tained in about 80% yields. The substances proved to be identical with that made by the condensation of *p*-nitrobenzoyl chloride with γ-hydroxypropylpiperidine.

Summary

1. β-Piperidylethyl and γ-piperidylpropyl *p*-aminobenzoates, β-(β-carbomethoxypiperidyl)-ethyl and γ-(β-carbomethoxypiperidyl)-propyl *p*-aminobenzoates have been prepared.

2. They are all local anesthetics, the substituted piperidyl derivatives being less effective than the unsubstituted.

3. *p*-Aminobenzoyl-γ-hydroxypropylpyridonium bromide had no anesthetic properties.

Urbana, Illinois

[Contribution from the Chemical Laboratories of Columbia University, No. 542]

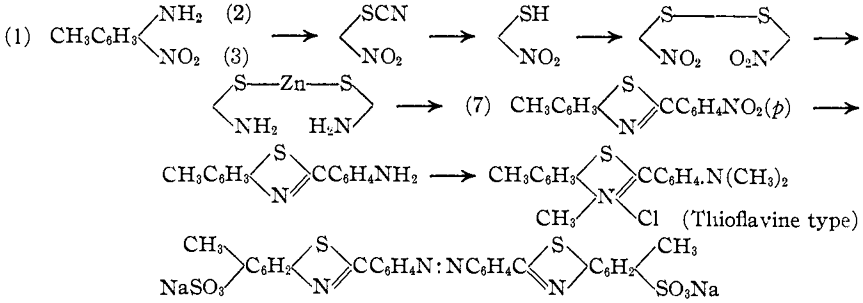
RESEARCHES ON THIAZOLES. XII. THE SYNTHESIS OF NEW ISOMERS OF DEHYDROTHIO-PARA-TOLUIDINE AND OF SOME RELATED COMPOUNDS: THE CONNECTION BETWEEN CHEMICAL CONSTITUTION AND TINCTORIAL PROPERTIES IN THE THIOFLAVINE AND CHLORAMINE YELLOW GROUPS[1]

By Marston Taylor Bogert and Roger William Allen

Received February 15, 1927 Published May 10, 1927

Introduction

Following up recent work from this Laboratory on dehydrothio-*p*-toluidine,[2] and on its 5-methyl isomer,[3] we have now completed the synthesis of other new isomers, carrying the methyl and amino groups in different positions. For the production of the isomer with the methyl group in Position 7, the following reactions were employed.



(Chloramine Yellow type)

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[1] Presented in abstract before the Dye Division of the American Chemical Society, at the Richmond Meeting, April, 1927.

[2] (a) Bogert and Meyer, This Journal, **44**, 1568 (1922). (b) Bogert and Snell, *Color Trade J.*, **14**, 109 (1924). (c) Bogert and Bergeim, *Proc. Nat. Acad. Sci.*, **10**, 318 (1924); (d) *Color Trade J.*, **15**, 63 (1924).

[3] Bogert and Allen, *Ind. Eng. Chem.*, **18**, 532 (1926).

For the conversion of the nitrotoluidine into the corresponding thiocyano derivative by the diazo reaction, cobalt chloride was used as catalyst instead of cuprous thiocyanate, following the recommendation of Korczynski,[4] and gave excellent results.

From the 2-(*p*-aminophenyl)-7-methyl-benzothiazole by sulfonation and hypochlorite oxidation, a direct cotton yellow dye, analogous to Chloramine Yellow (Colour Index No. 814) was prepared, whose physical, chemical and tinctorial properties varied but slightly from those of the Chloramine Yellow itself. Hence, it seems to make but little difference in compounds of this type whether the methyl group is carried in Positions 5, 6 or 7. Of the three isomers, the depth of shade obtained in direct cotton dyeings decreases as the methyl group is moved in the direction 5 ⟶ 6 ⟶ 7 although, as just stated, the differences are but slight.

All of these dye tests were carried out as described by Bogert and Bergeim[2d] in their article on Columbia Yellow, or as recommended by Knecht, Rawson and Lowenthal.[5]

By direct methylation of the 5- and 7-methyl isomers, thioflavines were prepared analogous to Thioflavine T (Colour Index No. 815), and here again the three isomeric thioflavines exhibited a striking similarity in physical, chemical and tinctorial properties. Comparative dyeings upon silk indicated that the position of the methyl group, at least so far as Positions 5, 6 and 7 are concerned, was of almost negligible influence upon the shade.

