanine (Method B).—The above piperidine salt, when recrystallized from acetic acid or treated with a mixture of acetone and hydrochloric acid, yielded 5-piperidinomethylenerhodanine as a yellow solid, m.p. 253° dec.

Dicyclohexylamine Salt of 5-Ethoxymethylenerhodanine.—Dicyclohexylamine (45 ml.) was added to a solution of 5-

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[7] Z. P. Sytnik, I. I. Levkoev and M. V. Deichmeister, *J. Gen. Chem., USSR*, **21**, 768 (1951); *C. A.*, **45**, 9352 (1951).

[8] Literature value[7] 240–242°.

TABLE III

AMINE SALTS OF RHODANINES AND 2,4-THIAZOLIDINEDIONES

Rhodanine (Rh) or 2,4-thiazolidinedione (Th)	Amine	Yield, %	M.p., °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
Rh	$t\text{-}C_8H_{17}NH_2$[a]	89	150–152[b]	$C_{11}H_{12}N_2OS_2$	10.7	10.7	24.4	24.8
Rh	$(i\text{-}C_3H_7)_2NH$	88	140–142[b]	$C_9H_{18}N_2OS_2$	12.0	11.8	27.4	27.0
Rh	$C_5H_{10}NH$[c]	50	99–101[b]	$C_8H_{14}N_2OS_2$	12.8	12.3	29.4	29.6
Rh	$(C_2H_5)_3N$	77	102–104	$C_9H_{18}N_2OS_2$	12.1	11.9	27.4	27.4
5-Isopropylidene-Rh	$C_6H_{11}NH_2$[d]	71.5	134–135[b]	$C_{12}H_{20}N_2OS_2$	10.3	10.4	23.6	23.3
5-Isopropylidene-Rh	$C_5H_{10}NH$[c]	79	122–123[b]	$C_{11}H_{18}N_2OS_2$	10.9	10.6	24.8	24.5
5-Benzylidene-Rh	$C_6H_{11}NH_2$[d]	90	160[b]	$C_{16}H_{20}N_2OS_2$	8.8	8.7	20.0	20.0
5-Benzylidene-Rh	$C_5H_{10}NH$[c]	60	137[b]	$C_{15}H_{18}N_2OS_2$	9.2	9.0	20.9	20.9
Th	$C_6H_{11}NH_2$[d]	88	163–165	$C_9H_{16}N_2O_2S$	13.0	12.9	14.8	14.5
Th	$t\text{-}C_8H_{17}NH_2$[a]	85	138–139	$C_{11}H_{22}N_2O_2S$	11.4	11.3	13.0	12.6
Th	$C_5H_{10}NH_2$[c]	83	91–92	$C_8H_{14}N_2O_2S$	13.8	13.6	15.9	16.3
5-Benzylidene-Th	$C_6H_{11}NH_2$[d]	80	167–168	$C_{16}H_{20}N_2O_2S$	9.2	9.0	10.5	10.3
5-Benzylidene-Th	$C_5H_{10}NH$[c]	77	115–117	$C_{15}H_{18}N_2O_2S$	9.7	9.5	11.0	10.9

[a] 1,1,3,3-Tetramethylbutylamine. [b] With decomposition. [c] Piperidine. [d] Cyclohexylamine.

ethoxymethylenerhodanine (19 g.) in acetone (100 ml.). A reaction took place with evolution of heat and deposition of solid. After cooling, the solid was collected and washed with cold acetone. The dicyclohexylamine salt of 5-ethoxymethylenerhodanine was obtained as an orange solid (34.5 g., 93%) which decomposed at 153°.

Anal. Calcd. for $C_{18}H_{30}N_2O_2S_2$: N, 7.6; S, 17.3. Found: N, 7.6; S, 17.8.

This amine salt, upon treatment with acetic acid, yielded 5-ethoxymethylenerhodanine identified by m.p. and analysis.

Dicyclohexylamine Salt of 5-Dicyclohexylaminomethylenerhodanine.—A mixture of 5-ethoxymethylenerhodanine (19 g.), dicyclohexylamine (40 g.), and methyl isobutyl ketone (150 ml.) was heated under reflux for 2.5 hours. The solid which separated upon cooling was collected and air-dried. The dicyclohexylamine salt of 5-dicyclohexylaminomethylenerhodanine was obtained as an orange solid (44 g.) which melted at 170–172°.

