

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

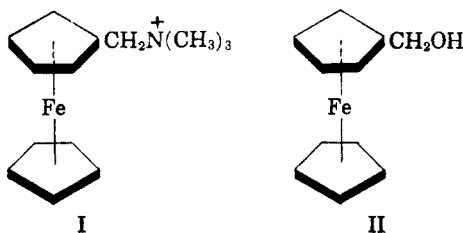
Reaction of the Methiodide of *N,N*-Dimethylaminomethylferrocene with Potassium Cyanide to Form Ferrocylacetonitrile¹

DANIEL LEDNICER, JACQUE K. LINDSAY, AND CHARLES R. HAUSER

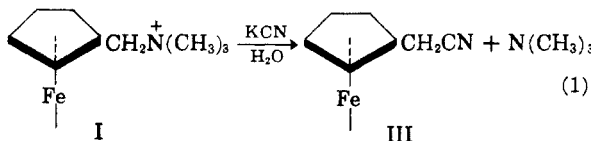
Received August 27, 1957

The methiodide of *N,N*-dimethylaminomethylferrocene was treated with potassium cyanide to afford ferrocylacetonitrile. This nitrile was converted to various derivatives. Evidence is presented for the structures of these compounds. An anomalous Leuckart reaction is reported.

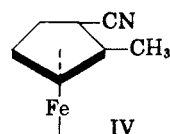
The displacement of trimethylamine from quaternary ammonium ion I by hydroxide ion to form alcohol II has previously been described.²



The analogous displacement reaction with the cyanide ion to give nitrile III is described in the present paper.

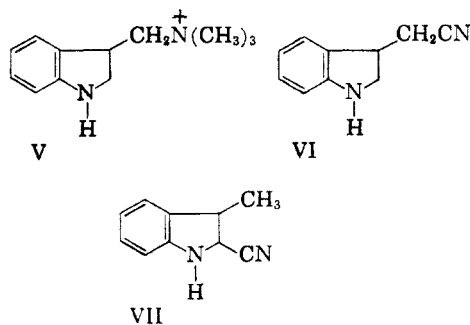


Before presenting the evidence that this nitrile has structure III, it should be mentioned that the erroneous structure IV for this nitrile was assigned recently in a communication.³



This structural misinterpretation arose in the preparation of the tertiary amine from the reduction product of the nitrile employing the Eschweiler-Clarke modification of the Leuckart reaction.⁴ This transformation has now been found to follow an anomalous course (see below).

It should also be mentioned that quaternary ammonium ion V has been observed by other workers⁵ to produce with sodium cyanide both nitrile VI (60%) and nitrile VII (14%), which would be analogous to the ferrocene nitriles III and IV respectively.



(1) Supported by the Office of Ordnance Research, U. S. Army. Presented before the Southeastern Regional Meeting of the American Chemical Society, Nov. 15, 1957, Durham, N. C.

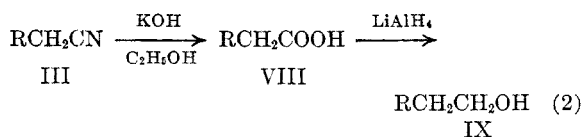
(2) C. R. Hauser and J. K. Lindsay, *J. Org. Chem.*, **22**, 355 (1957).

(3) C. R. Hauser, J. K. Lindsay, D. Lednicer, and C. E. Cain, *J. Org. Chem.*, **22**, 717 (1957).

(4) See M. L. Moore, *Org. Reactions*, **5**, 303, 307 (1949).

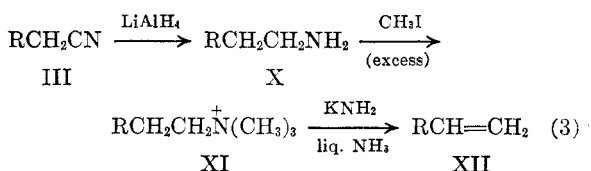
(5) See H. R. Snyder and E. L. Eliel, *J. Am. Chem. Soc.*, **70**, 1857 (1948).

Evidence for nitrile III. The nitrile prepared according to Equation 1 was hydrolyzed to the corresponding acid (VIII) which was reduced to the alcohol (IX) as indicated in Equation 2.