None of these dyed cotton directly, but imparted to silk beautiful, fluorescent, greenish-yellow shades, which resembled one another very closely, the depth of shade almost imperceptibly decreasing, according to the location of the methyl groups, in the order 5 ⟶ 6 ⟶ 7, the 5-methyl being clearly of deeper shade than its 7-methyl isomer. After-treatment with dil. sulfuric acid caused all these dyeings to assume a more greenish tone, at the expense of the yellow, and generally increased somewhat their fluorescent appearance. All showed approximately the same fastness to light and to washing.

To discover to what extent the position of the amino group influenced the tinctorial properties of these thioflavines, 2-(*o*- and *m*-aminophenyl)-5- and 7-methyl-benzothiazoles were synthesized, converted into the corresponding thioflavines, and dyeing tests upon silk carried out with the latter. These dyeings compared favorably in fastness with those obtained with Thioflavine T, but differed decidedly from the latter in other tinctorial properties, showing clearly that in dyes of this type the position of the amino is a much more important factor than that of the methyl group.

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[4] Korczynski, *Compt. rend.*, **171**, 182 (1920). Korczynski, Kniatowna and Kaminski, *Bull. soc. chim.*, **31**, 1179 (1922).

[5] Knecht, Rawson and Lowenthal, *Manual of Dyeing*, **2**, 747 (1925).

When the amino group occupied the *para* position, the shade produced on silk was a fluorescent, brilliant greenish-yellow, as already noted. With the amino group in the *ortho* position, however, the dyeings were a paler and duller yellow, with little fluorescence. In the *meta* position, the amino group appeared to exert a bathochromic influence, the greenish tinge of the *ortho* isomers being replaced by a reddish one. As with the *ortho* isomers, the dyeings with the *meta* compounds were still duller and paler, with but little or no fluorescence, and were rendered still paler by after-treatment with dil. sulfuric acid.

All of the thioflavine dyeings were carried out with 1 g. of pure white silk, 20 cc. of 0.1% dye solution (0.02 g. of dye), 25 cc. of water, 10 cc. of neutral 2% soap solution, 5 cc. of 2% sodium chloride solution; the silk was entered lukewarm and the bath kept at a simmer for half an hour.

Although we had encountered no difficulty in the conversion of 3-nitro-4-iodotoluene into the 2-nitro-4-methylphenyl disulfide,[3] the reaction failed completely when applied to the 3-nitro-2-iodo and 2-nitro-3-iodo isomers. If the non-reactivity of the 2-iodo derivative be ascribed to steric hindrance, some other explanation must be found for the similar behavior of the 3-iodo isomer.

The syntheses of the isomers carrying the methyl group in Position 4 as yet are uncompleted, due largely to the cost of preparing an adequate quantity of 2-nitro-3-aminotoluene and the difficulties encountered in the hydrolysis of the thiocyano derivative obtained therefrom. Because of the withdrawal of the junior author, however, the results secured to date are reported in this paper.

Experimental Part

2,3-Dinitrotoluene.—The method used by Sandmeyer[6] for the preparation of nitrobenzene from aniline was applied to the conversion of the 2-amino-3-nitrotoluene into the dinitro compound by the action of cuprous oxide upon the diazonium salt.

A suspension of 14.7 g. of 2-amino-3-nitrotoluene in a hot solution of 15.5 cc. of concd. sulfuric acid and 15 cc. of water was cooled to 0° and treated drop by drop with 7 g. of sodium nitrite dissolved in 25 cc. of water, while the mixture was vigorously agitated. After standing for five minutes, the slight amount of unchanged initial material was filtered off and the filtrate treated with 19 g. of anhydrous sodium carbonate dissolved in a small amount of water, adding the carbonate very slowly to the well-cooled solution of the diazo salt. After the evolution of carbon dioxide had ceased, a solution of 10 g. of sodium nitrite in a little water was added, and this caused the color of the solution to change immediately from a light yellow to light red. The solution was then poured at once over a previously prepared paste of cuprous oxide[7]

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[6] Sandmeyer, *Ber.*, 20, 1494 (1887).

