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CHAPTER XXX

The Aromatic Hydrocarbons

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I. General Considerations

A. NOMENCLATURE, SOURCES, AND USES OF AROMATIC HTDROCARBOSS

The aromatic hydrocarbons contain one or more benzene rings. They are classified into three principal groups, depending on the number of benzene rings and the type of linkage between the rings in the molecule. These groups are: (1) benzene and its aliphatic and alicyclic derivatives, (2) polyphenyls—two or more noncondensed rings, and (3) polynuclear — twa or more condensed rings.

From the industrial hygiene standpoint, the most important aromatic hydrocarbons belong to the first group, consisting of benzene and its aliphatic and alicyclic derivatives. In general, these compounds are liquids with a significant vapor pressure at room temperature which, combined with their toxicity, may present potential working hazards. Included in this group are benzene (benzol), toluene, ethylbenzene, styrene, the xylenes, cumene, *p-tert*-butyltoluene, and tetralin.

Benzene and its alkyl derivatives are obtained as by-products of the coke-oven industry and the petroleum industry. From coke-oven operations they are recovered from the gases and the coal tars. As petrochemicals they are separated from crude oil by fractionation, distillation, or solvent extraction, or converted chemically by dehydrogenation of naphthene fractions, alkylation of benzene with olefins, or produced from paraffins by catalytic cyclization and aromatization.

Benzene is extensively used as a solvent in the chemical and drug industry, as a starting material and intermediate in the synthesis of numerous chemicals, and as a constituent of motor fuels. Toluene and the xylenes are used as solvents for synthetic rubber, paint and lacquers, and are also constituents of motor fuels. p-Xylene is the intermediate in the synthesis of synthetic fibers. Toluene is the starting material in the manufacture of the explosive trinitrotoluene. Ethylbenzene is used principally as the source of styrene, which is the constituent of polymers such as synthetic rubber, plastics, and packaging films. Cumene and *p-tert*-butyltoluene are used for synthesis in the chemical industry. Cumene is also a Constituent of certain aromatic solvents and motor fuels. Tetralin is prepared by

the hydrogenation of naphthalene and is used as a constituent of solvents, motor fuels, and lubricants.

The polyphenyls of industrial importance are diphenyl (biphenyl) and the terphenyls (triphenyls). Diphenyl is produced by thermal dehydrogenation of benzene; terphenyls are by-products in the manufacture of diphenyl. Diphenyl is one of the most thermally stable of known organic compounds. This forms the basis for its use either alone or mixed with diphenyl oxide as a low-pressure, high-temperature, heat-transfer medium. Dowtherm A is a eutectic mixture of 73.5 per cent diphenyl ether (diphenyl oxide) and 26.5 per cent diphenyl. The terphenyls are also used as heat-storage and heat-transfer agents. Because of their low vapor pressure and low order of toxicity these hydrocarbons do not present industrial hygiene hazards and do not warrant detailed discussion in this chapter.

Naphthalene is the most extensively used polynuclear hydrocarbon in industry. It is the most abundant single constituent of coal tar and is available from this source in technical grades at a low price. It is important as a starting material and intermediate in the synthesis of numerous chemicals and is used also as a moth repellent and insecticide.

B. TOXICOLOGY OF THE AROMATIC HYDROCARBONS

The liquid aromatic hydrocarbons are primary irritants which on repeated or prolonged contact with the skin will cause dermatitis due to their dehydrating and defatting action. Contact of the liquid hydrocarbons with lung tissue (aspiration) will cause severe pulmonary edema, pneumonitis, and hemorrhage. Because of their low surface tension a small volume of liquid will cover a large area so that extensive lung injury can result from the aspiration of a few cubic centimeters of a liquid hydrocarbon. The vapors are more irritating to the mucous membranes than equivalent concentrations of the aliphatic and alicyclic hydrocarbons.

Systemic injury can result from the inhalation of vapors of the aromatic hydrocarbons. It is well established that benzene (benzol) is an insidious toxicant which has a specific destructive effect on the blood-forming tissue. The preponderance of the evidence from animal experimentation indicates that the alkyl derivatives do not possess this property and that benzene appears to be unique among hydrocarbons as a myelotoxicant. Because the name "alkylbenzenes" suggests to the uninformed that these compounds are similar to benzene, the term "phenylalkanes" has been suggested to dissociate them from benzene.[1] Pharmacologically, the phenylalkanes can be classified with the central nervous system depressants.