The acid obtained in this manner not only had a melting point in good agreement with that reported for acid VIII prepared from acetylferrocene (Wilgerodt reaction),⁶ but its infrared spectrum was identical with that of a sample of acid VIII synthesized by this method.⁷ Moreover, the acid exhibited an ultraviolet spectrum having a maximum at 320 m μ , which is close to that of 323 m μ observed for hydroxymethylferrocene, and considerably different from that shown by ferrocene-carboxylic acid. This may be considered evidence for the lack of conjugation of the carboxyl group with the ring as in structure VIII.

Also, nitrile III was reduced to the corresponding primary amine X which was exhaustively methylated to form quaternary ammonium ion XI. This quaternary ion underwent β -elimination with potassium amide in liquid ammonia to form vinylferrocene (XII) as described previously.⁸

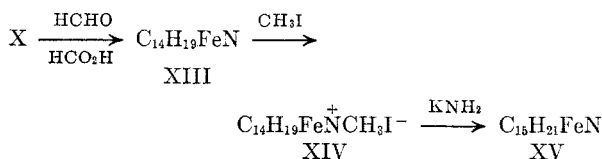


The conversion of the nitrile III to vinylferrocene as represented by Equation 3 confirms its two-carbon sidechain.

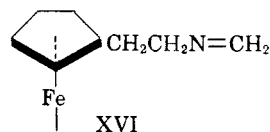
It should be pointed out that quaternary ammonium ion I, from which nitrile III was prepared (Equation 1), may be obtained from ferrocene in two convenient steps,² and that nitrile III should be a useful intermediate for the synthesis of not only the derivatives shown above but also of other compounds. A study is in progress on certain condensations involving the reactive methylenic hydrogens of this nitrile.

Anomalous Leuckart reaction. When the primary amine X prepared by the reduction of nitrile III was treated with formaldehyde and formic acid by the common method for effecting the *N,N*-dimethylation of primary amines,⁴ a tertiary amine (XIII) was obtained. This tertiary amine produced

a methiodide (XIV) that was different from, but isomeric with, the methiodide XI prepared by the exhaustive methylation of primary amine X. Whereas the methiodide XI underwent β -elimination with potassium amide to form vinylferrocene (Equation 3), the unidentified methiodide XIV produced a new tertiary amine XV that was homologous with tertiary amine XIII.



Apparently in the acidic medium of the first step of this series of reactions, there occurred a reaction other than (or in addition to) the expected *N,N*-dimethylation. It might be thought that the presumably first formed methylene derivative XVI underwent cyclization involving the ferrocene nucleus, since an acid catalyzed cyclization of similar Schiff bases from β -phenylethylamines has been reported.⁹ However, the analytical data for our products have not been consistent with cyclic structures that might be expected from XVI.



EXPERIMENTAL¹⁰

Ferrocylacetonitrile (III). A solution of 84.4 g. (0.22 mole) of the methiodide of *N,N*-dimethylaminomethylferrocene¹¹ and 85 g. of potassium cyanide in 850 ml. of water was brought to reflux. Within 5 min. the copious evolution of trimethylamine was noted as an oil separated from the solution. At the end of 2 hr., the reaction mixture was cooled and extracted with ether. The ethereal solution was then washed well with water, percolated through anhydrous sodium sulfate, and taken to dryness. The solid residue thus obtained was recrystallized from hexane to afford 47.9 g. (95%) of the nitrile as bright yellow crystals, m.p. 76–79°. Since this compound darkens quickly on standing it is advisable to use it as soon as possible after preparation.

A small sample was recrystallized from hexane to a constant m.p. of 81–83°.

Anal. Calcd. for C₁₂H₁₁NFe: C, 64.03; H, 4.93; N, 6.22; Fe, 24.81. Found: C, 64.00; H, 4.98; N, 6.05; Fe, 24.52.

Ferrocylacetic acid (VIII). A suspension of 34.3 g. (0.15 mole) of the nitrile (III) in 340 ml. of ethanol was added to a solution of 85 g. of potassium hydroxide in 850 ml. of water. The reaction was then brought to reflux. After the evolution of ammonia had ceased (5 hr.), ethanol was removed *in vacuo* to bring the volume to about 100 ml. The residual suspension was dissolved in 800 ml. of water, extracted twice with ether and filtered. Acidification of the alkaline solution with 85% phosphoric acid afforded flaky

(9) J. S. Buck, *J. Am. Chem. Soc.*, **56**, 1769 (1934).

(10) All melting points are uncorrected and reported as obtained on a Fisher-Johns apparatus. All analyses are by Galbraith Laboratories, Knoxville, Tenn.

