to that described for the reduction of I, about 7.5 g. of sodium was added to a solution of 2.00 g. (0.0051 mole) of II in 75 ml. of absolute ethanol at 60–70°. Following addition of the sodium, 25 ml. of additional ethanol was added to the thick yellow solution and the mixture was stirred for 1 hr. at room temperature. Water was added and the yellow crystals which separated were dried and recrystallized from hot ethanol. Long yellow needles of III were obtained weighing 1.00 g., m.p. 105–106°. From the methanol mother liquor an additional 0.49 g. of III was recovered, for a total yield of 80%.

Anal. Calcd. for $C_{24}H_{22}Fe$: C, 78.70; H, 6.06; Fe, 15.24. Found: C, 78.40, 78.35; H, 6.16, 6.16; Fe, 15.05, 15.02.

A mixed melting point test of a sample of III prepared above and a sample obtained by means of catalytic hydrogenation melted intermediate between the two melting points. The infrared spectra of the two samples were identical.

In another experiment, a 72% yield of III was obtained by this procedure.

Reduction of II by lithium aluminum hydride. To a slurry of 1.52 g. (0.04 mole) of powdered lithium aluminum hydride in 250 ml. of ether was added 11.8 g. (0.030 mole) of II in 150 ml. of benzene and 50 ml. of ether over a 1 hr. period. The reaction mixture was refluxed with stirring for 16 hr., cooled, and moist ether followed by dilute ammonium chloride solution was added. After filtering, the ether phase was washed with water and dried over Drierite. The solvent was evaporated leaving a dark viscous oil which was induced to crystallize by dissolving it in hot methanol and rapidly cooling in a Dry Ice-acetone bath. Seven g. of a yellow solid was thus obtained, m.p. 115–125° (uncorr.). After repeated crystallization from either methanol or ethanol, 5.0 g. of VIII was obtained in the form of yellow leaflets, m.p. 136–137°.

Anal. Calcd. for $C_{24}H_{22}FeO_2$: C, 72.37; H, 5.57; Fe, 14.02. Found: C, 72.42, 72.62; H, 5.85, 5.86; Fe, 14.04, 14.04.

Reduction of I by sodium borohydride. To a solution of 2.90 g. (0.01 mole) of I in 80 ml. of methanol was added 3.8 g. (0.10 mole) of sodium borohydride in 20 ml. of water. The mixture was stirred for 2 hr. and then filtered. The filtrate was cooled in ice and the excess sodium borohydride was decomposed with acetone. Following the addition of 50 ml. of water and 100 ml. of ether, the ether portion was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent and two recrystallizations from ether–petroleum ether produced 1.9 g. (66% yield) of yellow crystals of VII, m.p. 80.3–80.5°.

Anal. Calcd. for $C_{17}H_{16}FeO$: C, 69.88; H, 5.52; Fe, 19.12. Found: C, 70.10, 69.92; H, 5.57, 5.67; Fe, 19.18, 19.22.

Reduction of I by aluminum isopropoxide. A solution of 4.37 g. (0.015 mole) of I and 7.4 g. (0.036 mole) of aluminum isopropoxide in 150 ml. of redistilled isopropyl alcohol was slowly distilled for 1 hr.; however, the presence of acetone in the distillate could not be detected. In order to raise the reaction temperature, 300 ml. of xylene was added and the isopropyl alcohol was removed by distillation. Continued slow distillation at 134–135° produced a distillate containing acetone. After hydrolysis with 150 ml. of 10% hydrochloric acid, the organic phase was washed with water and the solvent evaporated. Recrystallization of the residue produced 0.6 g. of benzylferrocene (IV), m.p. 73–74°. A mixed melting point test with an authentic sample was not depressed.

Acknowledgment. The authors wish to express their appreciation to Mr. F. F. Bentley and Mrs. N. E. Srp for the infrared spectra. We are also very grateful to Dr. Roy Pruett of the Linde Co., and to Dr. Eric Barthel of the E. I. du Pont de Nemours & Co., Inc., for generous samples of ferrocene used in our research program.

WRIGHT-PATTERSON AIR FORCE BASE, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Some Typical Aldehyde Addition and Condensation Reactions of Formylferrocene[1]

CHARLES R. HAUSER AND JACQUE K. LINDSAY

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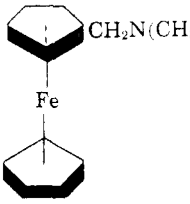
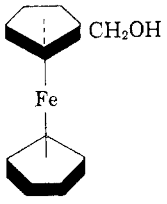
Formylferrocene was found to undergo typical addition and condensation reactions with methylmagnesium iodide, dimethylamine and sodium cyanide, lithio *t*-butyl acetate, and acetophenone and alkali. These processes together with further reactions of certain of the products illustrate useful methods for the synthesis of a number of ferrocene derivatives. Formylferrocene failed to condense with acetophenone in the presence of boron fluoride.

