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Working with Hazardous Chemicals

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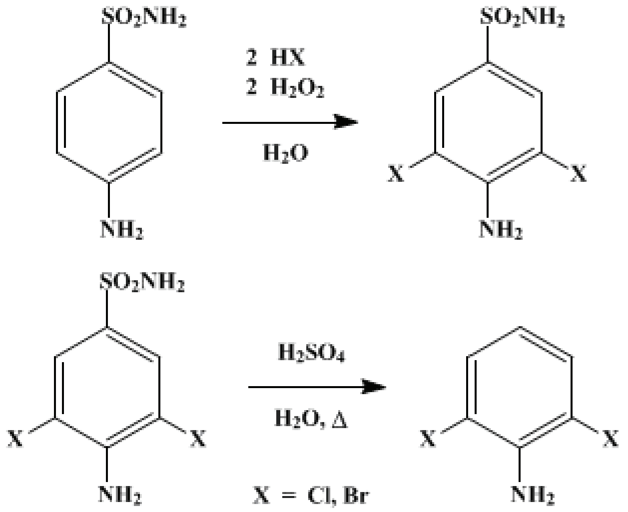
DOI:10.15227/orgsyn.024.0047

Organic Syntheses, Coll. Vol. 3, p.262 (1955); Vol. 24, p.47 (1944).

2,6-DICHLOROANILINE AND 2,6-DIBROMOANILINE

[Aniline, 2,6-dichloro- and 2,6-dibromo-]



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1. Procedure

A. 3,5-*Dichlorosulfanilamide*. In a 2-l. round-bottomed flask, fitted with a two-holed stopper carrying a mechanical stirrer and a thermometer, are placed 50 g. (0.29 mole) of sulfanilamide and 500 ml. of water. About 50 ml. of a 500-ml. portion (approximately 6 moles) of pure concentrated hydrochloric acid is added, and the mixture is stirred until a clear solution results (Note 1). The remainder of the 500 ml. of hydrochloric acid is then added. If the internal temperature does not rise to 45°, the stirred solution should be warmed gently with a free flame until this temperature is reached. At this point 65 g. (59 ml., 0.58 mole) of 30% hydrogen peroxide (sp. gr. 1.108) is added and rapid stirring is initiated (Note 2). The heat of reaction causes a progressively faster rise in temperature. After 5 minutes the solution fills with a white precipitate which increases rapidly in amount and becomes delicately colored. When the temperature has reached 60°, about 10 minutes after adding the peroxide (Note 3), any further rise is preferably prevented by judicious cooling (Note 4). The reaction is allowed to proceed for 15 minutes more at 60°, and then an ice bath is raised about the flask while stirring is continued. When the temperature has fallen to 25–30°, the mixture is filtered at once. The yield of 3,5-dichlorosulfanilamide is 45–50 g. (65–71%), and the crude dusky pink product melts over a range of 1–2° in the region 200–205° (Note 5).

B. 2,6-*Dichloroaniline*. The crude 3,5-dichlorosulfanilamide is added to 200–250 ml. (5 ml./g.) of 70% sulfuric acid (50 ml. of concentrated acid diluted with 31 ml. of water) in a 500-ml. flask, and the mixture is boiled gently for 2 hours; heat is supplied by an oil bath kept at 165–195° (Note 6). The dark mixture is then poured into 1 l. of water in a 2-l. round-bottomed flask, whereupon partial separation of a suspension of black oil occurs. The flask is attached to a condenser by a gooseneck of glass tubing; the tubing entering the flask is bent at a slight angle and cut so that its opening is at right angles to the level of the solution (Note 7). The product is steam-distilled by boiling the mixture with a free flame; the collecting vessel should be immersed in an ice bath. The solid product is separated from the distillate and dried in the air (Note 8); the white 2,6-dichloroaniline weighs 23.5–26 g. (75–80% based on 3,5-dichlorosulfanilamide or 50–55% based on sulfanilamide) and melts at 39–40°. If the product is colored it can be purified by a second steam distillation; recovery is over 90%.

