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A Review Paper on Benzidine

Dr. Anjum Ansari
Assistant Professor, Department of Chemistry
Shri Makhanlal Chaturvedi Government College, Babai, Hoshangabad, M.P., India
ansari.anjum@rediffmail.com

Abstract: *Benzidine is a manufactured chemical that does not occur naturally. It is a crystalline solid. It will evaporate slowly from water and soil. In the environment, benzidine is found in either its "free" state (as an organic base), or as a salt (for example benzidine dihydrochloride or benzidine sulfate). In air, benzidine is found attacked to suspended particles or as a vapor. It is a di-acid base and forms salts with the mineral acids. It is readily brominated and nitrated; when the nitration is carried out in presence of sulphuric acid, the nitro groups take up the meta-position with regard to the amino groups. Benzidine is stable, combustible and incompatible with strong oxidizing agents. Benzidine-based dyes are relatively stable in air and in solution at ambient temperatures but degrade in aqueous solution at high temperatures, particularly in presence of iron. Benzidine is a manufactured chemical that does not occur naturally in the environment. Benzidine and its breakdown products can be detected in urine but only within about two weeks after exposure. Benzidine is an important product in the dye industry and is a common constituent of several hair dyes, despite its well-known carcinogenic effects particularly with regard to bladder tumors. Benzidine and its derivative are widely used in the manufacture of dyestuffs and are common constituents of pigments, hair-dyes, inks, polymers and rubber compounding. Benzidine is widely used for the analysis of sulphate and for detection of hydrogen cyanide and phenol in atmosphere.*

Keywords: Benzidine, Environment, Dye, Atmosphere, Carcinogenic

I. INTRODUCTION

Benzidine is an aromatic amine having molecular weight 184.2. It presents as a grayish-yellow, white, or reddish-gray crystalline solid, darkens when exposed to air and light. Benzidine is partially soluble in water, boiling alcohol. and ether. It may burn but does not readily ignite.

Benzidine is the trivial name for 4,4'-diaminobiphenyl. Benzidine synonyms are 4, 4'-Biphenyldiamine, 4, 4'-Biphenyleneldiamine C.I. azoic diazo component 112, 4, 4'-Diamino-1, 1'-biphenyl para, para'- Diamino biphenyl, 4, 4'-Diaminodiphenyl para-Diamino diphenyl, 4, 4'-Diphenyleneldiamine Fast Corinth base B. Benzidine used in the synthesis of dyes & as part of a test for cyanide. It has been linked to bladder cancer and pancreatic cancer.

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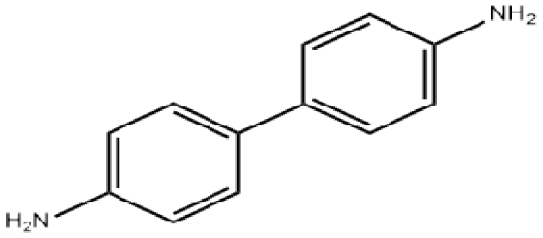
II. STRUCTURE OF BENZIDINE



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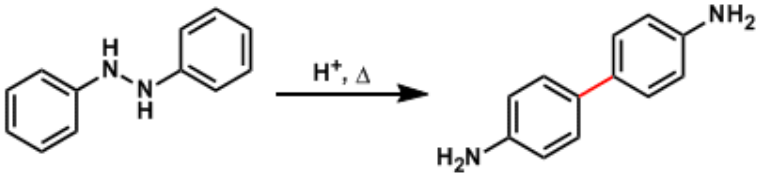
III. Benzidine Rearrangement

In rearrangement reaction benzidine is formed by the reaction of 1,2-diphenylhydrazine (Ph NH NH Ph) with acids.



IV. Environmental Exposure

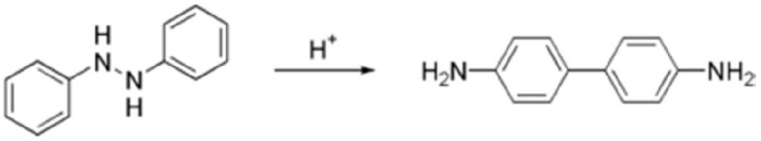
The primary routes of exposure to benzidine based dyes are inhalation, accidental ingestion, dermal absorption etc. According to the U.S. EPA's Toxics Release Inventory, no environmental releases of benzidine-based dyes have been reported since 1989. The National Occupational Hazard Survey (1972-1974) estimated that 79,200 workers in 63 occupations (primarily the dye manufacturing, textile dyeing, printing, paper and leather industries) potentially were exposed to benzidine-based dyes.

Benzidine has been found to be a useful reagent for sugar detection on paper chromatograms and for quantitative determination in test-tubes.

