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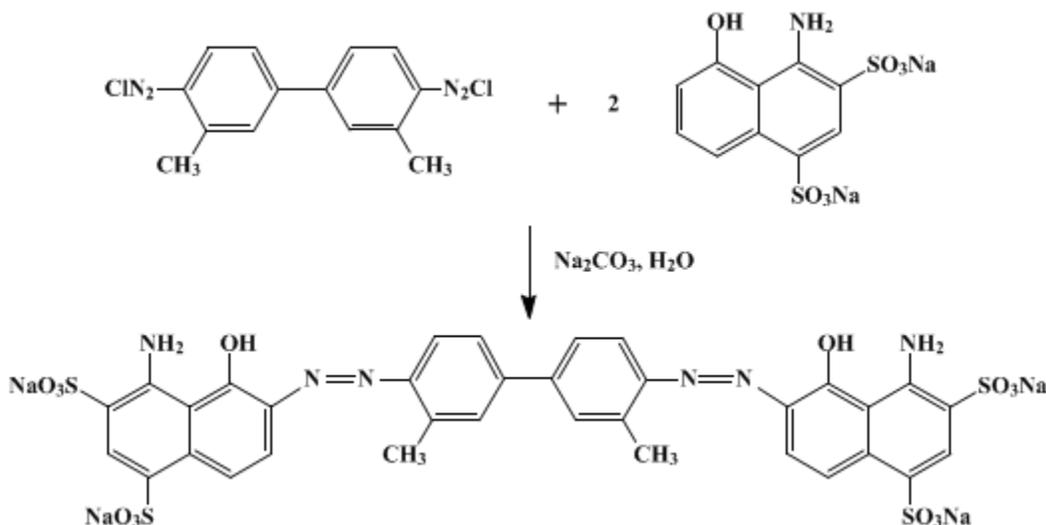
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.145 (1943); Vol. 16, p.12 (1936).

COUPLING OF *o*-TOLIDINE AND CHICAGO ACID

[Preparation of a Salt-Free Azo Dye]

[1,3-Naphthalenedisulfonic acid, 6,6'-[(3,3'-dimethyl[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[4-amino-5-hydroxy-, tetrasodium salt]



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1. Procedure

In a 1-l. beaker 21.2 g. (0.1 mole) of *o*-tolidine is made into a thin paste with 300 cc. of water and dissolved by the addition of 20 cc. (23.6 g., 0.23 mole) of concentrated hydrochloric acid (sp. gr. 1.18), warming a little if necessary. The solution is cooled to 10° with ice, mechanical agitation is started, and 21 cc. (25 g., 0.24 mole) more of concentrated hydrochloric acid is added (Note 1). This causes partial separation of *o*-tolidine dihydrochloride. The temperature being kept at 10 – 15° , a solution of 14.5 g. (0.2 mole) of 95 per cent sodium nitrite in 40 cc. of water is run in rapidly, the last 10 per cent being held back and added slowly as needed to give a distinct positive test for nitrous acid on starch-iodide paper. This excess is maintained for one-half hour. Throughout the diazotization an excess of hydrochloric acid should be present as shown by a strong test on Congo red paper. When the diazotization is complete, the excess nitrous acid is eliminated by the careful addition of a small amount of *o*-tolidine hydrochloride solution, using starch-iodide paper to arrive at an exact balance (Note 2).

In a 3-l. beaker a paste is made from 82 g. (0.21 mole) of 88 per cent technical Chicago acid (1-amino-8-naphthol-2,4-disulfonic acid) (Note 3) and 500 cc. of water, and solution effected by the addition of 8 g. (0.2 mole) of sodium hydroxide in 30 cc. of water, testing with litmus toward the end and leaving the reaction still acid (Note 4). The solution is cooled to 18° by the addition of ice, and just before the coupling 35 g. (0.33 mole) of anhydrous sodium carbonate is added.

With vigorous mechanical agitation the diazonium salt solution is run into the Chicago acid solution rather rapidly. The blue dye which separates at first, gradually dissolves on further stirring. After one-half hour the solution is tested for alkalinity (Note 5) and for completeness of coupling (Note 6) and (Note 7).

