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RESEARCHES ON THIAZOLES. II. 2-PARA-TOLYL-BENZOTHIAZOLE, DEHYDROTHIO-PARA-TOLUIDINE, AND SOME RELATED COMPOUNDS

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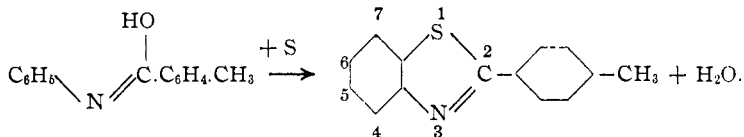
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Introductory

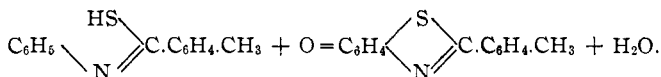
2-Phenyl-benzothiazole is remarkable for its very agreeable odor, which resembles that of tea roses or the rose geranium, a fact which led to its being called "Rosenkoerper" by the earlier workers in this field.

In searching for an explanation of this fragrance, so unexpected and so unusual in an organic sulfide, we have prepared and studied the corresponding 2-*p*-tolyl compound, and find that it has a somewhat similar but very much fainter aroma. An isomer, 6-methyl-2-phenyl-benzothiazole, is recorded in the literature¹ but no mention is made of its possessing any noteworthy or characteristic odor.

The first method utilized for the synthesis of the 2-*p*-tolyl-benzothiazole was one entirely analogous to that employed by Hofmann and others² for the production of 2-phenyl-benzothiazole, and consisted in fusing *p*-tolanilide with sulfur, with or without naphthalene.³



The yields were so poor, however, that the method was abandoned and recourse had to the process of Jacobsen⁴ which depends upon the action of mild oxidizing agents upon the appropriate thio-anilide.



Using an aqueous solution of potassium ferricyanide as the oxidizing agent upon an alkaline solution of the thio-anilide, the thiazole sought was obtained in yields of 60–65%.

With fuming nitric acid, or with a mixture of conc. nitric and conc. sulfuric acids, the new thiazole is easily nitrated, and the resulting mono-nitro derivative can be reduced without difficulty to the corresponding amine, but the position of these groups in the molecule remains to be deter-

¹ *Ber.*, **14**, 493 (1881); **22**, 424, 1065 (1889).

² Hofmann, *et al.*, *ibid.*, **12**, 2360 (1879); **13**, 1225 (1880); **14**, 493 (1881); **22**, 424, 1065 (1889); etc.

³ Ger. pat., 53,938; Friedlaender, **2**, 293 (1890).

⁴ *Ber.*, **19**, 1069 (1886).

mined. Various azo dyes were prepared from the amino thiazole, and certain of the secondary disazo products showed good tinctorial power and fastness on unmordanted cotton.

As is well known, when a mixture of *p*-toluidine and sulfur is heated at 180–250°, the chief products are dehydrothio-*p*-toluidine and primuline. In the earlier years of their history, primuline was considered the more valuable component of the melt, on account of its extensive use and low price. To-day, however, the situation is reversed, and dehydrothio-*p*-toluidine is the more important, since from it are prepared such useful dyes as Columbia Yellow, thioflavine T, etc., and primuline has lost much of its former market, because of its fugitive character in the light. Some further work has, therefore, been undertaken with dehydrothio-*p*-toluidine and with compounds closely related thereto.

When subjected to the Skraup reaction, dehydrothio-*p*-toluidine behaves like a normal aromatic primary amine, and gives the corresponding quinoline. This quinoline, on its part, showed characteristic quinoline behavior, adding methyl iodide directly, and giving a deep purple-red product when a mixture of this methiodide and that of quinaldine was treated with caustic alkali.

An effort to prepare a cinchophen (atophan) from the dehydro base proved fruitless, although various modifications of the usual methods were tried.