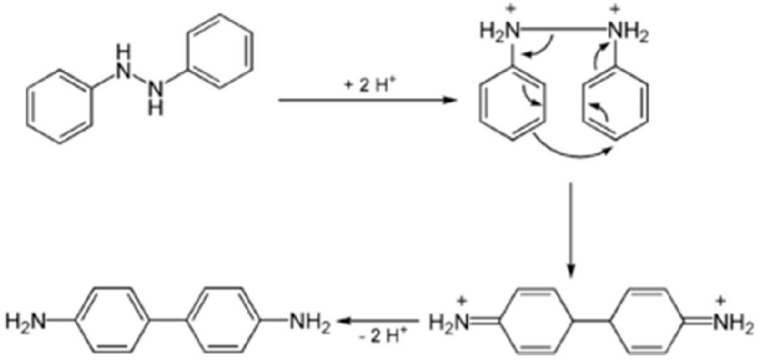
Benzidine salts can dissolve more easily in water than free benzidine. Only a very small portion of dissolved benzidine will pass into the air. Benzidine exists in the air as very small particles or as a vapour, which may be brought black to the earth's surface by rain or gravity. In soil, most benzidine is likely to be strongly attached to soil particles, so it does not easily pass into underground water.

V. Benzidine Production

Benzidine is prepared in a two-step process from nitrobenzene. First, the nitrobenzene is converted to 1,2-diphenylhydrazine, usually using iron powder as the reducing agent. Treatment of this hydrazine with mineral acids induces a rearrangement reaction to 4,4'-benzidine.



The conversion is described as a [5,5] sigmatropic reaction.



Conversion of benzidine to the bis(diazonium) salt was once an integral step in the preparation of direct dyes (requiring no mordant). Treatment of this bis(diazonium) salt with 1-aminonaphthalene-4-sulfonic acid gives the once popular congo red dye. In the past, benzidine was used to test for blood. An enzyme in blood causes the oxidation of benzidine to a distinctively blue-coloured derivative. The test for cyanide relies on similar reactivity. Such applications have largely been replaced by methods using phenolphthalein/hydrogen peroxide and luminol.

Benzidine may be prepared by the reduction of the corresponding dinitro diphenyl, or by the reduction of azobenzene with tin and hydrochloric acid.

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Benzidine is no longer manufactured for commercial scale in the United States. All large-scale production was discontinued in 1976, and only relatively small quantities remain available for use in diagnostic testing. All benzidine production must be for captive consumption (in-house, use) and take place in closed systems under stringent workplace controls.

5.1 Properties

It appears as white or light pink crystalline powder with a melting point of 125 ℃, the boiling point of 400 ℃, (98.7kPa) and the relative density of 1.250 (20/4 ℃). It is soluble in boiling ethanol, acetic acid and diluted hydrochloric acid, slightly soluble in ether, slightly soluble in boiling water and slightly soluble in cold water. Its color is darkened under air and light. Analysis reagents are usually benzidine hydrochloride or acetate, which is more soluble, and sulfate is commonly used in the industry. Benzidine acetate is white or nearly white crystals, being soluble in water, acetic acid and hydrochloric acid, as an indicator. Benzidine sulfate is a white crystalline powder or flaky crystal, being soluble in ether, very slightly soluble in water, dilute acid and alcohol.

In terms of its physical properties, 4,4'-benzidine is poorly soluble in cold water but can be recrystallized from hot water, where it crystallises as the monohydrate. It is dibasic, the deprotonated species has K_a values of 9.3×10^{-10} and 5.6×10^{-11}. Its solutions react with oxidizing agents to give deeply coloured quinone-related derivatives. Physical and chemical properties of benzidine are listed in Table 1.

Table 1: Physical and chemical properties of benzidine

Property	Information
Molecular weight	184.2[a]
Specific gravity	1.250 At 20 °C/4 °C[a]
Melting point	120 °C[a]
Boiling point	401 °C[a]
Log K_{ow}	1.34[a]
Water solubility	0.322 g l^{-1} at 25 °C[a]
Vapor pressure	8.98×10^{-7} mm Hg at 25 °C[b]
Vapor density relative to air	6.36[a]
Dissociation constant (pK_a)	4.3[a]
a The figures are from HSDB 2009. b The figures are from ChemIDplus 2009.	

5.2 Uses

Benzidine-based dyes were used primarily to colour textiles, leather, and paper products and also in the petroleum, rubber, plastics, wood, soap, fur, and hair-dye industries.