C. 3,5-*Dibromosulfanilamide*. The bromination of sulfanilamide is carried out in much the same way as the chlorination. The stirrer must be more efficient (Note 9); a glass stirrer with two sets of blades is satisfactory if run at high speed. Fifty grams (0.29 mole) of sulfanilamide is dissolved in a mixture of 850 ml. of water (Note 9) and 100 ml. (0.68 mole) of 40% hydrobromic acid (Note 10). The solution is heated as above, but to 70–75°, and 65 g. (59 ml., 0.58 mole) of 30% hydrogen peroxide is added (Note 2) and (Note 11). A precipitate settles in 2–3 minutes, and the solution becomes yellow. The heat of reaction causes the internal temperature to rise without further application of heat to a maximum of 85–90° after 10 minutes; by the end of the reaction time the temperature will have fallen to about 70° (Note 12). After a total reaction time of 30 minutes (Note 13), during which the mixture has become almost solid and is very difficult to stir, the material is filtered hot (Note 14). The yield of 3,5-dibromosulfanilamide is 85–90 g. (90–94%), and the crude tan product (Note 15) melts over a range of 1–2° in the region 230–237° (Note 16).

D. 2,6-*Dibromoaniline*. In a 2-l. flask, equipped with a two-holed stopper carrying an exit tube to a condenser and an entrance tube for steam, 50 g. of crude 3,5-dibromosulfanilamide (Note 17) and (Note 18) and 250 ml. (5 ml./g.) of 70% sulfuric acid are heated in an oil bath; when the temperature of the bath reaches 175–180°, steam is passed rapidly through the mixture (Note 19). The hydrolysis is continued in this way for 2 hours; small amounts of the dibromoaniline distil (Note 20). The bath is then allowed to cool to 105–110°. At this temperature the main mass of the product is steam-distilled. The slightly colored 2,6-dibromoaniline melts at 84–86° and weighs 25–30 g. (66–79% based on 3,5-dibromosulfanilamide) (Note 21). It may be purified by recrystallization from 70% alcohol (7 ml./g.); after recrystallization the product is obtained as long colorless needles which melt at 87–88°. The recovery is 85–90%.

2. Notes

1. Solution of sulfanilamide is more readily obtained in this way than by treating the amide at once with 6 *N* acid for, in the latter case, the salt precipitates at first and redissolves only slowly. If acid stronger than 6 *N* is used, a larger volume is required to dissolve the sulfanilamide hydrochloride, and the product is partly held in solution as dichlorosulfanilamide hydrochloride unless the solution is diluted. If 4 *N* acid is used, the reaction is much slower without any worthwhile decrease in the color of the product.
2. Equivalent quantities of sulfanilamide and hydrogen peroxide are used in order to minimize the cost since no better yields are obtained with either in excess. If sulfanilamide is in excess, the product is tinged more orange-tan than pink and never becomes red from subsequent oxidation. If hydrogen peroxide is in excess, the reaction is faster but rapid oxidation giving dark-colored materials occurs toward the end.
3. When smaller amounts of reactants are employed, it is necessary to apply heat to reach and maintain a temperature of 60°.
4. Without cooling, the temperature rises above 70° and the precipitate becomes deep rose from oxidation by-products. The color, however, does not seem to affect the yield or purity of the dichloroaniline to any great extent.
5. The color of the product varies; higher temperatures, larger excesses of peroxide, longer reaction times, higher acidity, and higher concentrations of the reactants lead to the formation of more deeply colored materials. The color may be removed by several recrystallizations from glacial acetic acid with decolorizing carbon. As a preparative method for dichlorosulfanilamide, when a pure product is desired, the following procedure is recommended. For each 10 g. (0.058 mole) of sulfanilamide, 200 ml. of water, 200 ml. of concentrated hydrochloric acid, and 24 ml. (0.23 mole or 2 equivalents) of 30% hydrogen peroxide are used and the reaction is run at 25° for not more than 2 hours. A practically white product is obtained in 45–60% yield. It may be recrystallized from a very large volume of water, from 95% ethanol, or from glacial acetic acid; the recrystallized product melts at 205–205.5°.
6. Desulfonamidation is brought about faster by 75% sulfuric acid, but the yield is lower. The reaction is inconveniently slow with 65% sulfuric acid.
7. This bend prevents the mechanical carry-over of dark materials from the spray rising from the boiling dark solution. A distilling flask is not employed because dark oil creeps out the side arm.
8. It is difficult to measure the yield accurately; the material must be air-dried on account of its low melting point; the substance volatilizes to a significant extent on standing.
9. The larger amount of product obtained requires a more dilute initial solution coupled with violent

stirring to maintain sufficient agitation.