Recently[2] *N*,*N*-dimethylaminomethylferrocene (I) was prepared from ferrocene and the methiodide of this tertiary amine converted to the corresponding alcohol and aldehyde, II and III, respectively.

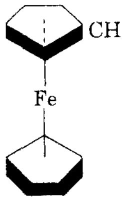
In the present investigation aldehyde III (formylferrocene) was shown to undergo the addition and condensation reactions represented in Chart I. The crude aldehyde, which was obtained by the oxidation of alcohol II with manganese dioxide, was employed in these reactions, the yields being based on the alcohol.



I



II



III

It can be seen from Chart I that the yields of the products (IV–VII) were good to excellent (63–

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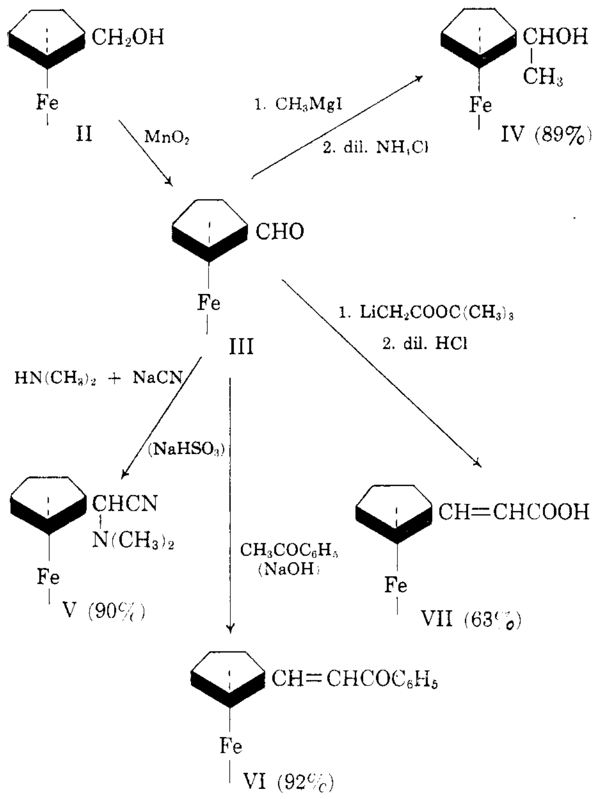
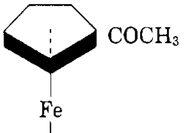
[1] Supported by the Office of Ordnance Research, U. S. Army.

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



92%). The carbinol (IV) from the addition reaction of aldehyde III with methylmagnesium iodide was shown to be identical with that obtained by the lithium aluminum hydride reduction of acetylferrocene (VIII). This ketone was prepared by the Friedel-Crafts type of acetylation of ferrocene with acetic anhydride by means of boron fluoride.[3]

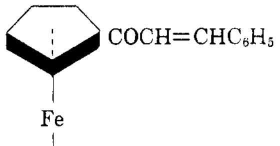


VIII

The reaction of aldehyde III with dimethylamine and sodium cyanide to form aminonitrile V was effected through the sodium bisulfite addition compound of the aldehyde similar to that described for benzaldehyde.[4] The aminonitrile (V) was shown to react with methylmagnesium iodide to form tertiary amine IX (Equation 1). Such a substitution of the cyanide group by the alkyl or aryl group of a Grignard reagent is known to be characteristic of α-aminonitriles.[5]

(1)

The condensation of aldehyde III with acetophenone by means of alkali produced an α,β-unsaturated ketone (VI) that was isomeric with another α,β-unsaturated ketone (X) prepared recently[3] from benzaldehyde and acetylferrocene (VII). Both of these α,β-unsaturated ketones are purple although of different shades.



X

The condensation of aldehyde III with lithio t-butyl acetate was effected by a modification of the method developed recently[6] for that of certain aldehydes and ketones with this metallo ester which was prepared from lithium amide and t-butyl acetate. The intermediate β-hydroxy ester was dehydrated and hydrolyzed by means of hydrochloric acid in dioxane to form α,β-unsaturated acid VII which is an analog of cinnamic acid.

The reactions represented in Chart I together with that of aminonitrile V with the Grignard reagent (Equation 1) illustrate useful methods for the synthesis of a number of new ferrocene derivatives. Although carbinol IV would usually be prepared by the reduction of acetylferrocene, certain other carbinols could probably be synthesized more conveniently through formylferrocene.