Benzidine has been used for over a century as an intermediate in the production of azo dyes, sulfur dyes, fast color salts, naphthols and other dying compounds. Most of the uses have been discontinued because of concerns about benzidine's potential carcinogenicity. Some dyes that may contain benzidine as an impurity still are used as stains for microscopy and similar laboratory applications.

Benzidine finds commercial application since its tetrazo compound couples readily with amino-sulphonic acids, phenol carboxylic acids, and phenol and naphthol-sulphonic acids to produce substantive cotton dyes.

5.3 Effects of Benzidine

1. **Acute Effects:** Benzidine is considered to be very acutely toxic to humans by ingestion, with an estimated oral lethal dose of between 50 and 500 mg/Kg. Symptoms of acute ingestion exposure include cyanosis, headache, mental confusion, nausea, and vertigo. Dermal exposure may cause skin rashes and irritation. Tests involving acute exposure of animals, such as the LD50 test in rats and mice, have shown benzidine to have high toxicity from oral exposure.

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2. **Chronic effects (Noncancer):** Chronic exposure to benzidine in humans may result in bladder injury. Animal studies have reported effects on the blood, liver, kidney, and central nervous system from oral exposure to benzidine. The RfD for benzidine is 0.003 mg/Kg/d based on brain cell vacuolization in mice and liver cell alterations in female mice.
3. **Cancer Risk:** Numerous epidemiological studies have shown occupational exposure to result in an increased risk of bladder cancer. Animal studies have reported various tumor types at multiple sites from benzidine exposure via oral, inhalation, and injection exposure. EPA has classified benzidine as a group A, human carcinogen. EPA's office of Air Quality planning and standards, for a hazard ranking under section 112 (g) of the clean Air Act Amendments, has ranked benzidine in the non-threshold category. The 1/ED10 value is 2,200 per (mg/Kg)/d and this would place it in the high category under superfund's ranking for carcinogenic hazard.

5.4 Medical Test for Determination of Benzidine

Several tests have been developed. Although these tests must be performed by experts in special laboratories. Benzidine and its breakdown products can be detected in urine but only within about 2 weeks after exposure. Benzidine and some of its changed forms will bind to proteins within red blood cells, and this can be detected for up to 4 months after exposure.
Benzidine test is a specific test used for the determination of blood (RBCs or haemoglobin) in urine. Kidney diseases or any injury to the urinary tract may result in leakage of blood in the urine. Blood (Haemoglobin) may occur in the urine as intact corpuscles (RBC) as in haematuria or free in the solution (Haemoglobin). Haemoglobinuria occurs in a certain condition in which the RBCs are haemolysed, and haemoglobin is liberated into the plasma. This haemoglobin is excreted by the kidneys and appears in the urine.

A. Toxicity

Benzidine is highly toxic, can be absorbed through the respiratory tract, skin and digestive tract, and is highly toxic, belonging to a carcinogen. Both solid and vapor are quickly absorbed through the skin, causing blood damage and causing bladder cancer. Mistakenly eating it can cause nausea, vomiting, liver and kidney damage. Mice oral LD50: 214mg / kg (body weight), rat oral LD50: 309 mg / kg (body weight). Rabbits and dogs have an oral minimum lethal dose of 200mg / kg (weight). The major toxic effect is hemorrhagic cystitis. The effect on the formation of methemoglobin is weak. It has stimulation effect on the skin and mucous membranes, being capable of causing contact dermatitis. It can cause liver cancer in mice and hamsters, causing rat liver, Zymbal gland, breast and colon cancer and cause bladder cancer in dogs. A variety of short-term mutagenicity test has given positive results. The International Agency for Research on Cancer (IARC) classifies it as a human carcinogen (well-documented) with the targets being bladder. The relative risk of bladder cancer in dyes chemical worker is 19 with the incubation period of about 19 years.

VI. CONCLUSION

Benzidine is no longer produced in the United States, although benzidine-based dyes may be imported into this country. No information is available on the acute (short-term) effects of benzidine in humans by inhalation exposure but benzidine is considered to be very acutely toxic to humans by ingestion. Chronic (long-term) exposure to benzidine in humans may result in injury to the bladder. Epidemiological studies have shown occupational exposure to benzidine to result in an increased risk of bladder cancer. Animal studies have reported various tumor types at multiple sites from benzidine exposure via oral, inhalation, and injection exposure in 1973, Occupational Safety and Health Association (OSHA) regulations banned United States production of benzidine. Benzidine has been detected in soil and water near industrial sources, especially those that have disposed of benzidine solid wastes improperly. The Reference Dose (RfD) for benzidine is 0.003 milligram per kilogram body weight per day (mg/kg/d) based on brain cell vacuolization in mice and liver cell alterations in female mice. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999. 4. California Environmental Protection Agency (CalEPA). Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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