

hydrolytic products an aldobionic acid precipitable by basic lead acetate. Since in our work the sugar solution was purified by repeated precipitation with 95% ethyl alcohol, such an acid might have been overlooked. Ehrlich and von Sommerfeld⁹ report a di-uronic acid obtained by the hydrolysis of pectinic acid. This acid appeared as an insoluble mass in the hydrolysate. In our work a very small amount of insoluble matter was observed in the acid solution after hydrolysis and this material apparently did possess acidic properties. However, the method of hydrolysis used was more drastic than that employed by either Heidelberger and Goebel or Ehrlich and von Sommerfeld, as it was desired to obtain only the products of complete hydrolysis. If compounds of either of these types were present, they must have constituted only a small part of the products of hydrolysis.

Summary

Glucuronic acid has been identified as a constituent of the gum produced by the root nodule bacteria of pea and red clover. The gum was subjected to acid hydrolysis and the glucuronic acid separated from the hydrolysis products as the barium salt. The *p*-bromophenylosazone of this salt had the melting point and the barium and the nitrogen content required for this derivative of glucuronic acid.

The sugar produced by hydrolysis of the gum of the pea bacteria was crystallized, and its specific rotation agreed with that of glucose. In the case of the sugar from the gum of the red clover bacteria, crystallization could not be effected. However, the phenylosazone of this sugar possessed the melting point and the nitrogen content required for phenylglucosazone.

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THE MIGRATION OF ACYL FROM SULFUR TO NITROGEN

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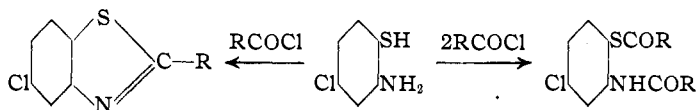
The work of Raiford,¹ from a study of sixteen different substituted *o*-aminophenols, has shown that when the radicals acetyl and benzoyl are introduced, identical diacyl derivatives are obtained regardless of the order of introduction. This clearly involves a migration of acyl between oxygen and nitrogen during acylation. The present investigation was undertaken to determine whether a similar migration of the radicals acetyl and benzoyl would take place between sulfur and nitrogen in an *o*-aminothiophenol.

The base employed, 2-amino-4-chloro-thiophenol is readily prepared and isolated in the form of the hydrochloride, by reducing 4,4'-dichloro-2,2'-

⁹ F. Ehrlich and R. von Sommerfeld, *Biochem. Z.*, **168**, 263 (1926).

¹ See papers of Raiford, *THIS JOURNAL* (1919-1926).

dinitrodiphenyldisulfide with tin and hydrochloric acid. The acylation of the hydrochloride in dimethylaniline, with acetic anhydride or benzoyl chloride easily could be controlled to give either the diacyl derivative or benzothiazole. Heating the mixture at the temperature of the water-bath gave a smooth conversion to the diacyl derivative; upon boiling the mixture, however, only benzothiazole was obtained.²



2-Benzoylamino-4-chlorothiophenol and 2-acetylamino-4-chlorothiophenol, upon drying for several hours in a desiccator or upon recrystallization from alcohol, were completely converted into the corresponding benzothiazoles.³ Hofmann⁴ prepared 2-phenylbenzothiazole by heating *o*-aminothiophenol hydrochloride with benzoyl chloride. He called attention to the probable formation of the *N*-benzoyl derivative as an intermediate product but did not isolate it. Reissert⁵ upon saponifying 2-benzoylamino-4-chlorothiophenol thiobenzoate obtained a product which upon recrystallization from alcohol proved to be 2-phenylbenzothiazole. He reports no melting point for the crude product. It is probable that the initial product was the *N*-benzoyl derivative, which upon recrystallization formed the benzothiazole.

2-Benzoylamino-4-chlorothiophenol gave upon treatment with acetyl chloride a different diacyl derivative from that obtained by treating 2-acetylamino-4-chlorothiophenol with benzoyl chloride. This shows that no migration of acyl occurs during acylation.

Saponification of the two isomeric benzoyl acetyl derivatives gave the same product, 2-benzoylamino-4-chlorothiophenol, which was identified in one case as the corresponding benzothiazole. This shows that the benzoyl radical displaces acetyl from nitrogen upon saponification of 2-acetylamino-4-chlorophenyl thiobenzoate.