10. Speedier reactions can be run at lower temperatures, producing lighter-colored crude materials if the amount of hydrobromic acid is doubled (30 minutes at 45°) or quadrupled (20 minutes at 25°); the use of the minimum quantity recommended above (approximately 1.15 times the required amount) produces as high yields of as high-melting materials with an attendant reduction in cost.

The 100 ml. of 40% hydrobromic acid can be replaced by 75 ml. of 48% hydrobromic acid.

11. The use of excess peroxide in the bromination also causes the formation of tribromoaniline.[1,2,3,4] If only 0.29 mole of hydrogen peroxide is used, the monobromo derivative is obtained.

12. When small runs are made, it is necessary to use a bath to attain and maintain an internal temperature of 80–85° during the reaction time of 30 minutes.

13. The reaction is considered complete when a sudden increase in or appearance of the brownish yellow color of free bromine is noted. This may or may not be evident under the above conditions, for the solution is deeply colored because of the high temperature and a very slight excess of hydrobromic acid is used; it is clearly evident whenever the excess is greater or the temperature lower.

14. Hot filtration removes traces of the monobromo compound, which is soluble in water and acids.

15. When the reaction is run at lower temperature with excess hydrobromic acid, the crude product is lighter colored. However, it melts no higher and is purified with no greater ease and with only slightly better recovery.

16. The purification of the crude material is effected by recrystallization from glacial acetic acid or, preferably, 95% ethanol (25 ml./g.), using decolorizing carbon; colorless needles, which melt at 239–240°, are obtained after two recrystallizations.

17. The crude material to be used for desulfonamidation should be tested for absence of *sym*-tribromoaniline by ascertaining its solubility in 1 *N* alkali. A clear, though colored, solution should result. If the solution is cloudy, purification of the impure material by dissolving it in alkali, filtering the solution, and reprecipitating the amide is essential.

18. Fifty-gram lots seem to be the maximum size if consistently high-melting pure material is to be obtained under the conditions employed. If a very pure product is desired, less starting material should be used.

19. The use of a current of steam in the desulfonamidation of the dibromo compound as recommended by earlier investigators[1,3,5] was found to be absolutely necessary in this instance. Without the steam, considerable amounts of *sym*-tribromoaniline are formed;[6] superheated steam is not necessary. The purity of the crude product varies directly with the ratio of the amount of steam to the size of the reaction mixture; the current of steam should be very rapid or the amount of material in a single operation should be small.

20. One and a half liters of distillate was collected in the time given.

21. If the crude product melts lower, it contains too much tribromoaniline to permit satisfactory purification. Recrystallization effects no separation; repeated fractional steam distillation is very slowly effective.

3. Discussion

2,6-Dichloroaniline was prepared by Beilstein[7] and by Körner[8] by reduction of 2,6-dichloronitrobenzene. A better method, more recently reported,[9] involves the chlorination of sulfanilic acid in 1% solution with free chlorine, subsequent evaporation of the solution, and desulfonation as above. The present method (reported earlier in slightly different form and for small amounts[10]), although requiring more expensive raw materials, is more convenient and gives higher yields.

2,6-Dibromoaniline has been prepared many times[1,3,5,6,11] by bromination of sulfanilic acid and desulfonation of the product or its salts. Fuchs[12] brominated sulfanilamide with free bromine and desulfonamidated it in the usual manner. Reduction of the corresponding nitro compound[13] and other methods[14] also have been employed.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

sym-tribromoaniline

Aniline, 2,6-dichloro- and 2,6-dibromo-

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

HYDROBROMIC ACID (10035-10-6)

bromine (7726-95-6)

decolorizing carbon (7782-42-5)

chlorine (7782-50-5)

hydrogen peroxide (7722-84-1)

sulfanilic acid (121-57-3)

tribromoaniline

2,6-Dichloroaniline (608-31-1)

2,6-Dibromoaniline (608-30-0)

sulfanilamide (63-74-1)

3,5-Dichlorosulfanilamide (22134-75-4)

3,5-Dibromosulfanilamide (39150-45-3)

dibromoaniline

sulfanilamide hydrochloride

dichlorosulfanilamide hydrochloride

dichloroaniline

dichlorosulfanilamide

2,6-Dichloronitrobenzene (601-88-7)