pension was added, with stirring, 50 g. (0.415 mole) of acetophenone followed, after 30 min., by 52 g. (0.415 mole) of benzyl chloride in 75 ml. of dry toluene. The mixture became warm reaching approximately 80°. The suspension was stirred until it had cooled to room temperature (about 2 hr.) and worked up as in A to give 15.7 g. (31%) of acetophenone, b.p. 75–77° at 10.3 mm. (reported[14] b.p. 83–85° at 12 mm.), 38.5 g. (46%) of X, and 32.8 g. (23%) of XI. Both of these derivatives crystallized, and were shown to be identical with those prepared in A by mixed melting points.

DURHAM, N. C.

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[14] I. Heilbron, *Dictionary of Organic Compounds*, Oxford, New York, 1953, Vol. 1, p. 16.

[CONTRIBUTION FROM DUKE UNIVERSITY AND UNION CARBIDE CORP.]

Mannich Reaction of Acetylferrocene with Formaldehyde and Secondary Amines[1,2]

CHARLES R. HAUSER, ROY L. PRUETT,[3] AND T. ARTHUR MASHBURN, JR.

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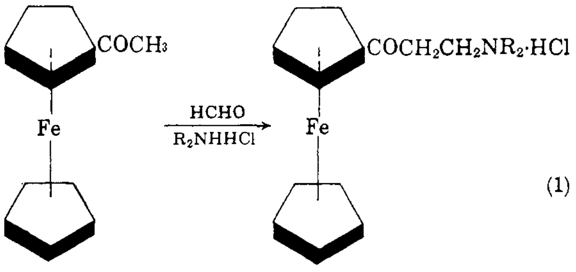
Acetylferrocene was condensed with formaldehyde and dimethylamine hydrochloride or diethylamine hydrochloride to form Mannich type salts, which were converted to the free amines and to acryloylferrocene. One of the salts was cyclized with phenylhydrazine to form a pyrazoline. One of the free amines was hydrogenated to give the hydroxyamine.

Rausch and Coleman[4] have recently reported the Mannich reaction of acetylferrocene (I) with formaldehyde and dimethylamine hydrochloride to form salt II (Equation 1); this salt was pyrolyzed by steam distillation to give a polymeric material.

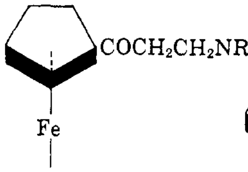


(1)

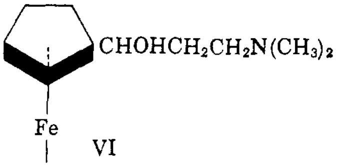
I

II. $R = CH_3$
III. $R = C_2H_5$

In the present investigation, which was initiated some time ago,[2] I was found to undergo the Mannich reaction with certain secondary amines, and the products were shown to exhibit reactions that are typical of ordinary Mannich salts.[5] Thus, salts II and III were prepared in good yields as indicated in Equation 1, and aqueous solutions of them were treated with sodium bicarbonate to liberate the free bases IV (80%) and V, respectively. The use of sodium hydroxide instead of bicarbonate brought about decomposition. Free base IV was then hydrogenated over Raney nickel to give the hydroxyamine VI in 80% yield.

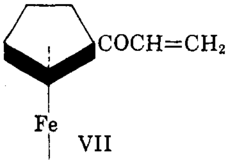


IV. $R = CH_3$
V. $R = C_2H_5$



VI

Another reaction of salts II and III involved heating aqueous solutions of them on the steam bath for one hour, under which condition the elements of the secondary amine were eliminate to form the α,β-unsaturated ketone VII. Good yields of VII were isolated, however, only under carefully controlled conditions since this product tends to undergo polymerization. The product was shown to have structure VII not only by analysis but also by its infrared spectrum, which exhibited strong bands at 6.04 and 6.22 μ for the carbonyl group[6] and conjugated carbon-carbon double bond,[7] respectively.



VII

Still another reaction of salt III involved its cyclization with phenylhydrazine to form the pyrazoline VIII in 49% yield. Two or more courses of reaction appear possible in the formation of such a compound.[8] The structure of the product was supported by analysis and by its infrared spectrum,

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[1] Supported in part by Grant CY-4455 from the National Institutes of Health.

[2] A portion of this work was completed in 1955 by R.L.P. at Linde Air Products Company, Tonawanda, N. Y.

[3] Present address: Research Dept., Union Carbide Chemicals Company, South Charleston, W. Va.

[4] M. D. Rausch and L. E. Coleman, Jr., *J. Org. Chem.*, 23, 107 (1958).

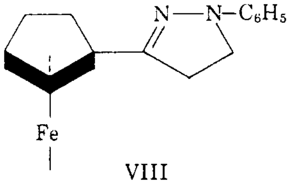
[5] F. F. Blicke, *Org. Reactions*, 1, 303 (1942).

[6] See L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Wiley and Sons, New York, 1958, p. 136.

[7] See Ref. 6 p. 24.

[8] See Ref. 5, p. 320.

which showed no band for a carbonyl group and showed strong bands at 6.25 and 6.64 μ, which may be attributed to a carbon-nitrogen double bond.[9]



VIII

Besides II and III, the corresponding salt (m.p. 158–160° dec.) was evidently obtained from the reaction of I with morpholine hydrochloride; its analysis was satisfactory for iron, nitrogen, and hydrogen but not for carbon. Also, bisacetylferrocene produced a similar salt (m.p. 176–179° dec.) with four molecular equivalents each of formaldehyde and dimethylamine hydrochloride. The analysis for iron and hydrogen fitted the bis-salt, but analyses for carbon and nitrogen did not fit the bis- or mono-salt. Like II and III, these salts were very soluble in water, moderately soluble in ethanol, and insoluble in diethyl ether.