5-(1,1,3,3-Tetramethylbutylaminomethylene)-rhodanine (Method C).—1,1,3,3-Tetramethylbutylamine (15.5 g.) was added to a mixture of 5-ethoxymethylenerhodanine (10 g.) and acetone (40 ml.). To this solution was added a solution of hydrochloric acid (7 g.) and water (10 ml.). The solid which separated upon cooling was collected and washed with aqueous acetone (1:1). The air-dried product was a yellow solid (11.7 g.), m.p. 175–176°.

5-Di-*n*-butylaminomethylenerhodanine (Method D).—Di-*n*-butylamine (15 g.) was added to a mixture of 5-ethoxymethylenerhodanine (10 g.) and petroleum ether (40 ml.). The heavy oil which formed was separated by decantation, dissolved in acetone and acidified with hydrochloric acid. The solid which separated was collected and washed with aqueous acetone (1:1). The 5-di-*n*-butylaminomethylenerhodanine thus obtained was a yellow solid (12 g.), m.p. 132–132.5°. After recrystallization from aqueous acetone it melted at 140–141°.

5-Aminomethylene-3-methylrhodanine (Method E).—5-Ethoxymethylene-3-methylrhodanine (30 g.) was added to an ethanolic ammonia solution (8 g. of anhydrous ammonia in 160 ml. of ethanol). The solid which separated upon cooling was collected and washed with acetone. The 5-aminomethylene-3-methylrhodanine was a green solid (13 g.), m.p. 174–175.°

3-Alkyl-5-aminomethylenerhodanines. General Procedure (Method F).—The 3-alkyl-5-ethoxymethylenerhodanine (0.10 mole) was dissolved or suspended in 100 ml. of the reaction medium (acetone, ethanol or petroleum ether). The amine (0.11 mole) was added. If a solution was not obtained, the mixture was warmed slightly on a steam-bath to a clear solution. The solid separated upon cooling was collected, washed with the proper solvent and air-dried.

5-Anilinomethylene-3-phenylrhodanine (Method G).—A mixture of 5-ethoxymethylene-3-phenylrhodanine (7 g.), aniline (3.5 g.), and methyl ethyl ketone (150 ml.) was heated under reflux on a steam-bath for 30 minutes. The product was isolated in the usual manner. It weighed 6 g. (73%) and melted at 246–247° (lit.[6] m.p. 247°).

If the above reaction was carried out in boiling acetone for 15 minutes, the product (m.p. 245–247°) was obtained in 39% yield (58.5% of crude 5-ethoxymethylene-3-phenylrhodanine, m.p. 145–165°, was recovered).

Amine Salts of Rhodanines and 2,4-Thiazolidinediones (General Procedure).—The amine (0.11 mole) was added to a solution or a suspension of rhodanine, 2,4-thiazolidinedione or their 5-alkylidene derivatives (0.10 mole) in acetone (100 ml.). Reaction took place with generation of heat and formation of a clear solution. (In some cases, slight warming of the mixture was necessary to bring forth a solution.) The crystalline amine salt which separated upon cooling was collected, washed with cold acetone and air-dried. The analytical sample was obtained by recrystallization from acetone.

The thirteen amine salts thus prepared are listed in Table III.

Treatment of the Amine Salts of Rhodanines and 2,4-Thiazolidinediones with Acid. A. With Acetic Acid.—Cyclohexylamine salt of 5-benzylidene-2,4-thiazolidinedione (1.5 g.) was dissolved in hot acetic acid (25 ml.). The solid separated upon cooling was identified as 5-benzylidene-2,4-thiazolidinedione by m.p. and mixture m.p. (247–249°). It weighed 0.96 g. (95%).

1,1,3,3-Tetramethylbutylamine salt of rhodanine when similarly treated with acetic acid yielded rhodanine (75%), m.p. 164–165°.

B. **With Hydrochloric Acid.**—The piperidine salt of 5-benzylidenerhodanine (1.35 g.) was dissolved in acetone and acidified with diluted hydrochloric acid (10%). The yellow solid isolated weighed 0.9 g. (92%) and was identified as 5-benzylidenerhodanine by m.p. and mixture m.p. (204–206°).

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