II. Specific Aromatic Hydrocarbons

BENZENE, C_6H_6 (Benzol)

1. *Sources, Uses, and Industrial Exposures*

Benzene (not to be confused with petroleum benzin, a hydrocarbon mixture discussed in Chapter 28) is obtained as a by-product of the coke-oven industry

[1] H. W. Gerarde, *A.M.A. Arch. Ind. Health*, **19**, 403 (1959).

and the petroleum industry. From coke-oven operations it is recovered from the gases and coal tar. As a petrochemical it is obtained by dehydrogenation of naphthene fractions or by cyclization and aromatization of paraffin hydrocarbons. Benzene is used extensively as a solvent in the chemical and drug industries, as a starting material and intermediate in the synthesis of numerous chemicals, and as a constituent of motor fuels.

2. *Physical and Chemical Propertirr*

See Table 1.

3. *Determination in the Atmosphere*

In the presence of other gases the most satisfactory method of determining benzene is the nitration procedure described by Schrenk and co-workers.[1] The interferometer (Vol. I, page 179), a properly calibrated and serviced benzol indicator, and the M.S.A. aromatic hydrocarbon detector may be used for air analysis.

1 mg./liter ≅ 313 p.p.m. and 1 p.p.m. ≅ 3.19 mg./cu. meter at 25°C., 760 mm. Hg.

4. *Physiological Resporrse*

Acute Toxicity. Acute poisoning by benzene is due to its nnrcotic action and in many respects resembles that caused by other low molecular weight petroleum hydrocarbons. Flury[3] gives the following figures for a single exposure for man: 3000 p.p.m.—endurable for 0.5 to 1 hour; 7500 p.p.m.—dangerous after 0.5 to 1 hour; 20,000 p.p.m.—fatal after 5 to 10 minutes. The inhalation of a high concentration of benzene may cause exhilaration followed by drowsiness, fatigue, vertigo, nausea, and headache. With higher concentrations or longer exposure times, convulsions followed by paralysis and loss of consciousness may result. An initially rapid respiration soon diminishes in rate and circulatory collapse may follow. Death may ensue quickly from respiratory paralysis after severe exposure. Dautrebande[4] found that dogs inhaling benzene initially developed hypertension. This was soon followed by paralysis of the vasomotor system due to the effect of benzene on the smooth muscle of the blood vessels. High concentrations of benzene are irritating to the mucous membranes of the eyes, nose, and respiratory tract. Liquid benzene is irritating to the skin and direct contact of liquid benzene with the lung (aspiration) will cause severe pulmonary edema and hemorrhage which may be fatal depending on the volume aspirated.

Brief exposures to high concentrations in the air may cause chronic benzene intoxication. It is not good practice to encourage or to condone exposure to 100 p.p.m. or more for even brief periods without suitable respiratory protection. A

[1] H. H. Schrenk, S. J. Pearce, and W. P. Yant, *U. S. Bur. Mines Rept. Invest. No.* 3287 (1935).

[3] F. Flury, Arch. *exptl. Pathol.* Phannakol., 138, 65 (1928).

[4] L. Dautrebande, Arch. *intern. pharmacodynamie,* 44, 394 (1933).

TABLE

Physical and Chemical Properties of

Property	Benzene	Toluene	Xylenes		
			o-	*m-*	*p-*
Mol. wt.	78.11	92.13	106.16	106.16	106.16
B.p., °C.	80.103	110.623	144.414	139.102	138.348
F.p., °C.	5.533	−94.991	−25.175	−47.872	13.263
n_D (25°C.)	1.49790	1.49405	1.50282	1.49455	1.49319
Vapor pressure	100 mm. (26.085°C.)	30 mm. (26.04°C.)	10 mm. (32.11°C.)	10 mm. (28.26°C.)	10 mm. (27.30°C.)
Density (25°/4°C.)	0.87368	0.86220	0.87583	0.85985	0.85666
Vapor density (air = 1)	2.7	3.2	3.7	3.7	3.7
Per cent in satd. air, 760 mm.	13.15 (26°C.)	3.94 (26°C.)	1.32 (32°C.)	1.32 (28.3°C.)	1.32 (27.3°C.)
Density of satd. vapor—air mixture at 760 mm. (air = 1)	1.22 (26°C.)	1.09 (26°C.)	1.03 (32°C.)	1.03 (28°C.)	1.03 (27°C.)
Specific dispersion	189.6	184.4	180.3	181.1	181.8
Solubility in water (20°C.)	0.082 g. per 100 ml. (22°C.)	0.047 g. per 100 ml. (16°C.)	Insoluble	Insoluble	Insoluble
Solubility in ethyl alcohol	Miscible	Miscible	Very soluble	Very soluble	Very soluble
Solubility in ethyl ether	Miscible	Miscible	Very soluble	Very soluble	Very soluble
Flammable limits (% by vol. in air)	1.35–7.90	1.17–7.10	1.09–6.40	1.09–6.40	1.08–6.60
Flash point (closed cup)	12°F.	40°F.	63°F.	77°F. (t.o.c.)	77°F.

