

The Preparation of Ferric Mesoporphyrin Chloride

BY T. HARRISON DAVIES*

Ferric mesoporphyrin chloride is readily obtained from ferric protoporphyrin chloride by reduction of the latter with hydrogen and palladium charcoal in alkaline methyl alcohol solution. The method leads to higher yields with less labor than the procedure of Fischer and Pützer¹ and Fischer and Stängler,² in which ferric protoporphyrin chloride is first reduced to mesoporphyrin by the action of formic acid and colloidal palladium and the iron is then reintroduced in acetic acid solution. The yields are higher and the general procedure is less troublesome than the method of Fischer and Röse,³ in which ferric mesoporphyrin is obtained directly by heating ferric protoporphyrin in pyridine-methyl alcohol or pyridine-potassium methyl alcoholate solution in a bomb at 225°.

Experimental

Ferric protoporphyrin chloride (4 g.), prepared and recrystallized by the usual methods, is dissolved in 450 ml. of methyl alcohol and 50 ml. of 0.5 *N* potassium hydroxide. Palladinized charcoal (2 g. of a preparation 12% in palladium) is added. The mixture is refluxed with hydrogen bubbling until a test drop in a few ml. of 0.5 *N* sodium cyanide solution gives no evidence of the absorption bands of cyanide ferrous protoporphyrin upon reduction with a little sodium dithionite. About eight hours is ordinarily required. The solution is cooled and filtered. The catalyst, after thorough washing, drying, and shaking with air, can be used again. The filtrate is treated with 1 *N* hydrochloric acid to precipitate the metalloporphyrin. The latter is collected on a filter, washed with a little water and dried *in vacuo* over sodium hydroxide. The semi-crystalline material is dissolved in 100 ml. of chloroform containing 4 g. of quinine. The chloroform solution is added dropwise to 150 ml. of glacial acetic acid saturated with sodium chloride and held above 90° on a water-bath. During the addition, air is bubbled through the acetic acid to assist in the removal of the chloroform. The solution is allowed to cool slowly. After a few hours the crystalline ferric mesoporphyrin chloride is collected on a hardened filter, washed with 50% acetic acid, then with water, and finally dried over potassium hydroxide: yield in one preparation 2.7 g., in a second 3.2 g.

The absorption spectra of cyanide ferrous mesoporphyrin and of ethanalamine ferrous mesoporphyrin from this preparation were identical with those of a preparation of ferric mesoporphyrin chloride made by the method of Fischer and Stängler from an authentic sample of mesoporphyrin hydrochloride.

(* National Research Fellow in Medicine.

(1) Fischer and Pützer, *Z. physiol. Chem.*, **154**, 39 (1926).

(2) Fischer and Stängler, *Ann.*, **459**, 53 (1927).

(3) Fischer and Röse, *Z. physiol. Chem.*, **88**, 9 (1913).

ABSORPTION SPECTRA

Sample	In NaCN soln. + Na ₂ S ₂ O ₄	In NH ₂ CH ₂ - CH ₂ OH soln. + Na ₂ S ₂ O ₄
Ferric protoporphyrin chloride	531-541; 565-574	(525); 550-562
Ferric mesoporphyrin chloride from mesoporphyrin hydro- chloride	527-535; 555-562	(515); 542-551
Ferric mesoporphyrin chloride by this procedure	526-536; 555-562	(516); 541-550

GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA RECEIVED DECEMBER 28, 1939

Reaction of *bis*-β-Chloroethyl Ether with Ethylenediamine

BY M. E. HULTQUIST AND E. H. NORTHEY

The reaction of *bis*-β-chloroethyl ether with ammonia, aliphatic monoamines, and aromatic amines and diamines is well known.^{1,2,3,4} We sought a simpler method for the preparation of 4-(β-aminoethyl)-morpholine than the reaction of *N*-(β-bromoethyl)-phthalimide with morpholine followed by hydrolysis and found one in the action of *bis*-β-chloroethyl ether with a large excess of ethylenediamine.

To 1.875 kg. of 57.5% ethylenediamine (18 moles anhydrous) in a 5-liter flask equipped with agitator, reflux condenser and dropping funnel, 863 g. (6 moles) of *bis*-β-chloroethyl ether was added during one hour. Thirty minutes later, 505 g. of flake sodium hydroxide was added cautiously. The mixture was cooled and the precipitated salt filtered. The liquor was dried over solid sodium hydroxide and then distilled through a 60 cm. × 50 mm. packed column. After distillation of excess ethylenediamine, 370 g. (47.5% of theoretical) of 4-(β-aminoethyl)-morpholine boiling at 121-123° (68 mm.), b. p. 204.5° (768 mm.), was obtained as a water-white liquid with a refractive index of 1.4742 (25°). These values were in agreement with those of 4-(β-aminoethyl)-morpholine prepared by the phthalimide process.

Anal. Calcd. for C₆H₁₄N₂O: N, 21.55. Found: N, 21.4.

On fractionation of the residues, the following cuts were obtained: 50 g. 123° (68 mm.) to 164° (30 mm.); 69 g. 164-166° (30 mm.); 8.5 g. 166-200° (30 mm.); 7.3 g. 200-203° (30 mm.); 5.5 g. 203° (30 mm.) to 220° (4 mm.).

Fraction 2 was mainly ethylenedi-(4-morpholine). It solidified to a light yellow solid. After two recrystallizations from hexane, it was obtained as colorless, coarse prisms; m. p. 70-73°, setting point 71.3°. It was converted to the dihydrochloride by dissolving in alcohol and adding concentrated hydrochloric acid, then twice recrystallizing from dilute alcohol.

(1) Axe and Freeman, *THIS JOURNAL*, **56**, 478 (1934).

(2) A. L. Wilson to Carbide & Carbon Chemical Corp., U. S. Patent, 2,096,441, October 19, 1937.

(3) A. L. Wilson to Carbide & Carbon Chemical Corp., U. S. Patents 2,105,828, January 18, 1938.

(4) Marion C. Reed to Goodrich Tire & Rubber Co., U. S. Patent, 2,001,584, May 14, 1935.