[7] This was obtained by adding a solution of 40 g. of sodium hydroxide in 120 cc. of water to a boiling solution of 100 g. of copper sulfate and 30 g. of glucose in 200 cc. of water, then neutralizing with acetic acid and allowing the mixture to cool.

moistened with a little water. Evolution of nitrogen occurred in the cold and dinitrotoluene separated as a brown solid. The dinitro compound was freed from cuprous oxide by extraction with alcohol, and the crude product obtained by concentration of these extracts. After repeatedly decolorizing and crystallizing the crude product from alcohol, it formed nearly colorless, minute needles and scales; m. p., 63° (corr.); yield, 7 g., or 40%. This melting point agrees with that reported by Rozanski,[8] who obtained the product by a different method.

2-Nitro-3-aminotoluene.—The 2,3-dinitro compound was reduced partially with an absolute alcohol solution of stannous chloride saturated with dry hydrogen chloride, following the method employed by Burton and Kenner.[9] Recrystallized from a 1:1 mixture of petroleum ether and benzene, it formed beautiful orange-red prisms, m. p. 108° (corr.), in agreement with the value recorded by them; yield, 42%.

3-Nitro-2-aminotoluene was prepared from aceto-*o*-toluidide by nitrating it at low temperature with a mixture of fuming nitric and glacial acetic acids, following the method of Reverdin and Crépieux.[10] The melting point of the purified crystalline orange product was 96° (corr.); yield, 35%. Reverdin and Crépieux give the melting point as 96°.

2-Nitro-3-iodotoluene was prepared by diazotizing the corresponding nitrotoluidine, according to the method used by Willgerodt and Simonis[11] for the production of the 3-nitro-4-iodotoluene from the corresponding nitrotoluidine; yield, 80%. It crystallized from alcohol in pale, yellowish, short, thick prisms, m. p. 65° (corr.), in agreement with the figure reported by Wheeler and Liddle,[12] who prepared it by a different method.

By the action of ferrous hydroxide, this compound was reduced to the 2-amino-3-iodotoluene, but the yield was so low that the method was abandoned.

3-Nitro-2-iodotoluene was prepared by diazotization of 3-nitro-2-aminotoluene, following the method of Wheeler and Liddle;[13] yield, 77%. Our product crystallized from alcohol in pale yellow leaflets, m. p. 68° (corr.), in practical agreement with the melting point of 67–68° recorded by them.

3-Nitro-4-iodotoluene was obtained from the corresponding nitrotoluidine (m. p., 116°) by the method of Willgerodt and Simonis,[11] in sheaves of pale yellow needles; m. p., 55° (as given by them); yield, 80%.

2-Nitro-3-thiocyanotoluene was prepared by the method described beyond for the 3-nitro-2-thiocyano isomer. It was obtained in beautiful long, pale yellow, silky needles; m. p., 86° (corr.); yield, 68%.

Anal. Calcd. for $C_8H_6O_2N_2S$: C, 49.46; H, 3.12. Found: C, 49.33; H, 3.28.

Because of the instability of the cobalt chloride diazonium precipitate in this case and the ease with which it gave up its nitrogen, we could not work safely with more than 3 or 4 g. at a time.

Attempts to hydrolyze satisfactorily this thiocyano derivative to the disulfide by methods entirely similar to those used for its isomers, proved futile. When 2 *N* sodium hydroxide solution was used in the cold, it failed to hydrolyze the compounds whereas, when the reaction mixture was warmed, decomposition ensued. A very small quantity of yellow needles, m. p. 159° (corr.), was obtained from the decomposition product, but they were not identified.

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[8] Rozanski, *Ber.*, **22**, 2681 (1889).

[9] Burton and Kenner, *J. Chem. Soc.*, **119**, 1051 (1921).

[10] Reverdin and Crépieux, *Ber.*, **33**, 2498 (1900).

[11] Willgerodt and Simonis, *Ber.*, **39**, 269 (1906).

[12] Wheeler and Liddle, *Am. Chem. J.*, **44**, 138 (1910).

[13] Wheeler and Liddle, *ibid.*, **42**, 451 (1909).

3-Nitro-2-thiocyanotoluene was prepared from the nitrotoluidine by the use of a modified diazo reaction employing cobalt chloride as catalyst following the recommendation of Korczynski.[4] The following is a typical experiment.