brief exposure may be warranted in case of an emergency, but should not be permitted in addition to the routine exposure to the threshold limit of 25 p.p.m.

Chronic Toxicity. The chronic effects of inhaling small amounts of benzene over a prolonged period of time are of the greatest importance in the industrial use of this chemical. The symptoms, signs and blood changes in chronic benzene poisoning may not invariably present a typical picture of severe anemia and leukopenia. Greenburg and his associates[5] did complete blood studies on 102 workmen exposed to benzene in the rotogravure industry. A positive diagnosis of

[5] L. Greenberg, M. R. Mayers, L. Goldwater, and A. R. Smith, *J. Ind. Hyg. Toxicol.*, **21**, 395 (1939).

TABLE 1

Some Aromatic Hydrocarbons

Ethyl-benzene	Cumene	Styrene	*p-tert-* Butyl-toluene	Naphthalene	Tetralin
106.16	120.19	104.14	148.24	128.16	132.20
136.187	152.393	145.2	192.8	217.9	207.2
−94.950	−96.028	−30.628		80.22	−30.0
1.49319	1.48874	1.5441	1.4892	1.58218 (at 99.6°)	1.54614 (at 20.2°)
10 mm. (25.90°C.)	10 mm. (38.33°C.)	4.3 mm. (15°C.)	0.65 mm. (25°C.)	Approx. 0.082 mm. (25°C.)	
0.86258	0.85748	0.9021	0.8575	1.145 (20°/4°C.)	0.971 (20°/4°C.)
3.7	4.2	3.6		4.4	4.6
1.32 (26°C.)	1.32 (38.3°C.)	0.57 (15°C.)		0.01 (25°C.)	
1.03 (26°C.)	1.03 (38°C.)	1.02 (15°C.)	1.00479 (25°C.)	1.00 (25°C.)	
174.6	166.2	265			
0.014 g. per 100 ml. (15°C.)	Insoluble	0.31 g. per 100 ml. (25°C.)	Insoluble	3 mg. per 100 ml.	Insoluble
Miscible	Soluble	Miscible	Miscible	4.2 g. per 100 ml. (20°C.)	Very soluble
Miscible	Soluble	Miscible	Miscible	Very soluble	Very soluble
0.99–6.70	0.88–6.50	1.10–6.10		0.88–5.9	
63°F	102°F.	86°F.	155°F. (t.o.c.)	176°F.	ca. 172°F.

chronic benzene poisoning varying in severity was made in 74 men in this group. It is significant that in this group were found men with clinical pictures of benzene poisoning whose blood was normal, and serious blood abnormalities in the complete absence of signs or symptoms of benzene poisoning. A few men developed blood abnormalities in a 60-day period after removal from the source of benzene exposure. The percentages of the positive diagnoses of benzene poisoning detected by any single laboratory blood test in this group are given in Table 2. The bone marrow in chronic benzene poisoning may appear normal, aplastic, or hyperplastic. Signs and symptoms may include headache, dizziness, fatigue, loss of appetite, irritability, nervousness, nosebleed, and other hemorrhagic manifestations.

TABLE 2

Detection of Benzene Intoxication by Blood Tests

Test	Per cent positive
Mean corpuscular volume of erythrocytes (above 94 cu.μ)	64.9
Erythrocyte count (below 4.5 million)	63.5
Platelet count (below 100,000)	41.9
Hemoglobin (less than 13 g. per 100 ml. blood)	40.5
Leucocyte count (below 5000)	40.5

Absorption and Excretion. Industrial benzene poisoning results almost exclusively from the inhalation of benzene in the atmosphere. Saturation of the circulating blood occurs rapidly, with 70 to 80 per cent saturation being reached within 30 minutes (see Vol. I, pages 156–158, and Figs. 2 and 3 for absorption and elimination curves for benzene). However, it requires several days for complete saturation of the body tissues and fluids. Benzene is rather insoluble in blood and the equilibrium constant or coefficient of distribution of benzene between room air and the blood of dogs breathing this air is 6.58, that is, milligrams of benzene per liter of blood/milligrams of benzene per liter of air. This may also be stated as follows: at equilibrium, the average concentration of benzene in the blood is 2.1 mg./liter for each 100 p.p.m. of benzene in the inhaled air. As the blood circulates, however, it comes to equilibrium with the tissues and the fatty tissues store quantities of benzene in this manner.[6] Elimination involves the same process in reverse because most of the benzene is eliminated through the lungs, being picked up by the blood in the capillaries and carried to the lungs, where equilibrium with the alveolar air is rapidly established, as previously explained.