It has been found that 2,4-dihydroxy-quinoline couples on the fiber with diazotized primuline to give an azo dye which colors unmordanted cotton orange, and that this dyeing is fast to light, acids and washing.⁵ Inasmuch as benzoylene urea (2,4-dihydroxy-quinazoline) is so closely related structurally to the above dihydroxy-quinoline, we tested it also as a coupler for diazotized primuline on the fiber under exactly the same conditions, and discovered that the azo compound so formed dyes unmordanted cotton a yellow-brown, of good fastness to acids, alkalies or bleach, but too fugitive to light to be of any commercial value.

Experimental

2-*p*-Tolyl-benzothiazole, $C_8H_4 \begin{array}{c} \diagup S \\ \diagdown N \end{array} C_6H_4.CH_3$.—*p*-Tolanilide was prepared from

p-toluyl chloride by the method of Fischli,⁶ and melted sharply at 145°. Fusion of this anilide with sulfur, in presence or absence of naphthalene, gave unsatisfactory results, so the method was dropped, and the Jacobsen method utilized with a few modifications.

Thio-*p*-tolanilide was obtained from phenyl-isothiocyanate, by a process based upon that of Friedmann and Gattermann⁷ using 15. g. of the isothiocyanate, 30 g. of

⁵ Ger. pat., 210,453; Friedlaender, 9, 411.

⁶ Fischli, *Ber.*, 12, 615 (1879).

⁷ Friedmann and Gattermann, *ibid.*, 25, 3527 (1892); *J. prakt. Chem.*, [2] 59, 575 (1899).

toluene and 30 g. of anhydrous aluminum chloride, and heating the mixture for 2 hours at 100° in a 1-liter flask equipped with mechanical stirrer. The mixture was left overnight at laboratory temperature, and the solidified product then decomposed carefully with ice and water, the unchanged toluene and isothiocyanate driven out by a current of steam, and the residual liquor allowed to cool. The crude anilide which separated from the solution on cooling was purified by solution in 10% aqueous potassium hydroxide solution and reprecipitation by 20% sulfuric acid. Yield, 80%. Recrystallized from alcohol, it was obtained in yellow needles, which melted at 142° (corr.). In our experience, the use in a single charge of much larger amounts than those given above invariably resulted in considerably lower yields.

Sixteen g. of the anilide was dissolved by warming with 700 cc. of water containing 60 g. of sodium hydroxide. This solution was cooled to room temperature, and 227 cc. of a 20% aqueous potassium ferricyanide solution added. The mixture turned milky immediately. After standing for 24 hours, the resinous precipitate was collected, extracted twice with conc. hydrochloric acid (using 150 cc. of acid for the first extraction, and 100 cc. for the second), the extracts were filtered through asbestos and the filtrate precipitated by the addition of a large volume of water. The bulky pale yellow precipitate was filtered out and purified by repeated crystallization from alcohol. Yield of crude product, 60-75% of that calculated.

Analyses. Calc. for $C_{14}H_{11}NS$: N, 6.22. Found: 6.46, 6.55.

The pure compound forms colorless needles, which melt at 85° (corr.), and are practically odorless when dry, but have a faint "Rosenkoerper" odor when moistened with alcohol.

MONONITRO DERIVATIVE, $O_2N.C_{14}H_{10}NS$.—The thiazole was dissolved in 4 parts of conc. sulfuric acid and nitrated by adding 4 parts of conc. nitric acid, finally warming to complete the reaction. When cold, the mixture was poured into ice water, the orange-yellow precipitate collected, washed with a little warm alcohol to remove colored impurities, and then crysted from toluene. There resulted pale, cream colored crystals, which melted at 219.5° (corr.). Yield, nearly theoretical.


Analyses. Calc. for $C_{14}H_{10}O_2N_2S$: N, 10.38. Found: 10.51, 10.56.

THE MONO-AMINO DERIVATIVE, $H_2N.C_{14}H_{10}NS$, prepared by reducing the nitro-derivative with zinc or tin and hydrochloric acid, was purified by crystallization from toluene and then appeared in pale brown crystals melting at 229° (corr.).

