Several residues, formed by the spontaneous oxidation of a number of amine hydrosulfides, had been standing in open tubes for eight months. The residue from *n*-butylamine hydrosulfide was large in comparison with the others at hand. Recrystallization of this product from water yielded a white crystalline compound which began to sublime at 175° and melted with decomposition and charring at 180–193°.

Analysis for nitrogen and titration with standard iodine gave the following results. Subs., 0.3000, 0.3000: 11.23, 11.20 cc. of 0.2485 *N* HCl. Found: N, 10.93, 10.90. Calcd. for $(C_4H_9NH_3)_2S_2O_3$: N, 10.85. Subs., 0.1000: 38.86 cc. of *N*/100 iodine. Calcd. for $(C_4N_9NH_3)_2S_2O_3$: 38.90 cc.

The residues from *n*-propyl and methylamine hydrosulfides were extracted with water and the solutions evaporated to dryness. The amount of product in each case was too small to be analyzed quantitatively, but qualitative tests were positive for the thiosulfate ion. The residues from trimethyl and trimethylamine hydrosulfides proved to be entirely free sulfur.

Summary

The hydrosulfides of twelve of the simple amines have been described. These include the hydrosulfides of methyl-, ethyl-, *n*-propyl-, *n*-butyl-, *i*-amyl-, dimethyl-, diethyl-, di-*n*-propyl-,di -*n*-butyl-, dibenzyl-, trimethyl- and triethylamines.

The amine hydrosulfides undergo rapid oxidation upon exposure to air. Those derived from the more volatile amines leave an almost quantitative deposition of sulfur. Those derived from the less volatile amines are oxidized to the corresponding thiosulfates. These oxidation reactions take place without evidence of polysulfide formation. A mechanism is suggested for the oxidation reactions which fully accounts for all the facts observed.

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[CONTRIBUTION FROM THE EXPERIMENTAL RESEARCH LABORATORIES, BURROUGHS WELLCOME AND COMPANY]

RHODANINES. I. DERIVATIVES OF β-PHENYLETHYLAMINES

BY JOHANNES S. BUCK AND CLIFFORD S. LEONARD

RECEIVED APRIL 15, 1931 PUBLISHED JULY 8, 1931

Apparently no rhodanine derivatives of β-phenylethylamines have been described previously in the literature. The pharmacological properties of such compounds may prove interesting on account of their relation to compounds such as adrenaline, epinine, etc. On the other hand, they also contain the rhodanine (keto-thioketo-thiazolidine) ring, which, when alkylated in the methylene carbon, has been shown by Leonard[1] to possess pharmacological properties of the same type as the barbituric acid derivatives. The compounds described in the present paper contain an unsubstituted or an ether-substituted benzene ring and a non-alkylated

[1] Leonard, *Medd. Vetenskapsakad. Nobelinst.*, Bd. 4, No. 14 (1921).

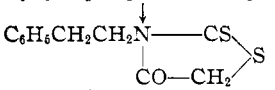
rhodanine ring. On account of their low solubility in water, they would probably not be of practical use in pharmacology. The authors are endeavoring to remedy this defect in solubility by (a) introducing hydroxyl groups in place of the ether groups, and (b) by modifying the rhodanine ring. The introduction of hydroxyl groups into the benzene ring would bring the compounds very close to the chemical type of epinine.

The preparation of the compounds here described is a relatively simple matter. The β-phenylethylamine is condensed with ammonia and carbon bisulfide to the ammonium dithiocarbamate[2] and this is then condensed, by means of potassium chloroacetate, to the dithiocarbamineglycolic acid.[3] This, on warming with dilute acetic acid, gives the rhodanine. The isolation of the dithiocarbamineglycolic acid may be omitted, and the rhodanine obtained directly by heating the dithiocarbamate with potassium chloroacetate, acidified with acetic acid.