A suspension of 7.4 g. of 3-nitro-2-aminotoluene in a hot solution of 7.8 cc. of concd. sulfuric acid and 7.5 cc. of water was cooled to 0° and diazotized with a cold solution of 3.5 g. of sodium nitrite in 12 cc. of water, added drop by drop with vigorous stirring. After standing for five minutes, the slight excess of the original nitrotoluidine was filtered off and a cold solution of 9.5 g. of anhydrous sodium carbonate in 25 cc. of water was added in small portions to the filtrate, after which addition of further amounts of carbonate should give no further evolution of carbon dioxide. A solution of 15 g. of potassium thiocyanate dissolved in a little water was then added and the mixture poured with good stirring into a solution of 6.6 g. of cobalt chloride dissolved in 25 cc. of water. A dark green, sticky precipitate separated which gradually decomposed with loss of nitrogen when the mixture was warmed at 100°. The thiocyano derivative separated as an oil which solidified on cooling and was purified by repeated crystallizations from alcohol, when it appeared in long, pale yellow needles; m. p., 45.5° (corr.); yield, 7.5 g., or 80%.

Anal. Calcd. for $C_8H_6O_2N_2S$: C, 49.46; H, 3.12. Found: C, 49.55; H, 3.18.

3-Nitro-4-thiocyanotoluene, obtained from 3-nitro-4-aminotoluene in a manner entirely similar to that employed for the preparation of the 2-thiocyano isomer, crystallized from alcohol in lustrous yellow laminas, m. p. 125° (corr.), in agreement with the figure reported by Zincke and Röse,[14] and by Challenger and Collins,[15] who prepared it by different methods; yield, 81%.

2-Nitro-3-methylphenyl Disulfide.—The experiments conducted for the production of this disulfide from 2-nitro-3-iodotoluene, or 2-nitro-3-aminotoluene, were similar in all respects to those described beyond for the production of the isomeric 2-nitro-6-methylphenyl disulfide from 3-nitro-2-iodotoluene or 3-nitro-2-aminotoluene, and were equally unsuccessful.

2-Nitro-4-methylphenyl Disulfide was obtained in a manner entirely analogous to that used for the preparation of the 6-methylphenyl isomer outlined beyond. It crystallized from glacial acetic acid in yellow needles; m. p., 175° (corr.); yield, 75%. This compound was obtained first by Zincke and Röse,[16] from the nitrochlorotoluene and sodium disulfide, and was subsequently prepared by Bogert and Allen[3] in a similar manner.

An intimate mixture of the products obtained from the two different processes likewise melted at 175° (corr.). Zincke and Röse[14] recorded a melting point of 176° for their product.

2-Nitro-6-methylphenyl Disulfide.—The method of Hugo Bauer[17] was followed, the thiocyano compound being hydrolyzed with caustic alkali to the thiophenol. The latter then oxidized in the air to the disulfide which was purified by crystallization from glacial acetic acid. Pale yellow, lustrous laminas were obtained; m. p., 149° (corr.); yield, 42%.

Anal. Calcd. for $C_{14}H_{12}O_4N_2S_2$: C, 49.98; H, 3.57. Found: C, 49.69; H, 3.64.

Repeated efforts to produce this disulfide from 3-nitro-2-iodotoluene by digestion

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[14] Zincke and Röse, *Ann.*, **406,** 111 (1914).

[15] Challenger and Collins, *J. Chem. Soc.*, **125,** 1379 (1924).

[16] Ref. 14, p. 108.

[17] Bauer, *Ber.*, **46,** 92 (1913).

with sodium disulfide in boiling ethyl or amyl alcohol solution for five hours proved fruitless.

Graebe and Mann[18] have shown that when hydrogen sulfide or ammonium sulfide acts upon a solution of a diazonium salt, the nitrogen is slowly evolved at ordinary temperatures with formation of the monosulfide in good yield. We therefore applied this reaction to the neutral solution of the diazonium salt prepared from the 3-nitro-2-aminotoluene, substituting aqueous solutions of the sodium or ammonium disulfide for the monosulfides, and carrying out the reaction at 0° in the presence of cracked ice, but the desired product was not obtained.

2-Amino-6-methylphenyl Mercaptan.—The zinc salt was prepared by a method entirely similar to that used in this Laboratory for the reduction of other nitro disulfides and described in previous papers.[2,3] It formed a pale, clay-colored, microcrystalline product; yield, 93%.

Anal. Calcd. for $C_{14}H_{16}N_2S_2Zn$: C, 49.26; H, 4.75. Found: C, 49.60; H, 4.83.