Although the condensation of aldehyde III with acetophenone to form α,β-unsaturated ketone VI was realized with alkali, the reaction failed with boron fluoride which is known to bring about the corresponding condensation between benzaldehyde and acetophenone.[7] Similarly the condensation of acetylferrocene (VIII) with benzaldehyde to form α,β-unsaturated ketone X was realized recently[3] with alkali but not with boron fluoride. Evidently the iron in aldehyde III and ketone VIII hinders this Lewis acid from serving as catalyst, the function of which would presumably involve the conversion of the aldehyde group to a carbonium ion and the ketone group, to an enol type intermediate.[8]

EXPERIMENTAL[9]

Hydroxymethylferrocene (II). This alcohol was prepared in

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[3] C. R. Hauser and J. K. Lindsay, *J. Org. Chem.*, **22**, 482 (1957).

[4] E. Knoevenagel and E. Mercklin, *Ber.*, **37**, 4087 (1904); D. B. Luten, Jr., *J. Org. Chem.*, **3**, 588 (1938).

[5] See L. H. Goodson and H. Christopher, *J. Am. Chem. Soc.*, **72**, 358 (1950).

[6] C. R. Hauser and W. H. Puterbaugh, *J. Am. Chem. Soc.*, **75**, 1068 (1953).

[7] D. S. Breslow and C. R. Hauser, *J. Am. Chem. Soc.*, **62**, 2385 (1940).

[8] In this connection see C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 99 (1954).

[9] Melting points are uncorrected. Analyses are by Galbraith Laboratories, Knoxville, Tenn.

three steps from ferrocene[10] as described previously.[2] Ferrocene was aminomethylated to form dimethylaminomethylferrocene (I) in 50% yield (80% conversion yield), and the methiodide of this tertiary amine (obtained in 95% yield) was treated with alkali to give hydroxymethylferrocene (II), m.p. 81–82°, in 94% yield.

Oxidation of alcohol II to aldehyde III and its reactions. Chart I. Alcohol II (10.7 g., 0.05 mole) was oxidized with manganese dioxide in chloroform to form aldehyde III as described previously.[2] The crude solid aldehyde, which was obtained quantitatively (10.8 g., 0.05 mole), was used in the reactions described below, the yields being based on alcohol II. Freshly prepared aldehyde was generally employed, although it was sometimes kept several hours under nitrogen before usage.

A. Reaction with methylmagnesium iodide to form carbinol IV. To a stirred ethereal solution of methylmagnesium iodide (prepared from 0.075 moles each of methyl iodide and magnesium) was added dropwise a solution of 0.05 mole of crude aldehyde III in 100 ml. of anhydrous ether. After 2 hr. stirring and refluxing, the yellow suspension was cooled in an ice bath, decomposed with excess ammonium chloride solution, and the ether layer of the product dried over magnesium sulfate. The solvent was removed to leave 10.2 g. (89%) of yellow powder of α-hydroxyethylferrocene (IV), m.p. 72–75°. Recrystallization from *n*-hexane gave large tan crystals, m.p. 78–79°; reported[11] m.p. 73–75°.

Anal. Calcd. for $C_{12}H_{14}OFe$: C, 62.64; H, 6.13; Fe, 24.27. Found: C, 62.73; H, 6.30; Fe, 24.22.

The melting point was not depressed by admixture with a sample of α-hydroxyethylferrocene (IV), m.p. 78–79°, prepared by the lithium aluminum hydride reduction of acetylferrocene (VIII) essentially as described by Arimoto and Haven.[11] The melting point of IV reported by these workers was 73–75° after recrystallization from a mixture of ether and petroleum ether. We obtained large tan crystals, m.p. 78–79°, after recrystallization from *n*-hexane.

B. Reaction with dimethylamine and sodium cyanide to form aminonitrile V. To a stirred solution of 5.2 g. (0.05 mole) of sodium bisulfite in 50 ml. of water was added 10.8 g. (0.05 mole) of crude aldehyde III in 30 ml. of methanol followed, after 5 min., by a solution of 3.0 g. (0.07 mole) of dimethylamine in 10 ml. of 50% methanol. The mixture was cooled in an ice bath, and a solution of 2.45 g. (0.05 mole) of sodium cyanide in 10 ml. of water was added dropwise with stirring. The color changed from red to orange. Ether (25 ml.) was added and the reaction mixture stirred at room temperature for 4 hr., then extracted three times with ether. The combined ethereal extract was dried over magnesium sulfate, and the solvent removed. The residual amber oil crystallized on adding petroleum ether to give 12.0 g. (90%) of (aminonitrile V), m.p. 83–86°. Recrystallization from *n*-hexane gave light brown plates, m.p. 86–88°.

Anal. Calcd. for $C_{14}H_{16}N_2Fe$: C, 62.71; H, 6.01; N, 10.45; Fe, 20.83. Found: C, 63.07; H, 5.75; N, 10.46; Fe, 20.74.