Another method is to form the phenylethylammonium dithiocarbamate by treating the amine with carbon bisulfide. On heating this with potassium chloroacetate acidified with acetic acid, the rhodanine is produced. The steps may be shown as follows

$C_6H_5CH_2CH_2NHCSSNH_4$ Ammonium dithiocarbamate type

$C_6H_5CH_2CH_2NHCSSCH_2COOH$ Dithiocarbamineglycolic acid type



Rhodanine type

$C_6H_5CH_2CH_2NHCSSNH_3CH_2CH_2C_6H_5$ β-phenylethylammonium dithiocarbamate type

Four series of compounds, derived from β-phenylethylamine, homoanisylamine, homopiperonylamine and homoveratrylamine are described. One compound, the dithiocarbamineglycolic acid from homoveratrylamine, could not be obtained in the pure state, as it spontaneously passes into the rhodanine.

Experimental

Ammonium Dithiocarbamates.—One mole of the amine, dissolved in twice its volume of absolute alcohol, is treated with one mole of ammonia (satd. aqueous soln.). Slightly more than one mole of carbon bisulfide is then slowly added, the mixture being cooled in ice throughout the above operations. After standing for a few hours the solid is filtered off and washed on the filter with alcohol and ether, and is then sufficiently pure. Recrystallization may be carried out by adding ether to a cold alcoholic solution, when the compound is obtained in the form of shiny leaves. Recrystallization, however, is not advisable on account of the instability of the compounds in solution. The yields are good. The ammonium dithiocarbamates are well-crystallized compounds, soluble in the cold in water, alcohol, acetic acid and ammonium hydroxide. They give colorless solutions in cold sulfuric acid, with the exception of the homopiperonyl derivative, which

[2] Hann, THIS JOURNAL, **47**, 1998 (1925).

[3] Holmberg, *J. prakt. Chem.*, [2] **79**, 253 (1909).

gives a deep claret color. The compounds are sparingly soluble in warm chloroform and moderately soluble in warm acetone. On melting, they froth violently.

β-Phenylethylammonium Dithiocarbamates.—The amine, dissolved in twice its volume of absolute alcohol, is cooled in ice, and one-half its volume of carbon bisulfide added slowly, with stirring. After standing for a few hours, the product is filtered off and washed with alcohol and ether and recrystallized by adding ether to the cold alcoholic solution. The compounds form well-defined crystals, soluble in warm water, alcohol, chloroform and acetone and soluble in the cold in acetic acid and in sulfuric acid. Only the homopiperonylamine derivative gives a color with the latter (deep red). The yields are excellent. On melting, pronounced frothing takes place.

Dithiocarbamineglycolic Acids.—The preparation of these compounds is simple. The ammonium dithiocarbamate is dissolved in a little warm water, and treated with a solution of an equal weight of chloroacetic acid which has been accurately neutralized with potassium bicarbonate. A white magma rapidly forms. After one hour the mixture is diluted with water and made slightly acid with acetic acid. The white, crystalline precipitate which forms is filtered off and washed on the filter with water. Although stable when dry, it is not possible to recrystallize the compounds. The dithiocarbamineglycolic acids are fairly soluble in water, the solution decomposing when heated. They are soluble in cold alcohol, acetic acid, ammonium hydroxide and ether and moderately soluble in cold chloroform. With cold concd. sulfuric acid, only the homopiperonyl compound gives a color (deep crimson). All attempts to prepare a homoveratryl derivative resulted in the isolation of products containing the corresponding rhodanine, formed by loss of water and cyclization. On melting, the acids froth violently.

Rhodanines.—The rhodanines are readily obtained by heating an aqueous solution of the ammonium or phenylethylammonium dithiocarbamate with an aqueous solution of potassium chloroacetate, made acid with acetic acid, on the water-bath for thirty minutes. They are also formed by warming the dithiocarbamineglycolic acid with dilute acetic acid. The rhodanines are best recrystallized from alcohol, in which they are moderately or readily soluble when heated. They are practically insoluble in water, very soluble in cold chloroform and acetone, soluble in warm acetic acid and insoluble in ammonium hydroxide. The rhodanines, when pure, are quite stable, but liquors and impure solutions soon develop red colors. For brevity, the individual compounds are tabulated.