(11) See. Ref. 2. This compound was prepared from ferrocene generously supplied by Linde Air Products Co. (Dr. R. L. Pruett), Tonawanda, N. Y.

(6) P. J. Graham, R. V. Lindsey, G. W. Parshall, M. L. Peterson, and G. M. Whitman, *J. Am. Chem. Soc.*, **79**, 3416 (1957).

(7) K. L. Rinehart, Jr., R. J. Curby, Jr., and P. E. Sokol, *J. Am. Chem. Soc.*, **79**, 3420 (1957); a sample of their acid was supplied by Dr. Rinehart.

(8) C. R. Hauser, J. K. Lindsay, and D. Lednicer, *J. Org. Chem.*, **23**, 358 (1958).

golden crystals. The product was collected by filtration and dried to yield 35.0 g. (94%) of ferrocylacetic acid, m.p. 152–156° (dec.); lit.,⁴ 150–152°.

The analytical sample, m.p. 152–155° (dec.) was obtained by sublimation at 130–135° at 0.2 mm.

Anal. Calcd. for $C_{12}H_{12}O_2Fe$: C, 59.05; H, 4.96; Fe, 22.88. Found: C, 59.13; H, 5.07; Fe, 22.78.

2-Ferrocylethanol (IX). Ferrocylacetic acid (24.4 g., 0.10 mole) was placed in a Soxhlet extractor attached to a flask containing a stirred refluxing suspension of 4.1 g. of lithium aluminum hydride in 450 ml. of ether. The heating was continued until all the acid had dissolved (12 hr.). The reaction mixture (ice-cooled) was then treated with water and 400 ml. of 20% hydrochloric acid. The ethereal layer was quickly separated, washed with 5% aqueous sodium hydroxide and water, and then dried over sodium sulfate. The oil which remained when the ether was removed was dissolved in 600 ml. of 30–60° petroleum ether. When this was cooled in ice, the alcohol (19.7 g., 86%) was deposited as light orange needles, m.p. 32.5–33.5°.

Three recrystallizations in the manner described above afforded alcohol of m.p. 41–41.5°.

Anal. Calcd. for $C_{12}H_{14}OFe$: C, 62.61; H, 6.13; Fe, 24.27. Found: C, 62.70; H, 6.04; Fe, 24.11.

β -Ferrocylethylamine (X). A suspension of 20.0 g. (0.54 mole) of lithium aluminum hydride in 1 l. of ether was stirred under reflux for 1 hr. A solution of 77 g. (0.35 mole) of the nitrile in 500 ml. of ether was then added at such a rate as to produce gentle refluxing. After an additional 2 hr. reflux, the reaction mixture was cooled in ice, and 20 ml. of water, 15 ml. of 20% aqueous sodium hydroxide, and 90 ml. of water were added consecutively. The ethereal layer was then decanted from the solid and the latter washed several times with more ether. The combined extracts were then saturated with hydrogen chloride; the resulting salt was separated by decantation under nitrogen. The solid (still soaked with ether) was added to 2*N* sodium hydroxide and the mixture extracted with ether. The ethereal layer was then dried over sodium sulfate and evaporated *in vacuo* to afford 70 g. of dark brown oil. Distillation at 0.5 mm. afforded 51.2 g. (66%) of the primary amine, b.p. 118–120°.

A sample was redistilled at the same pressure to afford the amine, n_D^{25} 1.6155.

Anal. Calcd. for $C_{12}H_{15}NFe$: C, 62.91; H, 6.60; N, 6.11; Fe, 24.38. Found: C, 62.79; H, 6.88; N, 6.04; Fe, 24.15.

Treatment of a sample of the product with saturated alcoholic picric acid afforded the picrate as purple crystals, dec. 185° (dark, 180°).

Anal. Calcd. for $C_{18}H_{18}N_4O_7Fe$: C, 47.18; H, 3.96; N, 12.23; Fe, 12.19. Found: C, 47.28; H, 4.05; N, 12.34; Fe, 12.08.

N,N,N-Trimethyl- β -ferrocylethylammonium iodide (XI). A solution of 1 g. (0.005 mole) of the primary amine (X) in 10 ml. of acetonitrile was treated with 10 ml. of methyl iodide. Evolution of heat was noted. After 30 min. a solution of 0.84 g. (0.01 mole) of sodium bicarbonate in water was added. The two-phase reaction mixture was then stirred for 2 hr., and at the end of this time poured into 100 ml. of ether. The resulting tan precipitate was collected by filtration and recrystallized from water, to afford 1.30 g. (65%) of the quaternary iodide, m.p. 237°. Further recrystallization raised the m.p. of the salt to 240° (dec.).