After stirring for a total of two hours, the mixture is heated to 85° , 15 g. of decolorizing carbon is added, and the solution stirred for fifteen minutes and filtered. The filtrate is reheated to 85° with agitation and the volume estimated. For each 100 cc. of the solution 27 g. of hydrated sodium acetate

(usually 450–500 g. in all) is added slowly, with vigorous stirring, in four or five portions (Note 8). The dye is thus caused to separate in an easily filterable form. On "spotting" a drop of the mixture on filter paper by means of a stirring rod, the dye should form a dark blue mass in the center of a red or violet rim (Note 9). The mixture, while still warm, is filtered with suction on a 20-cm. Büchner funnel, and as much as possible of the mother liquor is removed (Note 10). The filter cake is dissolved in 1.2 l. of water at 85° and resalted as above with about 300 g. of sodium acetate, in several portions, or until most of the dye is salted out. In a "spot" test on filter paper, little red should be left in the rim. The product is collected, redissolved in 1.2 l. of water at 85°, and salted again. This time enough sodium acetate should be added to give a small rim which shows no red impurity (Note 11). The product is collected, dried in an oven at 110° for at least twenty-four hours, ground, and passed through a 40-mesh sieve.

The sodium acetate is then extracted by digesting the sifted dye for ten to fifteen minutes with successive 500-cc. portions of boiling 95 per cent ethyl alcohol, filtering with suction after each extraction, and washing the product on the filter with a little alcohol (Note 12). After four alcohol extractions the filtrate should give a negative test for acetate. The product, which changes in appearance from bronze to green during the extraction, is dried in air at room temperature. The yield is 80–81 g. (83–84 per cent of the theoretical amount) of dye free from inorganic salts and organic impurities (Note 13).

2. Notes

1. If the hydrochloric acid is added all at once instead of in two portions as described, a solid will be obtained consisting of *o*-tolidine coated with its dihydrochloride and the diazotization will occur slowly.
2. If a clear solution is not obtained at this point, any solid may be removed by filtration.
3. Owing to the fact that this intermediate is a technical product and has been isolated by salting out, a knowledge of its purity is necessary. The compound is actually present as the acid sodium salt (molecular weight 341). A rapid method of analysis, sufficiently accurate for this preparation, is to titrate a known weight in dilute, strongly acid solution with 0.5 *N* sodium nitrite solution standardized against sulfanilic acid, using starch-iodide paper in obtaining the end points.

Some samples of technical Chicago acid may contain so much of an impurity giving rise to a red dye that the removal of this red dye by resalting, as recommended in (Note 9), presents considerable difficulty. When this occurs it is advantageous to purify the Chicago acid in the following fashion. Seven hundred grams of a Chicago acid paste, found by titration to contain 26.6 per cent of 1-amino-8-naphthol-2,4-disulfonic acid, is dissolved by heating in 2 l. of water; the solution is filtered, heated to 70°, and salted out by the addition of sodium chloride (600–650 g.) until a thick paste is obtained. The precipitate is collected at 40°, pressed well by means of a rubber dam, dissolved in 2 l. of water, and resalted exactly as before. After drying for thirty-six hours in a vacuum oven at 75°, the nearly white product weighs 150–155 g. and contains 78 per cent of active reagent. The dye ("Tolidine-1824") obtained from this material showed no red impurity in the capillary test after the second salting. (Louis F. Fieser and M. E. Gross, private communication.)

4. Aminonaphthols rapidly turn dark in alkaline solution owing to oxidation. For this reason the solution is left faintly acid until just before coupling.
5. This test is made by removing a few drops of the coupling mixture by means of a stirring rod to one of the depressions in a white porcelain spot plate, salting out the dye by stirring with a little c.p. sodium chloride, and bringing a piece of litmus paper in contact with the mass.
6. The test for completeness of coupling involves testing for excess diazonium salt (*a*) and for excess Chicago acid (*b*):

1. (*a*) A drop or two of the coupling mixture is dissolved in about 20 cc. of water in a test tube and the solution divided equally in two test tubes. To one tube is added a few drops of a 10 per cent solution of Schaeffer's salt (2-naphthol-6-sulfonic acid) or R salt (2-naphthol-3,6-disulfonic acid) prepared from 0.5 g. of the acid, 5 cc. of water, and just enough sodium carbonate solution to dissolve the material. The other tube acts as a control. Both tubes are brought rapidly nearly to boiling and the colors compared. If too dark, both tubes are diluted equally with water until the solutions are light blue. The colors may be compared by pouring solution from each tube onto

filter paper. If the color of the solution in the first tube is at all redder than that in the control tube, an excess of the diazonium compound is present in the coupling mixture.

- (b) A few drops of the coupling mixture are salted out as in (Note 5), the mass transferred to filter paper, and near the spot on the reverse side is placed a drop of solution of diazotized sulfanilic acid. A red or red-violet coloration at the meeting of the two spots shows the presence of excess Chicago acid.

7. Throughout the coupling an alkaline reaction should be maintained and sodium carbonate added if the alkalinity falls. If the mixture gives tests for both diazonium compound and Chicago acid, insufficient time has elapsed for complete coupling. A little more Chicago acid should be added (in alkaline solution) if a deficiency is shown.

8. The temperature of salting, speed of addition of salt, speed and duration of agitation, and alkalinity of the solution all affect the physical form of the dye and determine how well it will filter. The method described gives a product which filters rapidly.