2-Amino-6-methylphenyl Disulfide was obtained from the zinc salt of the corresponding mercaptan by the method of Bogert and Snell[19] and, after crystallization and decolorization, appeared in lustrous yellow needles and scales; m. p., 127° (corr.); yield, 70%.

Anal. Calcd. for $C_{14}H_{16}N_2S_2$: C, 60.82; H, 5.83. Found: C, 60.70; H, 5.93.

Nitro- and Aminotoluthiazoles

The derivatives which follow carry a methyl group in Position 5 or 7 of the benzothiazole nucleus, and a nitro or amino group in the *ortho*, *meta* or *para* position on the 2-phenyl group.

To economize space, yields of pure products, their corrected melting points and analytical results are given in Table I.

TABLE I

NITRO- AND AMINOTOLUTHIAZOLES

Position of CH_3	Substit. on 2-C_6H_5	Yield, %	M. p., °C., (corr.)	Analysis C, %		H, %	
				Calcd.	Found	Calcd.	Found
5	*o*-NO_2	32	91–92	62.22	62.48	3.73	3.95
5	*m*-NO_2	53	185	62.22	62.34	3.73	3.61
7	*o*-NO_2	35	108.5	62.22	62.81	3.73	3.90
7	*m*-NO_2	50	181	62.22	62.84	3.73	3.89
7	*p*-NO_2	64	209	62.22	62.09	3.73	3.88
5	*o*-NH_2	54	154	70.0	70.15	5.0	5.05
5	*m*-NH_2	69	179	70.0	69.65	5.0	5.04
7	*o*-NH_2	54	83	70.0	69.52	5.0	5.13
7	*m*-NH_2	73	132	70.0	70.04	5.0	5.04
7	*p*-NH_2	80	171	70.0	70.13	5.0	5.13

2-(*o*-Nitrophenyl)-5-methyl-benzothiazole, $C_{14}H_{10}O_2N_2S$.—To a solution of 2 g. of zinc 2-amino-4-methylphenyl mercaptide in 200 cc. of hot glacial acetic acid, 1.7 g. of *o*-nitrobenzaldehyde was added and a gentle stream of hydrogen sulfide passed into the hot solution for two hours, after which the solution was filtered, decolorized, diluted with an equal volume of hot water and allowed to cool. The yellow, gummy precipitate was crystallized repeatedly from alcohol and yielded pale yellow needles and scales.

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[18] Graebe and Mann, *Ber.*, **15**, 1683 (1882).

[19] Bogert and Snell, THIS JOURNAL, **46**, 1308 (1924).

2-(*m*-Nitrophenyl)-5-methyl-benzothiazole.—Zinc 2-amino-4-methylphenyl mercaptide (2 g.) and *m*-nitrobenzoyl chloride (2.5 g.) were ground up together and the mixture was heated at 100° for an hour, giving a viscous mass which solidified to a hard cake as it cooled. This cake was pulverized and warmed for 30 minutes with 1 *N* sodium hydroxide solution, to remove unchanged initial materials. The insoluble portion was crystallized from glacial acetic acid and gave fine, short, colorless needles.

2-(*o*-Nitrophenyl)-7-methyl-benzothiazole was prepared in exactly the same way as the 5-methyl isomer. Crystallized repeatedly from glacial acetic acid and from alcohol, it was obtained in pale yellow, lustrous scales.

2-(*m*-Nitrophenyl)-7-methyl-benzothiazole, prepared from the appropriate zinc mercaptide and *m*-nitrobenzoyl chloride, as described for the 5-methyl isomer, formed fine, short, colorless needles.

2-(*p*-Nitrophenyl)-7-methyl-benzothiazole, from the zinc amino mercaptide and *p*-nitrobenzoyl chloride, after decolorization and crystallization from alcohol, appeared in pale yellow, short needles.

2-(*o*-Aminophenyl)-5-methyl-benzothiazole.—To a solution of 1.5 g. of the nitro derivative in 100 cc. of hot glacial acetic acid, 5 g. of zinc dust was added gradually during two minutes, in such manner that the solution boiled gently. Reduction was rapid and the hot, colorless solution was filtered, the filtrate concentrated to 50 cc., decolorized and crystallized twice from glacial acetic acid and then twice from alcohol. Pale yellow, lustrous, short needles were obtained.