TABLE I

AMMONIUM DITHIOCARBAMATES

Ammonium ( )-dithiocarbamate	Formula	Appearance	M. p., °C.	Formula	Analyses, N, % Calcd.	Found
N-β-phenylethyl-	$C_6H_5CH_2CH_2NHCSSNH_4$	Large, transparent plates	132, froth.	$C_9H_{14}S_2N_2$	13.08	12.72
N-[3,4-dimethoxy-β-phenylethyl]-	$(CH_3O)_2C_6H_3CH_2CH_2NHCSSNH_4$	White, stout irreg. prisms	138, froth.	$C_{11}H_{18}O_2S_2N_2$	10.21	10.17
N-[4-methoxy-β-phenylethyl]-	$CH_3OC_6H_4CH_2CH_2NHCSSNH_4$	White, pearly leaves (plates)	139, froth.	$C_{10}H_{16}OS_2N_2$	11.47	11.66
N-[3,4-methylenedioxy-β-phenylethyl]-	$CH_2O_2C_6H_3CH_2CH_2NHCSSNH_4$	White, cryst. powder (prisms)	138, froth.	$C_{10}H_{14}O_2S_2N_2$	10.85	10.96

TABLE II

β-PHENYLETHYLAMMONIUM DITHIOCARBAMATES

Name and structure, ( )-dithiocarbamate	Appearance
β-Phenylethylammonium-N-β-phenylethyl- $C_6H_5CH_2CH_2NHCSSNH_3CH_2CH_2C_6H_5$	White, tiny, glittering plates
3,4-Dimethoxy-β-phenylethylammonium-N-[3,4-dimethoxy-β-phenylethyl]- $(CH_3O)_2C_6H_3CH_2CH_2NHCSSNH_3CH_2CH_2C_6H_3(OCH_3)_2$	White, powdery crystals
4-Methoxy-β-phenylethylammonium-N-[4-methoxy-β-phenylethyl]- $CH_3OC_6H_4CH_2CH_2NHCSSNH_3CH_2CH_2C_6H_4OCH_3$	White, felted needles
3,4-Methylenedioxy-β-phenylethylammonium-N-[3,4-methylenedioxy-β-phenylethyl]- $CH_2O_2C_6H_3CH_2CH_2NHCSSNH_3CH_2CH_2C_6H_3CH_2O_2$	Faint buff, tiny prisms

Formula	M. p., °C.	Analyses, N, % Calcd.	Found
$C_{17}H_{22}S_2N_2$	130, froth.	8.81	8.85
$C_{21}H_{30}O_4S_2N_2$	124, froth.	6.39	6.66
$C_{19}H_{26}O_2S_2N_2$	135, froth.	7.41	7.37
$C_{19}H_{22}O_4S_2N_2$	133, froth.	6.90	7.09

TABLE III

DITHIOCARBAMINEGLYCOLIC ACIDS

-Dithiocarbamineglycolic acid	Structure	Appearance
N-[β-Phenylethyl]-	$C_6H_5CH_2CH_2NHCSSCH_2COOH$	Felted, pearly leaves
N-[3,4-Dimethoxy-β-phenylethyl]-	$(CH_3O)_2C_6H_3CH_2CH_2NHCSSCH_2COOH$	Not isolable in pure state
N-[4-Methoxy-β-phenylethyl]-	$CH_3OC_6H_4CH_2CH_2NHCSSCH_2COOH$	Bulky, tiny leaves
N-[3,4-Methylenedioxy-β-phenylethyl]-	$CH_2O_2C_6H_3CH_2CH_2NHCSSCH_2COOH$	Chalky, cryst. mass

M. p., °C.	Formula	Analyses, N, % Calcd.	Found
125, froth.	$C_{11}H_{13}O_2S_2N$	5.49	5.43
.....	$C_{13}H_{17}O_4S_2N$	..	..
128, froth.	$C_{12}H_{15}O_3S_2N$	4.91	5.14
132, froth.	$C_{12}H_{13}O_4S_2N$	4.68	4.88