Experimental

2-Amino-4-chlorothiophenol Hydrochloride.—4,4'-Dichloro-2,2'-dinitrodiphenyldisulfide prepared by the method of Blanksma⁶ was suspended in five times its weight of alcohol and reduced with tin and hydrochloric acid. The best yields were obtained by stirring the mixture at a temperature of about 70°. Above this temperature a por-

² A further study of the acylation of this base has been made and will be reported in a later communication.

³ Mills and Whitworth, *J. Chem. Soc.*, 2738 (1927), have found that 2-cinnamoylaminothiophenol may be recrystallized from alcohol unchanged.

⁴ Hofmann, *Ber.*, 12, 2365 (1879).

⁵ Reissert, *ibid.*, 38, 3431 (1905).

⁶ Blanksma, *Rec. trav. chim.*, 20, 131 (1901).

tion of the aminothiophenol was further reduced, with the liberation of hydrogen sulfide. The resulting solution was filtered, the filtrate evaporated to about one-third its volume, and the hot solution treated with an equal volume of concentrated hydrochloric acid. Upon cooling, the hydrochloride separated out, contaminated with tin salts. It was purified by reprecipitation from alcohol with hydrochloric acid. It separated in firm colorless or straw colored needles; yield, 55-60%.⁷ That this product is 2-amino-4-chlorothiophenol hydrochloride was shown by the fact that it is soluble in cold aqueous alkali, and by the analysis for sulfur.

Anal. Calcd. for $C_6H_5NCl_2S$: S, 16.34. Found: S, 16.27.

The hydrochloride was converted into the free base by the action of an excess of ammonium carbonate solution. The free base separated as a light yellow precipitate, m. p. 198-201° with decomposition.⁸ Upon oxidation with ferric chloride it is converted into 4,4'-dichlorodi-*o*-thioaniline, m. p. 118-119°.⁹ The free base is very rapidly oxidized by the air to the alkali-insoluble disulfide.

2-Phenyl-5-chlorobenzothiazole.—One gram of 2-amino-4-chlorothiophenol hydrochloride was dissolved in 8 cc. of dimethylaniline and 1.2 g. of benzoyl chloride added. The mixture was boiled for thirty minutes. The thiazole was precipitated with dilute hydrochloric acid. It separated as colorless plates, insoluble in dilute alkali; yield, 1.2 g. Upon recrystallization from alcohol it separated in small colorless plates of m. p. 139°.

Anal. Calcd. for $C_{13}H_9NCIS$: S, 13.05. Found: S, 13.26.

2-Methyl-5-chlorobenzothiazole.—This product resulted when the hydrochloride was treated with acetic anhydride by the method described above. The benzothiazole was extracted from the acidified solution with ether. One gram of hydrochloride gave 0.5 g. of benzothiazole, m. p. 65-67°. Upon recrystallization from alcohol it separated in thin colorless plates melting at 68-69°.

Anal. Calcd. for C_8H_8NCIS : S, 17.45. Found: S, 17.36.

2-Benzoylamino-4-chlorophenyl Thiobenzoate.—A mixture of 1 g. of 4-chloro-2-aminothiophenol hydrochloride, 1.8 g. of benzoyl chloride and 5 cc. of dimethylaniline was heated on a water-bath for ten minutes. The dibenzoyl derivative was precipitated by hydrochloric acid; 1.35 g. of product melting at 140-154° was obtained. It was recrystallized from a mixture of benzene and alcohol from which it separated in colorless plates of m. p. 158-159°.

Anal. Calcd. for $C_{20}H_{14}SNClO_2$: S, 8.72. Found: S, 9.07.

2-Benzoylamino-4-chlorothiophenol.—0.74 g. of 2-benzoylamino-4-chlorophenyl thiobenzoate was saponified by allowing it to stand at room temperature with an excess of potassium hydroxide in alcohol. Upon diluting with water and acidifying, the mono-benzoyl derivative separated as a crystalline white solid, which upon drying melted at 105-106°; yield, 0.45 g. This compound was soluble in dilute aqueous sodium hydroxide and was precipitated unchanged on acidifying.

