

3rd Edition

CHEMISTRY
of
ORGANIC
COMPOUNDS

CARL R. NOLLER

Professor of Chemistry, Stanford University

W. B. SAUNDERS COMPANY
Philadelphia and London

1965

Chemistry of Organic Compounds

© 1965 by W. B. Saunders Company. Copyright 1951 and 1957 by W. B. Saunders Company. Copyright under the International Copyright Union. All rights reserved. This book is protected by copyright. No part of it may be duplicated or reproduced in any manner without written permission from the publisher. Made in the United States of America. Press of W. B. Saunders Company. Library of Congress catalog card number 65-10290.

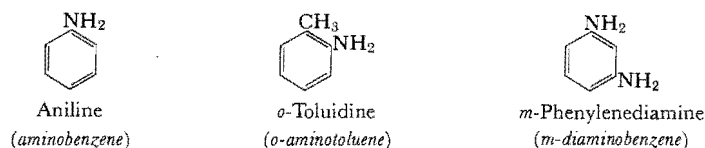
AROMATIC AMINES AND PHOSPHINES

Compounds classed as aromatic amines have an amino group or an alkyl- or aryl-substituted amino group attached directly to an aromatic nucleus. Usually they are made by a procedure different from those for aliphatic amines and undergo additional reactions. Aromatic phosphines resemble the amines only in structure. Their methods of preparation and reactions are entirely different.

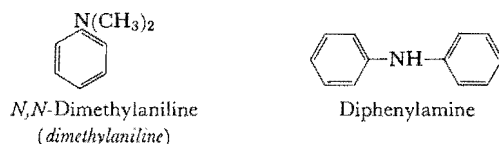
AMINES

Nomenclature

Aromatic amines may be primary, secondary, or tertiary, and in the secondary or tertiary amines, the second or third hydrocarbon group may be alkyl or aryl. Usually the primary amines are named as amino derivatives of the aromatic hydrocarbon or as aryl derivatives of ammonia, but some are known best by common names such as aniline or toluidine.



Secondary and tertiary amines are named as derivatives of the primary amine, or as derivatives of ammonia.

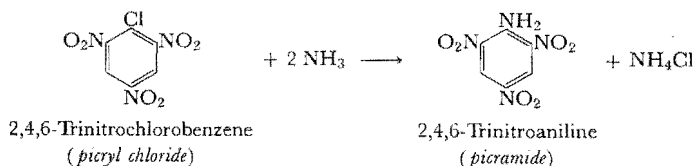


Preparation

1. **By Reduction of More Highly Oxidized Nitrogen Compounds.** Aromatic nitro compounds yield a series of reduction products, the final product being the primary amine (Fig. 23-1, p. 519). Therefore primary aromatic amines may be prepared from nitro compounds or from the less highly oxidized nitroso, hydroxylamino, azoxy, azo, and hydrazo compounds, by reduction with alkaline hydrosulfite or with sodium and ethanol.

2. **By Ammonolysis of Halogen Compounds.** Halogen attached to an aromatic nucleus usually is very stable to hydrolysis or ammonolysis, and rather drastic conditions are required to bring about reaction, which may occur with rearrangement (p. 495). If, however, electron-attracting groups are present in the *ortho* and *para* positions, the halogen

is more easily displaced. Thus 2,4,6-trinitrochlorobenzene (*picryl chloride*) reacts readily with ammonia to yield 2,4,6-trinitroaniline (*picramide*) by an S_NAr 2 mechanism (p. 496):



Physical Properties

The physical properties of the aromatic amines are about what would be expected. Just as benzene (b.p. 80°) boils at a higher temperature than *n*-hexane (b.p. 69°), so aniline (b.p. 184°) has a higher boiling point than *n*-hexylamine (b.p. 130°). The greater difference in the boiling points of the second pair may be ascribed to the fact that aniline has a higher dipole moment ($\mu = 1.6$) than *n*-hexylamine ($\mu = 1.3$). *N*-Methylaniline (b.p. 195°) boils at a higher temperature than aniline, but *N,N*-dimethylaniline (b.p. 193°) boils at a lower temperature than methylaniline despite the increase in the number of electrons because proton bonding is not possible for dimethylaniline.

Aniline is considerably more soluble in water (3.6 g. per 100 g. of water) than *n*-hexylamine (0.4 g. per 100 g. of water). Water dissolves in aniline to the extent of about 5 per cent. Aniline is miscible with benzene but not with *n*-hexane.

As is true for all of the disubstituted benzenes, the *para*-substituted anilines, being the most symmetric, have the highest melting point. Thus *p*-toluidine is a solid at room temperature whereas both the *ortho* and *meta* isomers are liquids.

