

ture at 213°) and had an $[\alpha]_D^{20}$ -33° (E. Späth and R. Göhring¹⁰ indicate -34.5° in water and a decomposition point of 217–218°).

From *dl*-mandelic amide, *dl*-ephedrine was obtained. The hydrochloride melted with decomposition at 183° (E. Späth and R. Göhring¹⁰ indicate a decomposition point of 188–189.5).

Anal. Subs., 5.050 mg.: 0.295 cc. N (740 mm. 20°). Calcd.: N, 6.97. Found: N, 6.72.

The salt was dissolved in absolute alcohol and dry barium hydroxide added. When the barium-free filtrate was mixed with petroleum ether, the free base began to crystallize out; m. p. 74.5°. Späth and Göhring indicate 73–74°.

Anal. Subs., 2.4 mg.: 0.183 cc. N (740 mm. 20°). Calcd.: N, 8.48. Found: N, 8.38.

Summary

l-Ephedrine has been synthesized from *d*-mandelic acid and the the configuration at the carbinol group shown.

MADISON, WISCONSIN, AND HEIDELBERG, GERMANY

[A CONTRIBUTION FROM THE CHEMICAL LABORATORIES, UNIVERSITY OF MISSOURI]

SOME REACTIONS OF DI-HALOGEN BARBITURIC ACIDS

BY DOROTHY NIGHTINGALE AND ARTHUR EDWARD SCHAEFER

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The 5,5-di-halogen barbituric acids have been known since 1864, but there is relatively little in the literature concerning their reactions. Baeyer¹ observed that there was a difference in the reactivity of the two halogens in 5,5-dibromobarbituric acid and states that one bromine is more readily replaced than the other. Trzcinski² reports the reaction of dibromobarbituric acid with thiourea and with potassium or ammonium thiocyanate. Whiteley³ prepared the hydrazone of 1,3-diphenylalloxan from 5,5-dibromo-1,3-diphenylbarbituric acid and phenylhydrazine. Biltz and Hamburger⁴ developed a method for the preparation of monobromobarbituric acid from the dibromobarbituric acid and ammonia.

These facts suggested the possibilities of reactions of various classes of nitrogen compounds, such as amines, carbazides, acid amides, etc., not only with the dibromobarbituric acid but also with the corresponding dichloro derivative.

Since one molecule of thiourea or one molecule of phenylhydrazine reacts with the dibromobarbituric acid with the elimination of two molecules of hydrogen bromide, it was expected that primary amines would

¹⁰ Späth and Göhring, *Monatsh.*, **41**, 319 (1920).

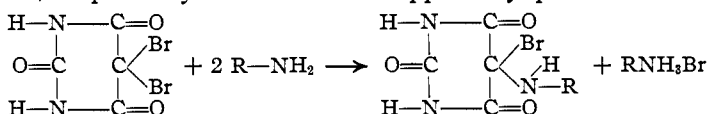
¹ Baeyer, *Ann.*, **130**, 33 (1864).

² Trzcinski, *Ber.*, **16**, 1057 (1883).

³ Whiteley, *J. Chem. Soc.*, **91**, 1334 (1907).

⁴ Biltz and Hamburger, *Ber.*, **49**, 635 (1916).

react similarly. However, only one bromine was found to react with either primary or secondary amines to form a 5-bromo-7-R- or a 5-bromo-7-R₂-uramil, respectively. The reaction apparently proceeds as follows



Alcohol was used as the solvent for the reaction. If the amine is added directly to the dibromobarbituric acid, a vigorous reaction occurs with charring and some tar formation.

Dibromobarbituric acid reacted normally with α -naphthylhydrazine, forming the α -naphthylhydrazone of alloxan. The 4,4-diphenyl semicarbazide and dibromobarbituric acid react readily to form a diphenyl semicarbazone of alloxan.

Other compounds which reacted with dibromobarbituric acid were formamide, formanilide and benzyl formate, but the results could not be interpreted satisfactorily.

As might be expected, dichlorobarbituric acid was relatively unreactive. In alcohol solution it did not react with any of the amines except benzyl and dibenzyl amines, but if the primary amine was added directly to the dichloro acid, a moderate reaction occurred with the formation of a dark gummy mass which would not yield crystals. It reacted with α -naphthylhydrazine and with 4,4-diphenyl semicarbazide.

Experimental

The condensation products of primary and secondary amines with dibromobarbituric acid are easily prepared. For the most part they are nearly colorless crystalline compounds, though some of them have a tendency to turn pink on standing. They are soluble in water, somewhat soluble in hot alcohol and insoluble in other usual organic solvents. Alkali decomposes them with the liberation of the amine. All of the condensation products were analyzed quantitatively for nitrogen and a quantitative bromine analysis was made on typical members of each series.

The reactions of ethylamine and of diethylamine with dibromobarbituric acid are typical of the reactions of the amines with the dihalogen barbituric acids.

5-Bromo-7-ethyl-uramil.—Seven grams (1 mol) of dibromobarbituric acid are dissolved in the smallest amount of hot alcohol. To this is added 3.6 g. (2 moles) of ethylamine. The ethylamine used was a 33% solution in water. The mixture was warmed and stirred vigorously. After a few minutes a pink crystalline solid separated from the solution. The crystals were collected on a Büchner funnel and washed with hot alcohol to remove any amine salt or dibromobarbituric acid. After repeated washing with warm alcohol, the melting point of the crystals was found to be 185° with decomposition. The compound shrinks at 180°; yield 3.5 g. or 57%; soluble in cold water and hot alcohol, insoluble in ether, benzene, acetone and chloroform.