9. The red impurity is another dye produced by coupling of the diazonium salt with an oxidation product which is present in the technical Chicago acid. It is usually easier to free the blue dye of this red impurity by resalting than to purify the Chicago acid. However, in the case of Trypan blue (tolidine coupled with two moles of H acid) the red impurity cannot be removed by salting. It may be removed completely by extraction with alcohol, in which it is more soluble than the blue component, preferably by precipitating a hot saturated aqueous solution of the dye with at least six times its volume of alcohol.

10. In this and subsequent filtrations it is advantageous to use a rubber dam held in place by rubber bands. The use of the rubber dam is especially advantageous for a slow filtration continuing overnight.

11. The most sensitive test for purity of the dye is the capillary test,¹ depending on the fact that the red impurity is more soluble in water than the blue compound and less readily adsorbed by filter paper. An amount of press cake corresponding roughly to 0.05 g. of solid dye is dissolved in 200 cc. of water in a 400-cc. beaker, 0.5 g. of common salt is added, and the temperature raised to 95°. A 2 by 15 cm. strip of filter paper is immersed in the liquid and is supported on a stirring rod pushed through it and placed across the top of the beaker. The temperature is maintained at 95° for fifteen minutes and the filter paper removed. Any red impurity will show plainly above the blue. If purification is found to be incomplete, further resalting will produce a pure product.

12. The progress of the extraction may be followed by adding three drops of concentrated sulfuric acid to 10 cc. of the alcoholic filtrate in a test tube. If a white precipitate of sodium sulfate does not form at once, the solution is chilled in an ice bath. A precipitate will form with 0.002 g. of sodium acetate in 10 cc. of alcohol.

13. Using this procedure, other diamines such as benzidine and dianisidine may be diazotized and coupled with other aminonaphthols, such as S acid (1-amino-8-naphthol-4-sulfonic acid), J acid (2-amino-5-naphthol-7-sulfonic acid), Gamma acid (2-amino-8-naphthol-6-sulfonic acid), and H acid (1-amino-8-naphthol-3,6-disulfonic acid), or with simple naphthols such as NW acid (1-naphthol-4-sulfonic acid), Schaeffer's acid (2-naphthol-6-sulfonic acid), and R acid (2-naphthol-3,6-disulfonic acid). The procedure would be varied only in the manner of salting out the dyes, each of which would require a set of optimum conditions peculiar to itself (see (Note 8)). If the alkalinity of sodium acetate leads to a considerable increase in solubility of the dye, ammonium bromide may be used. The latter is extracted easily by hot ethyl alcohol or, better, by hot methyl alcohol.

Naphthylamines cannot be used as second components by this procedure, as coupling takes place in acid solution.

3. Discussion

Dyes of the types described in the procedure and those mentioned in (Note 13) are described in the patent literature.² The ordinary methods of preparation give products that contain salt and other impurities.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 295

References and Notes

1. Mulliken, "Identification of the Commercial Dyestuffs," pp. 10–11, John Wiley & Sons, New York, 1910.
 2. Bayer and Company, Ger. pats. 35,341 and 38,802 [Frđl. 1, 469, 488 (1877–87)]; Cassella and Company, Ger. pat. 3949 [Frđl. 3, 685 (1890–94)]; Badische Anilin- und Soda-Fabrik, Ger. pats. 57,327 and 75,469 [Frđl. 3, 687, 690 (1890–94)].
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Trypan blue (tolidine coupled with two moles of H acid)

o-tolidine hydrochloride

1,3-Naphthalenedisulfonic acid, 6,6'-[(3,3'-dimethyl[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[4-amino-5-hydroxy-, tetrasodium salt

ethyl alcohol,
alcohol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

methyl alcohol (67-56-1)

sodium acetate (127-09-3)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

ammonium bromide (12124-97-9)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

sodium nitrite (7632-00-0)

nitrous acid (7782-77-6)

decolorizing carbon (7782-42-5)

1-amino-8-naphthol-2,4-disulfonic acid,
CHICAGO ACID (82-47-3)

sulfanilic acid (121-57-3)

2-naphthol-6-sulfonic acid (61886-35-9)

2-naphthol-3,6-disulfonic acid (148-75-4)

benzidine (92-87-5)

1-amino-8-naphthol-4-sulfonic acid (83-64-7)

2-amino-5-naphthol-7-sulfonic acid (87-02-5)

2-amino-8-naphthol-6-sulfonic acid (90-51-7)

1-amino-8-naphthol-3,6-disulfonic acid (5460-09-3)

1-naphthol-4-sulfonic acid (84-87-7)

o-TOLIDINE (119-93-7)

dianisidine (119-90-4)