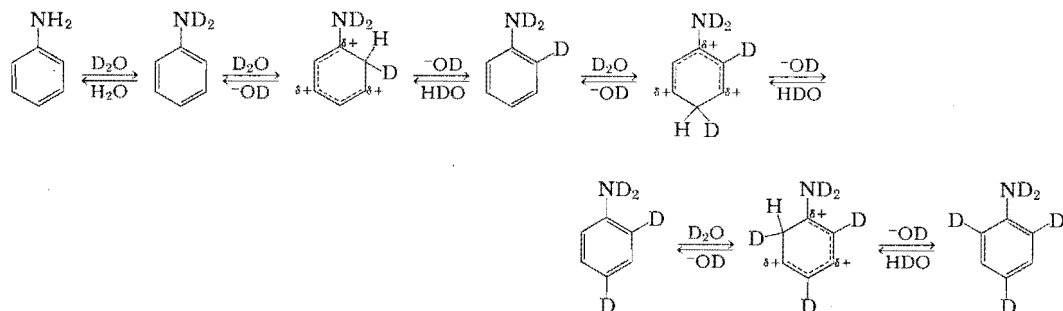
Physiological Properties

The aromatic amines, like the aromatic hydrocarbons and their halogen and nitro derivatives, are highly toxic. The liquids are absorbed readily through the skin, and low concentrations of the vapors produce symptoms of toxicity when inhaled for prolonged periods. Aniline vapors may produce symptoms of poisoning after several hours of exposure to concentrations as low as 7 parts per million. Aniline affects both the blood and the nervous system. Hemoglobin of the blood is converted into methemoglobin with reduction of the oxygen-carrying capacity of the blood and resultant cyanosis. A direct depressant action is exerted on heart muscle. Continued exposure leads to mental disturbances. Aromatic amines appear to be responsible also for bladder irritation and the formation of tumors in workers engaged in the manufacture of dye intermediates.

The chloro and nitro nuclear-substituted amines, the *N*-alkylated and acylated amines, and the diamines all are highly toxic. The *N*-phenylamines are considerably less toxic than the *N*-alkyl derivatives. The phenolic hydroxyl group also decreases the toxicity somewhat. Toxicity is greatly reduced by the presence of free carboxylic or sulfonic acid groups in the ring.

Reactions of the Nucleus

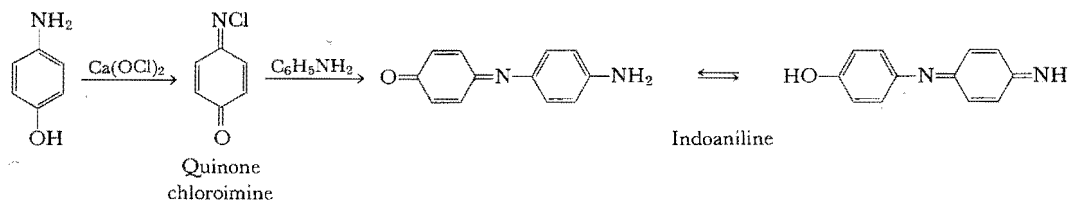
1. **Hydrogen Exchange.** Electrophilic substitution of deuterium for hydrogen of benzene takes place only with strong acids under anhydrous conditions (p. 469). The amino group is so strongly activating, however, that exchange with hydrogen in the *ortho* and *para* positions takes place readily in aqueous solutions, although less readily than with the amino hydrogen. As would be expected, these exchange reactions are catalyzed by acids.



2. **Oxidation.** Aliphatic amines are fairly stable to oxidation, but many aromatic amines oxidize readily. Unless carefully purified, they soon darken on standing in air. Stronger oxidizing agents produce highly colored products. Even the simplest aromatic amine, aniline, can give rise to numerous and frequently complex oxidation products. It is not surprising that, depending on the oxidizing agent used, azobenzene, azoxybenzene, phenylhydroxylamine, nitrosobenzene, and nitrobenzene have been isolated (p. 519), since aniline is a reduction product of these compounds. In addition to the amino group, however, the hydrogen atoms of the benzene ring that are *ortho* and *para* to the amino group can be oxidized to hydroxyl groups because the amino group increases the electron density at the *ortho* and *para* positions. Thus when sodium hypochlorite solution is added to aniline, *p*-aminophenol is formed along with azobenzene and other products.



These hydroxy amines are oxidized very readily to quinones (p. 566), which undergo further oxidation and condensation reactions. For example, the violet color produced when aniline is mixed with a solution of bleaching powder is due to a series of reactions that form a blue compound known as *indoaniline*.



Some of the more complicated reactions are considered in the discussion of quinones (p. 567) and of the Aniline Blacks (p. 765).

Amine salts are much less readily oxidized than the free amines because the positive charge makes the group electron-attracting rather than electron-donating. Similarly, electronegative substituents such as the nitro group decrease the electron density of the ring and greatly reduce the ease of oxidation.

3. **Halogenation.** Because of the strong activating effect of the amino group, no catalyst is required in the halogenation of the nucleus. Furthermore, halogenation takes place in aqueous solution and is so rapid that the only product readily isolated is 2,4,6-trichloro- or 2,4,6-tribromoaniline. The three halogen atoms in the *ortho* and *para* positions reduce the basicity of the amino group, and the salt does not form in aqueous solution.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.