A small sample (0.2 g.) was treated with 2 ml. of saturated

alcoholic picric acid. The quaternary picrate was deposited as ruby red crystals, m.p. 150–152°.

Anal. Calcd. for $C_{21}H_{24}O_7N_4Fe$: C, 50.41; H, 4.84; N, 11.20; Fe, 11.16. Found: C, 50.63; H, 4.77; N, 11.00; Fe, 9.90.

Reaction of primary amine X with formic acid and formaldehyde. To a solution of 34.4 g. (0.15 mole) of the primary amine, in 39.3 g. (0.75 mole) of formic acid, 33.6 ml. (0.45 mole) of 37% formaldehyde was cautiously added. After the frothing had subsided the reaction mixture was warmed on a steam bath for 8 hr. The dark mixture was then cooled, treated with 75 ml. of 4*N* hydrochloric acid and evaporated to a dark syrup *in vacuo*. This was dissolved in water, and made basic with 40% sodium hydroxide. The amine was taken up in ether, washed with water, and dried. The oil which remained (35 g.) when the solvent was removed was distilled at 0.7 mm. to afford 24.2 g. (63%) of dark amber product XIII, b.p. 123–125°.

The b.p. of the analytical sample was 113° at 0.35 mm.

Anal. Calcd. for $C_{14}H_{18}NFe$: C, 65.38; H, 7.45; N, 5.45; Fe, 21.72. Found: C, 65.19; H, 7.32; N, 5.43; Fe, 21.37.

The picrate of this compound was obtained as golden plates, m.p. 160–161° (dec.), in the usual manner.

Anal. Calcd. for $C_{20}H_{22}N_4O_7Fe$: C, 49.40; H, 4.56; N, 11.52; Fe, 11.49. Found: C, 49.29; H, 4.69; N, 11.66; Fe, 11.31.

Methiodide XIV of XIII was formed by cautiously adding 13 ml. of methyl iodide to a solution of 13 g. of the tertiary amine in 25 ml. of methanol. The solid which came out when the solution was cooled was collected by filtration to afford 18.3 g. of the methiodide, m.p. 258° (dec.).

A sample was recrystallized from methanol ether to afford golden needles, m.p. 258° (dec.).

Anal. Calcd. for $C_{15}H_{22}NFe$: C, 45.14; H, 5.56; N, 3.51; Fe, 13.99. Found: C, 45.34; H, 5.58; N, 3.51; Fe, 14.15.

Reaction of methiodide XIV with potassium amide. To a solution of 0.058 mole of potassium amide in 200 ml. of liquid ammonia there was added in portions over 30 min. 11.6 g. (0.029 mole) of the quaternary salt. Each addition was accompanied by a transient red color. At the end of 2 hr. a small amount of ammonium chloride was added to the brown reaction mixture and the solvent allowed to evaporate. The residue was washed several times with ether and the washes were combined. The ethereal solution was then washed with water, dried, and the solvent removed. A red oil having a strong amine odor XV remained (6.0 g., 77%). The infrared spectrum of this exhibits no N—H band but does suggest a ferrocene derivative substituted in one ring only.

One-half gram of the amine was treated with saturated ethanolic picric acid to give 0.83 g. (90% assuming XV to be a homolog of XIII) of orange crystals, m.p. 130–138°. This was recrystallized from ethanol to a constant m.p. of 138–140°.

Anal. Calcd. for $C_{21}H_{24}N_4O_7Fe$: C, 50.41; H, 4.84; N, 11.20; Fe, 11.16. Found: C, 50.20; H, 4.88; N, 11.29; Fe, 11.24.

The methiodide was prepared from 5.25 g. of the amine in 15 ml. of acetonitrile and 5 ml. of methyl iodide. The salt (5.9 g., 74%) was deposited as orange crystals, charring at 178°. A sample was recrystallized three times from acetonitrile-ether.

Anal. Calcd. for $C_{16}H_{26}NFe$: C, 46.51; H, 5.86; N, 3.39; Fe, 13.52. Found: C, 46.26; H, 5.67; N, 3.41; Fe, 13.64.

DURHAM, N. C.