The product dissolved in hot glacial acetic acid, and hot ethyl or amyl alcohol, but was much less soluble in benzene. It was reprecipitated from its solution in concd. hydrochloric acid by dilution. Its alcohol solution possessed a barely perceptible violet fluorescence, far less than that noted with the *p*-amino isomer.

2-(*m*-Aminophenyl)-5-methyl-benzothiazole; Dehydrothio-*m*-toluidine.—A mixture of 1.7 g. of the nitro derivative, 10 cc. of concd. hydrochloric acid, 90 cc. of water and 10 g. of granulated tin was boiled for three hours, the clear solution filtered hot and allowed to cool. A precipitate separated. The liquid containing the precipitate was made strongly alkaline with 4 *N* sodium hydroxide solution, warmed for 30 minutes, then cooled and filtered. The insoluble portion, crystallized from alcohol, formed pale, pinkish, short, glassy needles.

Its alcohol solution exhibited a very faint, greenish fluorescence. In other respects, it closely resembled the 2-(*o*-aminophenyl)-5-methyl isomer.

2-(*o*-Aminophenyl)-7-methyl-benzothiazole, prepared by reduction of the nitro compound in glacial acetic acid solution with zinc dust, as described for the 5-methyl-2-(*o*-aminophenyl) isomer, and purified by crystallization from glacial acetic acid and from alcohol, formed glassy, yellowish, flat needles, which resembled its 5-methyl isomer closely in physical and chemical properties.

2-(*m*-Aminophenyl)-7-methyl-benzothiazole, obtained from the nitro derivative by reduction with tin and hydrochloric acid, as described for the 2-(*m*-aminophenyl)-5-methyl isomer, crystallized from alcohol in nearly colorless, minute, short, felted hairs.

Its alcohol solution exhibited a very faint, greenish fluorescence, and in other respects also it resembled the 5-methyl isomer closely.

2-(*p*-Aminophenyl)-7-methyl-benzothiazole, prepared by reduction of the nitrothiazole with hydrochloric acid and tin, as outlined for the foregoing isomers, when crystallized from 50% alcohol and decolorized, formed dull, opaque, short, clay-colored needles.

It exhibited a beautiful violet fluorescence in alcoholic solution, and was soluble in hot amyl alcohol or in glacial acetic acid, but only sparingly in benzene. From its solution in concd. hydrochloric acid it was precipitated by dilution with water.

The Thioflavine from 2-(*o*-Aminophenyl)-5-methyl-benzothiazole was obtained by methylation under pressure as outlined beyond for the *p*-aminophenyl isomer, and appeared as a yellow crystalline product; yield, 38%.

It was easily soluble in water or alcohol. Its solution in concd. sulfuric acid exhibited a pale green fluorescence, much paler than that observed with the *p*-amino isomers from either the 5- or 7-methyl derivatives. Its dyeings on silk were likewise much paler than these *p*-amino isomers, as was also the fluorescence of these dyeings, although equally fast to light and washing. After-treatment of these dyeings with dil. sulfuric acid rendered them still paler, but did not noticeably increase their fluorescence.

The Thioflavine from 2-(*m*-Aminophenyl)-5-methyl-benzothiazole was obtained as a dark yellow, crystalline solid; yield, 0.2 g., from 0.4 g. of the amino derivative.

It was easily soluble in water or alcohol. Its solution in concd. sulfuric acid possessed a very slight, greenish fluorescence. The dyeings on silk were very pale yellow, with a reddish rather than a greenish tone and with scarcely any perceptible fluorescence. After-treatment with dil. sulfuric acid rendered these dyeings still paler, without developing any appreciable fluorescence. Their fastness to light and washing appeared to be approximately the same as that of the other thioflavines described.

The Thioflavine from 2-(*p*-Aminophenyl)-5-methyl-benzothiazole.—The aminothiazole was methylated by heating it with methanol and hydrochloric acid under pressure, following in the main the specifications of the original Cassella patent[20] for the manufacture of Thioflavine T.

A mixture of 2.4 g. of the aminothiazole, 3 g. of methanol and 1 g. of concd. hydrochloric acid was heated for 12 hours at 160–170°. The cooled tube then contained a mass of crystals, presumably the chloride of the methylated base. These crystals were boiled for a short time with 50 cc. of water, the solution was filtered, the filtrate warmed to 70° and sodium chloride added. As the solution cooled, the dye separated in yellow leaflets; yield, 2.1 g., or 66%.

