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 Pützer[1] 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 ethanolamine 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.

Absorption Spectra

Sample	In NaCN soln. + $Na_2S_2O_4$	In $NH_2CH_2CH_2OH$ soln. + $Na_2S_2O_4$
Ferric protoporphyrin chloride	531–541; 565–574	(525); 550–562
Ferric mesoporphyrin chloride from mesoporphyrin hydrochloride	527–535; 555–562	(515); 542–551
Ferric mesoporphyrin chloride by this procedure	526–536; 555–562	(516); 541–550

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[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).

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 $C_6H_{14}N_2O$: 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.

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[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.

The dihydrochloride crystallized as colorless plates decomposing and subliming over 250°.

Anal. Calcd. for $C_{10}H_{22}O_2N_2Cl_2$: N, 10.3; Cl, 25.9. Found: N, 10.5; Cl, 25.7.

Fraction 4 was mainly *bis*-{2-[N-(β-aminoethyl)-amino]-ethyl} ether, a light yellow oil. It was converted to the tetrahydrochloride and recrystallized three times from methanol giving small, colorless, thin plates; m. p. 185–187°.

Anal. Calcd. for $C_8H_{26}ON_4Cl_4$: N, 16.7; Cl, 42.2. Found: N, 16.9; Cl, 41.6.

By increasing the proportions of ethylenediamine in the reaction to 6 moles to 1, a 58% yield of 4-(β-aminoethyl)-morpholine, based on *bis*-β-chloroethyl ether, was obtained.

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Precipitation of Barium Sulfate in the Presence of Ammonium Chloride

BY J. T. MCHENRY, G. A. AMPT AND E. HEYMANN

It has been known for a long time that the analytical errors involved in the precipitation of the sulfate radical as barium sulfate are due to the presence of foreign material in the precipitate. Several explanations for the mechanism of this inclusion of foreign material have been considered.[1]

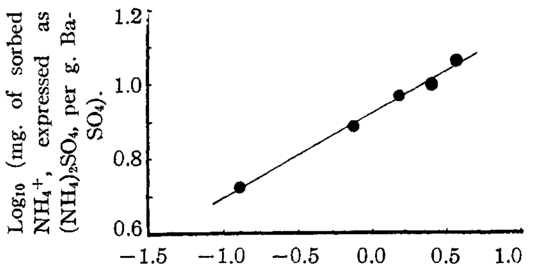

Fig. 1.

We performed a number of precipitations of barium sulfate by means of a barium chloride solution from sulfuric acid in the presence of ammonium chloride. To 200 ml. of boiling solution, containing 0.1859 equivalent of ammonium sulfate and varying amounts of ammonium chloride, 19.0 ml. of 1.96 *N* barium chloride solution was slowly added. Twenty hours after precipitation the precipitate was filtered, washed and dried in a vacuum desiccator.

The sorbed material was determined in two ways: (1) 1-g. aliquots were dissolved in 10 ml. of cold concentrated sulfuric acid, the solution poured into 200 ml. of boiling water, the liquid filtered, the precipitate washed and the filtrate made alkaline and distilled. The ammonia was collected in 0.1 *N* hydrochloric acid and the excess acid determined iodimetrically. Second extractions were carried out on the reprecipitated samples and the total extracted was regarded as the full amount of sorbed material, (2) one-gram aliquots were dissolved in 200 ml. of 50% sodium hydroxide by warming, the solution diluted to 500 ml. and then distilled. The ammonia was absorbed in 0.1 *N* hydrochloric acid. Both procedures gave results which did not differ by more than 4%.

Investigation of our precipitates, by a method first suggested by Hulett and Duschak,[2] showed that about 50% of the ammonia is present as sulfate.

Figure 1 shows that a linear relation exists between the logarithms of the amount sorbed and the ammonium chloride concentration (Freundlich's adsorption isotherm). It is, however, recognized that this empirical relation may also formally describe processes other than surface adsorption. Further it can be seen that barium sulfate, precipitated in the presence of *N* ammonium chloride contains 7.0 mg. of NH_4, expressed as ammonium sulfate, per 1 g. of barium sulfate.

The investigations of Kolthoff and MacNevin[3] and of Imre[4] indicate that the essential process in

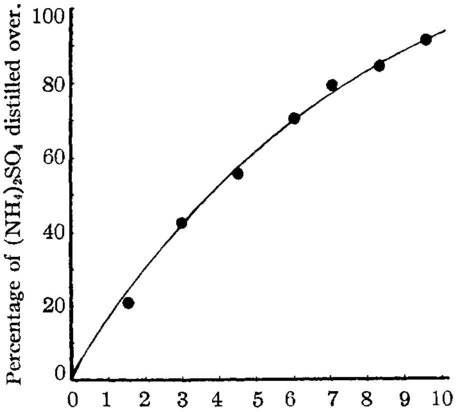

Fig. 2.

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(1) E. F. Allen and J. Johnston, THIS JOURNAL, **32**, 588 (1910); J. Johnston and L. H. Adams, *ibid.*, **33**, 829 (1911); I. M. Kolthoff, *J. Phys. Chem.*, **36**, 860 (1932); Z. Karaoglanow, *Z. anal. Chem.*, **106**, 129 (1936); *Z. physik. Chem.*, **A178**, 143 (1937); D. Balarew and co-workers, *Kolloid-Beihefte*, **30**, 249 (1929); **32**, 304 (1930); *Kolloid-Z.*, **67**, 203 (1934); **83**, 319 (1938); *Z. anal. Chem.*, **101**, 161 (1935); *Z. Krist.*, **89**, 268 (1934); *Kolloid-Beihefte*, **50**, 1 (1939).

(2) G. A. Hulett and L. A. Duschak, *Z. anorg. Chem.*, **40**, 196 (1904); cf. Treadwell and Hall, "Analytical Chemistry," Vol. II, p. 402.

(3) I. M. Kolthoff and W. M. MacNevin, THIS JOURNAL, **58**, 725 (1936).

(4) L. Imre, *Kolloid-Z.*, **87**, 12 (1939).