Analyses. Calc. for $C_{14}H_{12}N_2S$: N, 11.67. Found: 11.90, 11.80.

Its solutions in amyl alcohol, or in toluene, exhibit a beautiful bluish-green fluorescence, resembling alcoholic solutions of the isomeric dehydrothio-*p*-toluidine. Experiments to determine the position of the amino group (and of the nitro group in the antecedent nitro compound) in this amine have not been completed as yet.

Azo Dyes from Amino-2-*p*-tolyl-benzothiazole.—The amine was diazotized and coupled on the fiber with a considerable variety of the commoner azo couplers, and yielded thus mono- and disazo dyes which compared very favorably with the corresponding dyes from dehydrothio-*p*-toluidine in fastness to light, to soaping, to bleaching etc., and were in some cases superior in tinctorial power.

Benzothiazolyl-2-*p*-benzoic Acid, C_6H_4  $C_6H_4.COOH$.—2-*p*-Tolyl-benzo-

thiazole was oxidized by potassium permanganate, both in alkaline solution, and in a solution whose neutrality was maintained by the addition of magnesium sulfate. In each case, microscopic colorless needles were isolated from the product, and these crystals darkened but did not melt at 270°. Unfortunately, they were not obtained in sufficient amount for analysis. There seems little reason to doubt that this is the acid expected.

since it has been shown by others⁹ that a methylated benzothiazole yields the benzothiazole carboxylic acid on oxidation by potassium permanganate.

Primuline-azo-benzoylene Urea.—Primuline (a commercial sample) was diazotized on the fiber and coupled with the sodium salt of benzoylene urea, in alkaline solution, following in the main the process given in a German patent⁹ for the dye manufactured from primuline and 2,4-dihydroxy-quinoline. The product was subjected to the following tests: (a) boiling with a 5% hydrochloric acid solution; (b) boiling with a dil. (10%) aqueous sodium hydroxide solution; (c) boiling with a soap solution; (d) exposure to the action of bleaching powder, and (e) exposure to direct sunlight for 2 weeks. Parallel tests were run with cloth dyed with the same strength of Ingrain Red (primuline-azo- β -naphthol). The new dye gave yellowish-brown shades of approximately the same tinctorial power as Ingrain Red, and still more fugitive than the latter in sunlight, but fully as good or better in its fastness to acids and especially to alkalis.

Dehydrothio-*p*-toluidine was prepared by heating together 110 g. of *p*-toluidine and 60 g. of roll sulfur for 6 to 8 hours at 220°, purifying the crude product by distillation under diminished pressure, dissolving the cold pulverized distillate in alcohol, boiling this alcoholic solution with Norite, filtering and allowing the filtrate to cool. The crystals which separated were further purified by repeating the crystallization and treatment with Norite until beautiful pale yellow prisms were obtained which melted at 194.8° (corr.) and possessed a wonderfully brilliant iridescent luster, especially under strong artificial light.

BENZAL DERIVATIVE, $\text{CH}_3\cdot\text{C}_6\text{H}_5 \begin{matrix} \diagup \text{S} \\ \diagdown \text{N} \end{matrix} \text{C}_6\text{H}_4\cdot\text{N}:\text{CH}\cdot\text{C}_6\text{H}_5$.—This Schiff base

was formed immediately when alcoholic solutions of dehydrothio-*p*-toluidine and benzaldehyde were mixed and the solution warmed. The product separated in nearly theoretical yield as it is difficultly soluble in alcohol. Recrystallized from the same solvent, nearly colorless, odorless, glistening leaflets were secured, which melted at 193° (corr.). Its alcoholic solutions are pale yellow and strongly fluorescent.

Analysis. Calc. for $\text{C}_{21}\text{H}_{16}\text{N}_2\text{S}$: S, 9.76. Found: 9.80.