Anal. Calcd. for $C_{13}H_{10}ONClS$: S, 12.11. Found: S, 12.29.

Upon recrystallization from alcohol or ether this substance was completely converted into the alkali insoluble 2-phenyl-5-chlorobenzothiazole, m. p. 139°.

2-Acetylamino-4-chlorophenyl Thioacetate.—One and four-tenths grams of 2-amino-4-chlorothiophenol hydrochloride and 2.0 cc. of acetic anhydride were treated

⁷ The hydrochloride has a pronounced vesicant action upon the skin.

⁸ Hodgson and Wilson, *J. Chem. Soc.*, 127, 443 (1925), report 120° as the melting point.

⁹ Hodgson and Wilson, Ref. 8, report a melting point of 116° for this substance.

as described under benzylation of the base: 1.4 g. of product melting at 149–150° was obtained. It was recrystallized from alcohol, from which it separated as soft white needles melting at 150–151°.

Anal. Calcd. for $C_{10}H_{10}O_2NCl$: S, 13.17. Found: S, 12.90.

2-Acetylamino-4-chlorothiophenol.—One gram of 2-acetylamino-4-chlorophenyl thioacetate upon saponification with potassium hydroxide in alcohol gave 0.6 g. of monoacetyl derivative, m. p. 92–94°. This product was soluble in dilute sodium hydroxide solution and was precipitated unchanged on acidifying.

Anal. Calcd. for C_8H_8ONClS : S, 15.90. Found: S, 15.74.

This substance upon recrystallizing from alcohol separated in colorless plates, m. p. 68–69°. When melted with a sample of 2-methyl-4-chlorobenzothiazole the mixture melted without depression.

2-Acetylamino-4-chlorophenyl Thiobenzoate.—0.72 g. of 2-acetylamino-4-chlorothiophenol upon benzylation in dimethylaniline with 0.70 g. of benzoyl chloride gave 1.05 g. of product melting at 137–142°. Upon recrystallization from alcohol it separated in soft colorless needles of m. p. 141–142°.

Anal. Calcd. for $C_{18}H_{18}O_2NCIS$: S, 10.49. Found: S, 10.55.

2-Benzoylamino-4-chlorophenyl Thioacetate.—0.58 g. of 2-benzoylamino-4-chlorothiophenol and 1.0 g. of acetyl chloride were dissolved in a few drops of dimethylaniline and the mixture heated for ten minutes on a water-bath. Upon acidifying, the diacetyl derivative was precipitated: 0.55 g. of product melting at 108–116° was obtained. Upon recrystallization from alcohol it separated as long colorless needles melting at 129–130°. A mixture of this material with the isomeric 2-acetylamino-4-chlorophenyl thiobenzoate melted at 108–116°, showing that they are different substances.

Anal. Calcd. for $C_{18}H_{18}O_2NCIS$: S, 10.49. Found: S, 10.84.

Saponification of 2-Acetylamino-4-chlorophenyl Thiobenzoate.—Eight-tenths gram of this substance was saponified with excess potassium hydroxide in alcohol. The monoacetyl derivative obtained melted at 60–90° and was soluble in cold aqueous sodium hydroxide. Upon recrystallization from alcohol it melted at 138–139°. When melted with a sample of 2-phenyl-5-chlorobenzothiazole, m. p. 139°, the mixture melted at 138–139°, showing the identity of the two substances.

Saponification of 2-Benzoylamino-4-chlorophenyl Thiobenzoate.—0.46 g. of this substance upon saponifying with excess potassium hydroxide in alcohol gave 0.16 g. of product melting at 89–93°. Upon purifying by reprecipitating from aqueous sodium hydroxide it melted at 100–102°. A mixture of this product with 2-benzoylamino-4-chlorothiophenol melted without depression.

Summary

1. N-Acyl derivatives of 2-amino-4-chloro-thiophenol have been prepared. These lose water very readily to form the corresponding benzothiazoles.

2. No rearrangement of acetyl and benzoyl between sulfur and nitrogen occurs upon acylation of the N-acyl derivative of the *o*-aminothiophenol. This is unlike the typical behavior of an *o*-aminophenol.

3. Upon saponification of 2-acetylamino-4-chlorophenyl thiobenzoate a migration of benzoyl from sulfur to nitrogen occurs.