

A Small-scale Synthesis of Ferrocene

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Submitted in honour of the sixtieth birthday of our teacher, Professor *Arne Fredga*

A small-scale synthesis of ferrocene is described and applied to the preparation of ^{55}Fe - and ^{59}Fe -labelled ferrocene.

In connection with studies on the resorption of iron-containing remedies, it was of interest to analyze blood samples for their content of ^{55}Fe and ^{59}Fe . The purpose of the investigation was to determine the concentration of ^{59}Fe by its γ -radiation, and the ratio of the ^{55}Fe and ^{59}Fe concentrations by liquid scintillation counting based on their radiations. Since the liquid scintillation measurements were performed in toluene solution, it was desirable to convert the iron isotopes into toluene-soluble derivatives. For this purpose, ferrocene seemed to be suitable.

The synthesis of ferrocene from dry ferric chloride, iron powder and cyclopentadiene is described in Organic Syntheses¹. The method requires anhydrous conditions², since the presence of water decreases the yield appreciably*, and, therefore, the first problem we had to solve was to convert the iron of the blood into anhydrous ferric chloride. The destructed blood samples were electrolyzed, using platinum electrodes³. The cathode was prepared from coiled platinum wire, which could be heated electrically; allowing the deposited iron to be burned in chlorine. The ferric chloride obtained was dissolved in dry tetrahydrofuran, and used immediately in the synthesis. The ferric chloride solution could not be stored for long periods, since the solute afforded polymerization of the solvent⁴.

Usually the reduction of the ferric chloride to ferrous chloride is achieved by means of *ferrum reductum*. In the present case, however, the use of this reducing agent leads to an undesired dilution of the radioactivity. This difficulty was avoided by replacing the iron powder by zinc dust.

* Since the determination was based on the ratio between the ^{55}Fe and ^{59}Fe content of blood, the yield might not necessarily be quantitative; but it was desirable that it should be high.

The method described is quite useful for small-scale synthesis of ferrocene, but, unfortunately, it was impossible to determine the activity by liquid scintillation counting, since the ferrocene involved quenching of the radiation.

EXPERIMENTAL

Preparation of dry ferric chloride *: 30 mg of Fe, obtained as hydroxide from the destructed blood samples, were dissolved in a 5 % solution of oxalic acid, and the pH was adjusted to 4.5 with concentrated ammonia ³. The volume was then 50 ml. The platinum anode was applied as a stirrer. The cathode was made of a 0.2 mm platinum wire about 90 cm in length which was wound around a U-shaped glass tube. The solution was electrolyzed at 4.5 V and 0.4 A for 2.5 h. During the process it was necessary to correct the pH to 4.5 by adding a few drops of 5 M H₂SO₄. When the electrolysis was completed, the cathode was washed carefully with water and ethanol.

A three-necked flask (Fig. 1) was fitted with a gas inlet tube, a gas outlet

* The destruction of the blood samples was performed by Mr. H. Jenner ³, who also made important contributions to the electrolytical procedure.

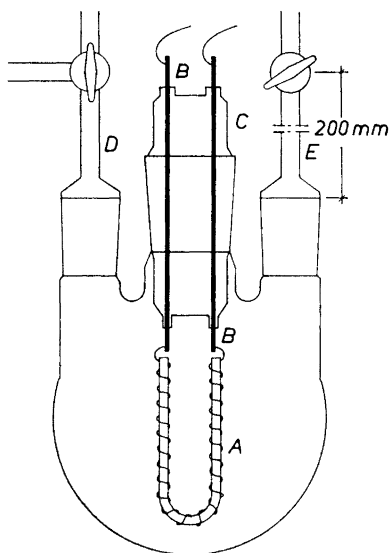


Fig. 1. A. The cathode. B. Pt-wires ($\text{\O} 2\text{ mm}$). C. Glass-stopper. D. Gas inlet tube. E. Gas outlet tube.

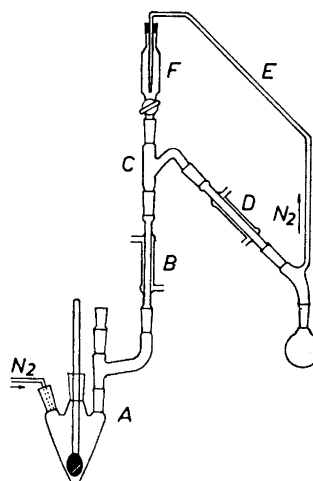


Fig. 2. A. A three-necked flask (25 ml) with a gas inlet tube ($\text{\O} 1\text{ mm}$) of stainless steel for oxygen-free N₂ and a stirrer. B. Reflux condenser. C. Stillhead. D. Distillation condenser. E. A glass tube ($\text{\O} 4\text{ mm}$) through which N₂ is conveyed from the receiver adapter up into the dropping funnel. F. Dropping funnel (10 ml). The upper conical joint is fitted with cotton-wool.

tube, and a glass-stopper through which two platinum wires were drawn. These functioned as holders and contacts for the cathode, thus allowing it to be heated electrically. When the cathode had been put in place, it was dried in a stream of dry nitrogen.

The nitrogen was replaced by chlorine, and the cathode was heated (15 V, 3–4 min), until the iron was burned to iron chloride, which was partly deposited on the walls of the flask. After cooling, the excess of the chlorine was removed by a slow stream of nitrogen, and the ferric salt was dissolved in 7 ml of dry tetrahydrofuran.

Preparation of ferrocene: 28 mg of zinc dust (90 % "active" zinc) was placed in a three-necked flask (Fig. 2) fitted with a gas inlet tube, a mechanical stirrer and a reflux condenser, connected to a distillation condenser via a stillhead. A stream of oxygen-free nitrogen was passed through the apparatus for 20 h.

The freshly prepared chloride solution was placed in a dropping funnel on the stillhead (Fig. 2), and a nitrogen stream was conveyed through the solution for a few minutes. Then the solution was poured out into the reaction vessel through the reflux condenser, and subsequently, the funnel was rinsed with 2 ml of tetrahydrofuran. The mixture was refluxed for 45 min and the bulk of the solvent was removed by distillation; the latter operation required about half an hour.

Meanwhile, 1.4 ml of freshly prepared cyclopentadiene⁵ was dissolved in 1.4 ml of diethylamine. The solution was placed in the dropping funnel and a stream of nitrogen was passed through the solution for a few minutes.

When the distillation was finished, the residue was cooled in an ice bath, and the cyclopentadiene solution was added while stirring vigorously. The dark mixture was stirred at room temperature overnight, and the excess of the amine was removed under reduced pressure. The residue was steam-distilled and the distillate extracted with petroleum ether. The solvent was removed and the ferrocene purified by sublimation *in vacuo*. Yield 71 mg (70 %, calculated on the iron content of the original ferric salt solution), melting at 171–174°C.

Acknowledgements. The authors are deeply grateful to Messrs. Adolf Berggren, Hans Jenner and Wolfgang Kirsten for valuable advice and discussions, and to Dr. Karl Johan Öbrink for making the radiation measurements.

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Received December 19, 1961.