***p*-Nitrobenzal-*p*-toluidine,** $\text{CH}_3\cdot\text{C}_6\text{H}_4\cdot\text{N}:\text{CH}\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2$.—Saturated alcoholic solutions of *p*-toluidine and of *p*-nitrobenzaldehyde were mixed and the mixture was boiled for an hour under a reflux condenser. On concentration, a crude product separated which was recrystallized from alcohol and then appeared in pale yellow needles, melting at 123° (corr.). This was the compound sought. The yield of pure substance amounted to approximately 50% of that calculated.¹⁰

It was hoped that the fusion of this nitrobenzal-toluidine with sulfur might result in the formation of dehydrothio-*p*-toluidine, but our expectations were not realized, in spite of many variations in the method of attack.

Experiments were also conducted which had as their object the conversion of dehydrothio-*p*-toluidine into the corresponding atophan (cinchopen) by methods similar to those employed by Doebner and Gieseke¹¹ and others¹² for the preparation of the ordinary atophan from aniline, benzaldehyde and pyruvic acid; but the only products

⁹ Ger. pat., 277,395; *C. A.*, 9, 865 (1915).

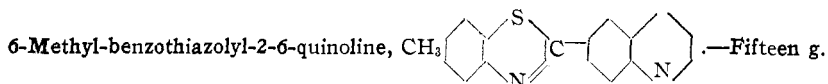
⁹ Ger. pat. 210,453, Badische Aniline-Soda Fabrik.

¹⁰ This preparation was completed and the product analyzed before the appearance of the article by Lowy and King in *THIS JOURNAL*, 43, 627 (1921), describing the same compound. These investigators give the melting point of their preparation as 122.5°.—M. T. B.

¹¹ Doebner and Gieseke, *Ann.*, 242, 291 (1887).

¹² *Ber.*, 32, 2276 (1889); *J. prakt. Chem.*, [2] 38, 583 (1888); 56, 293 (1897); *et al.*

isolated were the benzal derivative of dehydrothio-*p*-toluidine and a small amount of a brown, amorphous, difficultly-soluble compound which was not recovered in adequate amount to identify.



of pure dehydrothio-*p*-toluidine was dissolved in 20 cc. of conc. sulfuric acid, 21.7 g. of glycerol and 10.6 g. of arsenic acid added, and the mixture heated in a flask carrying a reflux air condenser. The reaction was vigorous and the mixture foamed considerably at first, turning red at the outset and later brown. After heating for an hour and a half at 190° , the mixture was cooled, 500 cc. of water added and the acid neutralized with solid sodium hydroxide. The black tarry mass which separated was collected, dried, and distilled under reduced pressure, when most of it passed over at about 250° at 45 mm. pressure. Purified by repeated crystallization from alcohol, it formed microscopic, pale brownish crystals, which melted at 147° (corr.), and possessed a peculiar faint tobacco-like odor. Yield, 15%.

Analyses. Calc. for $\text{C}_{17}\text{H}_{12}\text{N}_2\text{S}$: S, 11.59. Found: 11.69, 11.61.

The compound dissolves in alcohol to give an orange-red fluorescent solution. It adds methyl iodide directly. A mixture of equal moles of this methiodide with that of quinaldine reacts in the presence of caustic alkali with production of a substance of deep purple-red color, recalling the behavior of quinoline itself in the cyanine reactions.

Summary

1. 2-*p*-Tolyl-benzothiazole has been prepared by fusing *p*-tolanilide with sulfur, and also by the oxidation of thio *p*-tolanilide in alkaline solution with potassium ferricyanide.
2. Mononitro and mono-amino derivatives of this thiazole have been obtained, as well as various azo dyes from the latter.
3. The benzal derivative of dehydrothio-*p*-toluidine is easily obtained from the dehydro compound and benzaldehyde.
4. On applying the Skraup reaction to dehydrothio-*p*-toluidine, the corresponding quinoline results.
5. Diazotized primuline couples on the fiber with benzoylene urea, giving a product which dyes unmordanted cotton a direct yellowish-brown, of good fastness to acids, alkalies or bleach, but quite fugitive in daylight.

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