TABLE IV

RHODANINES

-2-Thioketo-4-keto-thiazolidine	Structure	Appearance
3-[β-Phenylethyl]-	$C_6H_5CH_2CH_2\underline{NCSSCH_2CO}$	Pale yellow flat needles
3-[3,4-Dimethoxy-β-phenylethyl]-	$(CH_3O)_2C_6H_3CH_2CH_2\underline{NCSSCH_2CO}$	Pale yellow pearly leaves
3-[4-Methoxy-β-phenylethyl]-	$CH_3OC_6H_4CH_2CH_2\underline{NCSSCH_2CO}$	Pale yellow flat needles
3-[3,4-Methylenedioxy-β-phenylethyl]-	$CH_2O_2C_6H_3CH_2CH_2\underline{NCSSCH_2CO}$	Pale flesh-colored tiny nodules

TABLE IV (*Concluded*)

M. p., °C.	Cold H_2SO_4	Formula	Analyses, % Calcd. C	H	S	N	Found C	H	S	N
107	No color	$C_{11}H_{11}OS_2N$	55.67	4.67	27.00	5.91	55.82	4.68	27.35	6.05
154	Intense yellow	$C_{13}H_{15}O_3S_2N$	52.50	5.09	21.55	4.71	52.56	5.25	21.52	4.92
106	No color	$C_{12}H_{13}O_2S_2N$	53.91	4.91	23.97	5.24	54.06	4.98	23.71	5.47
126	Intense yellow	$C_{12}H_{11}O_3S_2N$	51.23	3.94	22.77	4.98	51.15	4.09	22.82	5.31

The authors are indebted to Mr. W. S. Ide for the analyses (all micro) given above.

Summary

The ammonium dithiocarbamates, phenylethylammonium dithiocarbamates, dithiocarbamineglycolic acids and rhodanines derived from β-phenylethylamine, homoanisylamine, homopiperonylamine and homoveratrylamine are described, together with their preparations.

TUCKAHOE, NEW YORK

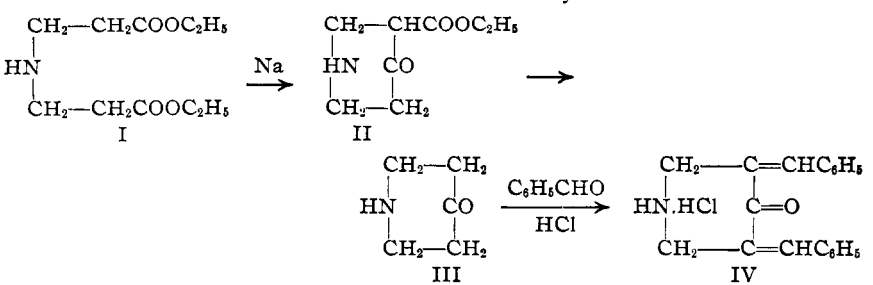
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

PIPERIDINE DERIVATIVES. XI. 3-CARBETHOXY-4-PIPERIDONE AND 4-PIPERIDONE HYDROCHLORIDE

BY GLEN M. KUETTEL AND S. M. McELVAIN

RECEIVED APRIL 18, 1931 PUBLISHED JULY 8, 1931

In an effort to prepare 4-piperidone, Ruzicka and Fornasir[1] carried out an internal acetoacetic ester condensation of β,β¹-dicarbethoxydiethylamine. No attempt was made to isolate the intermediate 3-carbethoxy-4-piperidone. The reaction mixture containing this latter compound was subjected directly to reaction conditions which would bring about its hydrolysis and decarboxylation. The resulting 4-piperidone was not obtained in the form of a crystalline salt and since the free base appeared to be quite unstable it was isolated in the form of the hydrochloride of the dibenzal derivative. These transformations may be illustrated as follows



[1] Ruzicka and Fornasir, *Helv. Chim. Acta*, **3**, 806 (1920).