A solution of 26.0 g. (0.1 mole) of aminonitrile V (m.p. 83–86°) in 100 ml. of dry ether was added dropwise to a stirred solution of methylmagnesium iodide prepared from 0.2 mole each of methyl iodide and magnesium in 150 ml. of dry ether. After stirring one hour and standing overnight, the reaction mixture was cooled and decomposed with ammonium chloride solution to give 23.0 g. (89%) of tertiary amine IX (clear amber oil) which distilled with partial decomposition at 111° at 0.65 mm., n_D^{25} 1.5883.

Anal. Calcd. for $C_{14}H_{19}NFe$: C, 65.38; H, 7.45; N, 5.45; Fe, 21.72. Found: C, 65.12; H, 7.50; N, 5.27; Fe, 21.53.

The amine was converted to a picrate which was recrystallized from 95% ethanol to give red plates, m.p. 136–137°.

Anal. Calcd. for $C_{20}H_{22}O_7N_4Fe$: C, 49.40; H, 4.56; N, 11.52; Fe, 11.49. Found: C, 49.55; H, 4.55; N, 11.68; Fe, 11.23.

C. Condensation with acetophenone to form α,β-unsaturated ketone VI. To a stirred solution of 2.56 g. (0.064 mole) of sodium hydroxide in 20 ml. of water (cooled to 15°) was added, successively, solutions of 6.0 g. (0.05 mole) of acetophenone in 10 ml. of 95% ethanol and 10.8 g. (0.05 mole) of crude aldehyde III in 30 ml. of 95% ethanol. The mixture was stirred at room temperature for 3 hr. and allowed to stand overnight. The thick purple suspension was filtered, and the solid washed thoroughly with water, followed by a small portion of ice-cold 95% ethanol. After drying, there was obtained 14.5 g. (92%) of α,β-unsaturated ketone VI (purple solid), m.p. 123–126°. Recrystallization from 95% ethanol gave deep purple needles, m.p. 126–128°.

Anal. Calcd. for $C_{19}H_{16}OFe$: C, 72.17; H, 5.10; Fe, 17.66. Found: C, 72.05; H, 5.23; Fe, 17.43.

D. Condensation with t-butyl acetate to form α,β-unsaturated acid VII. This reaction was effected by a modification of the general method developed previously in this laboratory.[6]

To a stirred suspension of 0.05 mole of lithium amide in 200 ml. of liquid ammonia was added a solution of 5.7 g. (0.05 mole) of *t*-butyl acetate in 10 ml. of anhydrous ether. To the resulting lithio ester was added, after 30 min., a solution of 10.8 g. (0.05 mole) of crude aldehyde III in 20 ml. of anhydrous ether. The yellow-green suspension was stirred for 2 hr., and excess solid ammonium chloride then added. The liquid ammonia was allowed to evaporate and, after the addition of 200 ml. of ether, the mixture was heated under reflux for 10 min., cooled slightly, and filtered. Removal of the solvent left 14 g. of the β-hydroxy ester as an amber oil. Samples of this oil failed to yield satisfactory crystals on treatment with *n*-hexane or benzene. A solution of 5 g. of this oil in 40 ml. of dioxane and 10 ml. of concentrated hydrochloric acid was refluxed for 1.5 hr.[6] After dilution with five volumes of water, the mixture was extracted with ether. The combined ethereal solution was extracted with 20 ml. portions of 1*N* sodium hydroxide. The combined alkaline solution (after extracting with ether) was chilled and acidified with 6*N* hydrochloric acid to precipitate acid VII which was collected on a funnel, washed with water, and dried. The bright red powder (2.9 g., 63%) melted at 176–178° dec., and at 177–179° dec. after careful sublimation at 130° at 0.1 mm.

Anal.[12] Calcd. for $C_{13}H_{12}O_2Fe$: C, 60.97; H, 4.72; Fe, 21.81. Found: C, 61.23; H, 4.74; Fe, 21.43.

Attempt to effect aldol condensation by boron fluoride. A solution of 0.5 mole of crude formylferrocene (III) and 0.10 mole of acetophenone in 100 ml. of methylene chloride was saturated with boron fluoride at 0°. After standing at room temperature for 3 hr. the reaction mixture was stirred with excess sodium acetate solution. Aldehyde III was recovered through its sodium bisulfite addition compound and converted to its semicarbazone, m.p. 217–219°.[2]

DURHAM, N. C.

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[10] We are indebted to Linde Co., Tonawanda, N. Y. (Dr. R. L. Pruett) for a generous sample of this compound.

[11] F. S. Arimoto and A. C. Haven, Jr., *J. Am. Chem. Soc.*, **77**, 6295 (1955).

[12] Galbraith Laboratories reported that acid VII was too insoluble for a satisfactory neutral equivalent.