It was readily soluble in water or alcohol. Its solution in concd. sulfuric acid possessed a dark green fluorescence. In sodium hydroxide solution, it gave a white, flocculent precipitate which dissolved in an excess of the alkali. Silk was dyed a brilliant greenish-yellow, scarcely distinguishable from the dyeings obtained when the same percentage of Thioflavine T was used. After-treatment with dil. sulfuric acid increased both the greenish tone and the fluorescence.

The Thioflavines from 2-(*o*-, *m*- and *p*-Aminophenyl)-7-methyl-benzothiazole were prepared in exactly the same manner as the 5-methyl isomer, and in physical, chemical and tinctorial properties were scarcely distinguishable from the latter.

The Chloramine Yellow Analog from 2-(*p*-Aminophenyl)-7-methyl-benzothiazole.—The process followed was the usual one of sulfonation followed by hypochlorite oxidation.

The sulfonation was accomplished by the use of fuming (50%) sulfuric acid upon the thiazole moistened with a little concd. sulfuric acid, maintaining the temperature for eight hours at 40–50°. The solution was then cooled and poured upon ice, when the product separated as a bright yellow solid.

For further purification this product was dissolved in water and converted into its sodium salt, the aqueous solution of the latter being then oxidized with a freshly prepared solution of sodium hypochlorite. The solution, which was at first nearly colorless, gradually became a deep reddish-yellow as the oxidation proceeded. The dye was precipitated by the addition of sodium chloride, and was then collected, washed with salt solution until free from hypochlorite, and dried. As thus prepared, it formed a brown powder which dissolved freely in water and dyed unmordanted cotton a bright yellow of a shade scarcely distinguishable from that produced with Chloramine

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[20] Cassella and Co., Ger. pat. 51,738 (1890); *Friedländer*, **2**, 299 (1891).

Yellow itself, although apparently somewhat paler for the same percentage of dye per gram of fabric. It was likewise fast to alkalies, acids and light, and insoluble in alcohol or in strong caustic alkali. Its solution in concd. sulfuric acid was a deep reddish-brown.

2-(*p*-Hydroxyphenyl)-5-methyl-benzothiazole.—To a solution of 2 g. of zinc 2-amino-4-methylphenyl mercaptide in 200 cc. of hot glacial acetic acid, there was added 1.4 g. of *p*-hydroxybenzaldehyde, and a gentle stream of hydrogen sulfide was passed through the solution for two hours. The hot solution was filtered, the filtrate decolorized, diluted with an equal volume of water and allowed to cool. Colorless, glassy, minute, short needles separated; m. p., 281° (corr.); yield, 1.7 g., or 61%.

Anal. Calcd. for $C_{14}H_{11}ONS$: C, 69.71; H, 4.56. Found: C, 69.39; H, 4.65.

2-(*p*-Hydroxyphenyl)-7-methyl-benzothiazole, prepared from the zinc 2-amino-6-methylphenyl mercaptide by the process just described, crystallized in nearly colorless leaflets; m. p., 232° (corr.); yield, 55%.

Anal. Calcd. for $C_{14}H_{11}ONS$: C, 69.71; H, 4.56. Found: C, 69.76; H, 4.68.

Summary

1. Five new isomers of dehydrothio-*p*-toluidine, carrying their methyl and amino groups in other positions, have been synthesized and studied.

2. From these new bases, new thioflavines have been prepared, analogous to Thioflavine T (Colour Index No. 815), but with their nuclear methyl and amino groups in different positions, and the effect of these changes upon tinctorial properties has been noted.

3. From the 2-(*p*-aminophenyl)-7-methyl-benzothiazole, by the usual sulfonation and hypochlorite oxidation, an isomer of Chloramine Yellow (Colour Index No. 814) has been obtained, which is scarcely distinguishable from it in physical, chemical or tinctorial properties.

4. In the course of the investigation, the following other new compounds were prepared and examined: 2-nitro- and 2-amino-6-methylphenyl disulfide, 2-amino-4- and 6-methylphenyl mercaptans (zinc salts), 3-nitro-2-thiocyano- and 2-nitro-3-thiocyanotoluenes, 2-(*o*-, *m*- and *p*-nitrophenyl)-5- and 7-methyl-benzothiazoles, 2-(*p*-hydroxyphenyl)-5- and 7-methyl-benzothiazoles.

NEW YORK, N. Y.