Small amounts of benzene are absorbed through the skin wherever the liquid touches the skin. It is not probable that systemic poisoning can arise from immersing the hands in benzene. However, well-recognized results of skin contact with benzene include skin defatting with erythema, dry scaling, and even secondary infections. In this respect, benzene is not considered to be as severe as toluene, xylene, and many other solvents, including certain of the petroleum distillates.

Some benzene is eliminated unchanged in the urine. Some is oxidized in the body to phenols and diphenols which, in turn, are conjugated in the liver with sulfate ions and excreted in the urine, thus increasing the ratio of ethereal sulfates to total sulfates in the urine. This is the basis of a test to determine the severity of the over-all daily exposure to benzene.

Tests Indicating Exposure. The exposure of an individual at any particular moment may be rather accurately determined by analysis of the benzene in a sample of arterial blood[7] and computation of the corresponding concentration in the air from the distribution coefficient of benzene between blood and room air.[6]

[6] H. H. Schrenk, W. P. Yant, S. J. Pearce, F. A. Patty, and R. R. Sayers, *J. Ind. Hyg. Toxicol.*, **23**, 20 (1941).

[7] S. J. Pearce, H. H. Schrenk, and W. P. Yant, *U. S. Bur. Mines Rept. Invest.* No. **3302** (1936).

The over-all or integrated exposure may be best arrived at by determining the ratio of inorganic to organic sulfates in a sample of urine collected near the end of the day's exposure, or within one hour after cessation of the day's exposure.[8,9] The ratio of inorganic sulfates to total sulfates in the urine is normally 85 per cent or above. Upon exposure to benzene this ratio is decreased, and the decrease is related quantitatively to the severity of the exposure to the point where nearly all sulfates are eliminated as organic sulfates. Ratios of less than 70 per cent inorganic are abnormal and may be indicative of benzene exposure and warrant investigation of exposure sources with a view toward correction. Ratios of 60 per cent or less inorganic indicate dangerous exposures warranting immediate correction. Concurrent exposure to carbon tetrachloride, or any other material having an adverse effect upon the liver, may decrease the sulfate response so that ratios on the order of 70 per cent inorganic would indicate exposures of great significance. As pointed out in the original paper,[8] the sulfate test must be made while the worker is on the job, and it is not to be considered a method for diagnosing benzene poisoning, because the changes are merely indicative of exposure, not of poisoning nor of damage. It is therein that the great preventive value of this test lies; the indication occurs in advance of any demonstrable harmful effects, but forewarns of their coming if exposures are not reduced. However, in complete disregard of these well-known facts, case histories of benzene poisoning too often carry enlightening comments to the effect that from a prognostic viewpoint repeated blood studies on the hospitalized patient are of greater value than concurrent repeated urinary sulfate determinations!

It seems logical to make periodic hematological studies of the blood of all workers coming in contact with any benzene vapors, perhaps every 30 days, and urine sulfate tests, perhaps weekly. Air analyses for benzene in suspected atmospheres should be made frequently. If these three control measures are consistently performed and heeded, as a guide for elimination of significant exposures, it is believed that no fear need be entertained regarding the careful use of benzene in industrial processes.

5. *Hygienic Standard of Permissible Exposure*

The threshold limit for benzene has been established at 25 p.p.m.

6. *Odor and Warning Properties*

Benzene has a distinctive odor which should be familiar to all industrial hygienists. The warning properties, however, are inadequate since 100 p.p.m. has an irritation rating of zero and an odor intensity between 1 and 2.

[8] W. P. Yant, H. H. Schrenk, R. R. Sayers, A. J. Horvath, and W. H. Reinhart, *J. Ind. Hyg. Toxicol.*, **18**, 69 (1936).

[9] W. P. Yant, H. H. Schrenk, and F. A. Patty, *J. Ind. Hyg. Toxicol.*, **18**, 349 (1936).