5-Bromo-7-diethyl-uramil.—Four grams (2 mols) of diethylamine was added with stirring to an alcoholic solution of seven grams (1 mol) of dibromobarbituric acid. After warming the reaction mixture for a few minutes, almost colorless fine needles separated rapidly. They were collected on a Büchner funnel and washed with warm alcohol to remove any contaminating amine salt or unchanged dihalogen barbituric acid. The purified product melted with decomposition at 167–168°; yield, 5 g., or 74%; soluble in cold water and hot alcohol, insoluble in ether, benzene, chloroform and acetone.

These procedures were used with all of the other primary and secondary amines listed in Table I.

TABLE I
SUMMARY OF THE REACTION PRODUCTS OF PRIMARY AMINES AND DIBROMO
BARBITURIC ACID

Amine	M. p. of product, °C. ^a	Nitrogen analyses, %	
		Calcd.	Found
Ethyl	185	16.80	16.96
Methyl	175–176	17.79	17.85
Butyl	178	15.10	14.84
Allyl	179–180	16.03	16.20
Benzyl	186	13.46	13.75
Ethanol	159	15.78	16.03
Diethyl	167–168	15.10	15.11
<i>n</i> -Dipropyl	216	13.72	13.95
<i>n</i> -Diamyl	Chars at 273	11.59	11.72
Diisoamyl	304	11.59	11.69
Dibenzyl	242	10.65	10.44

^a All melting points are with decomposition.

TABLE II
HALOGEN ANALYSES (THOMPSON AND OAKDALE)

Amine	Calcd.	Bromine analyses, %	
		Calcd.	Found
Ethyl	32.00		31.97
Ethanol	30.07		30.17
Diethyl	28.77		28.90
Benzyl	25.63		25.10
Dibenzyl	19.90		19.81

Benzylamine and Dibenzylamine with Dichlorobarbituric Acid.—These amines react readily with dichlorobarbituric acid, but the solubilities of the condensation products and the amine hydrochlorides are so similar that it was not possible to separate the hydrochlorides completely from the condensation products.

Butylaniline, isoamylaniline and diphenylamine did not react with either of the di-halogen barbituric acids even after long boiling of the alcohol solution.

Aromatic amines such as aniline, methylaniline, dimethylaniline, the toluidines, etc., when added to the halogen barbituric acids gave a dark tarry oil which would not yield crystals.

Alloxan α -Naphthylhydrazone.—A glacial acetic acid solution of 3.4 g. of α -naphthylhydrazine was added to 5 g. of dibromobarbituric acid dissolved in the smallest amount of hot glacial acetic acid. The mixture was boiled gently for a few minutes, then cooled to room temperature and poured into water. The brick red crystals which separated were collected on a Büchner funnel and washed with hot alcohol; melting

point, 264°, yield, 4 g. or 85%. The compound contains no bromine, is slightly soluble in hot alcohol, acetone and chloroform, and is insoluble in benzene, water and ether.

Anal. (Modified Kjeldahl). Calcd. for $C_{14}H_{10}N_3O_4$: N, 19.85. Found: N, 19.06.

The product formed in the same way from dichlorobarbituric acid and α -naphthylhydrazine was identical, melting at 264°. A melting point of mixtures of the two products was also 264°.

Dibromobarbituric Acid and 4,4-Diphenyl Semicarbazide.—A hot alcohol solution of 4 g. of dibromobarbituric acid was added to 3.2 g. of 4,4-diphenyl semicarbazide dissolved in alcohol. After warming the solution for a few minutes, 4 g. of a fine yellow powder separated, which after recrystallizing melted at 267°, with decomposition. It contained no bromine.

Anal. (Dumas) Calcd. for $C_{17}H_{13}N_3O_4$: N, 19.93. Found: N, 19.95.

This semicarbazone of alloxan is soluble in hot alcohol and insoluble in the other usual organic solvents.

Dichlorobarbituric acid reacted slowly with 4,4-diphenyl semicarbazide under the same conditions, but was expected to give the same semicarbazone of alloxan. However, the orange-yellow product, insoluble in alcohol and containing chlorine, was apparently a mixture which could not be purified. It contained 20.17% of nitrogen (Dumas) and 8.25% chlorine.

Summary

1. Further evidence is presented showing that one halogen in the 5,5-dihalogen barbituric acids is more reactive than the other.
2. Dibromobarbituric acid reacts readily with primary and secondary amines with the loss of one molecule of hydrogen bromide.
3. Dichlorobarbituric acid is much less reactive than the dibromo compound, reacting readily only with benzylamines.

COLUMBIA, MISSOURI

[CONTRIBUTION FROM THE CHEMICAL INSTITUTE OF THE PETROGRAD ACADEMY OF SCIENCE]

FORMATION OF NAPHTHENIC ACIDS¹

BY A. D. PETROV AND I. Z. IVANOV

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The mechanism of the formation of naphthenic acids present in petroleum is explained by two theories. According to C. Engler² naphthenic acids could have been formed² by cracking and cyclization of unsaturated fatty acids, which are considered as one of the original substances from which petroleum was formed, or³ by oxidation of naphthenes and polynaphthenes with air. G. Kraemer and Weger³ are in favor of the first theory from their experiments with acids from montan wax, while Kharichkov⁴ prefers the

¹ Translated from the manuscript, by K. T. Steik.

² Engler, "Das Erdoel," Vol. I, 1911, p. 452.

³ Kraemer and Weger, *Chem.-Ztg.*, **31**, 675-77, 734 (1907); *Chem. Zentr.*, II, 734 (1907).

⁴ Kharichkov, *J. Russ. Phys.-Chem. Soc.*, **40**, 1757 (1908); *Chem. Abstracts*, **3**, 1761 (1909).