EXPERIMENTAL[10]

β-Dimethylaminopropionylferrocene hydrochloride (II). A mixture of 13.7 g. (0.06 mole) of acetylferrocene (I), 3.6 g. (about 0.12 mole) of paraformaldehyde, and 9.8 g. (0.12 mole) of dimethylamine hydrochloride, 150 ml. of absolute ethanol, and 0.5 ml. of concd. hydrochloric acid was refluxed for 2.5 hr. The resulting solution was allowed to cool somewhat and an additional 3.6 g. of paraformaldehyde was added. The mixture was then refluxed for another 2.5 hr. and allowed to stand overnight. On cooling in an ice-salt bath, the red solution deposited brown crystals, which were collected and recrystallized from a minimum of isopropyl alcohol to give 9.0 g. (47%) of orange-yellow salt II, m.p. 170–171° dec; reported[4] m.p. 170–172°. In another experiment the product was obtained in 52% yield, m.p. 169–171° dec. (recrystallized from a minimum of absolute ethanol).

Hydrochloride II was very soluble in water, moderately soluble in ethanol, and insoluble in diethyl ether.

Treatment of salt II *to liberate free base* IV. To a cold solution of 1 g. of salt II in a minimum of water was added a cold, saturated solution of sodium bicarbonate to precipitate the free base IV, which was collected on a funnel and air-dried. The crude solid (1.2 g.) was stirred with hot *n*-heptane and the mixture filtered. The filtrate was cooled to give 0.70 g. (80%) of IV (fluffy orange crystals), m.p. 72–73 and at 72–72.5° after another recrystallization from *n*-heptane.

Anal. Calcd. for $C_{15}H_{19}FeNO$: C, 63.2; H, 6.7; Fe, 19.6; N, 4.9. Found: C, 63.2; H, 6.3; Fe, 19.8; N, 4.7.

Ketone-amine IV was soluble in chloroform and in dilute hydrochloric acid and moderately soluble in water.

Hydrogenation of IV *to form hydroxyamine* VI. A solution of 2 g. of ketone-amine IV in 150 ml. of absolute ethanol was shaken with 8 ml. of W-7 Raney nickel[11] in a Parr low-pressure hydrogenation apparatus under 57 p.s.i.g. Within 5 min. the theoretical absorption of hydrogen had occurred. The pressure was then released and the catalyst was removed by filtration under argon. The filtrate was evaporated to dryness in an air blast to give 1.6 g. (80%) of VI (yellow solid), m.p. 82–83.5°. Recrystallization from *n*-heptane gave a light yellow solid, m.p. 81–81.5°.

Anal. Calcd. for $C_{15}H_{21}FeNO$: C, 62.7; H, 7.3; Fe, 19.4; N, 4.9. Found: C, 62.6; H, 6.8; Fe, 19.5; N, 5.2.

Infrared bands: 2.8, 3.5, 6.8, 9.0, 9.4, and 9.98 μ.

Conversion of salt II *to acryloylferrocene* (VII). A solution of 3.5 g. (0.0109 mole) of salt II in 15 ml. of water was heated on the steam bath for 50 min. The resulting red mixture was cooled in an ice bath to precipitate a pasty red-brown solid which was collected on a funnel and air-dried. The solid was stirred with hot *n*-hexane and the mixture filtered. The filtrate was reduced in volume (steam bath) and cooled to give red crystals of acryloylferrocene (VII), m.p. 71–72°. After two recrystallizations from *n*-hexane, 1.0 g. (42%) of VII was obtained, melting at 73.5–74°.

Anal.[12] Calcd. for $C_{13}H_{12}FeO$: C, 65.0; H, 5,0; Fe, 23.1 Found: C, 65.0, 65.2; H, 5.2, 5.1; Fe, 22.5, 22.7.

Infrared bands: 6.04, 6.22, 6.89, 9.04, and 10.0 μ.

In certain other experiments the yield of VII was somewhat lower than that reported above and a considerable amount of polymeric material was obtained.

Although VII appeared to be stable at room temperature, it underwent thermal polymerization, as might be expected.

β-Diethylaminopropionylferrocene hydrochloride (III). This salt was prepared from 0.06 mole of acetylferrocene, 0.19 mole of paraformaldehyde and 0.12 mole of diethylamine hydrochloride essentially as described above for salt II, except that only 60 ml. of absolute ethanol were used. There was obtained 14.4 g. (69%) of crude III. After two recrystallizations from absolute isopropyl alcohol, the orange-brown crystals melted at 159–160°.

Anal.[12,13] Calcd. for $C_{17}H_{24}FeNOCl$: C, 58.4; H, 6.9; N, 4.0. Found: C, 58.7, 58.8; H, 7.3, 7.4; N, 3.7, 3.8.

Infrared bands: 6.0, 6.86, 8.04, 9.04, 10.0, and 12.22 μ.

Hydrochloride III was very soluble in water, moderately soluble in ethanol, and insoluble in diethyl ether.

Treatment of salt III *to liberate free base* V. To a cold solution of 1.5 g. of salt III was added cold aqueous sodium bicarbonate. Since no precipitate was obtained, the solution was extracted twice with chloroform. The red extracts were combined, and the solution washed with small amounts of cold water. Removal of the solvent left a dark red liquid, which failed to crystallize.

Anal. Calcd. for $C_{17}H_{23}FeNO$: C, 65.0; H, 7.3; Fe, 17.8; N, 4.5. Found: C, 64.8; H, 8.0; Fe, 18.0; N, 4.7.

Conversion of salt III *to acryloylferrocene* (VII). This reaction was carried out essentially as described above with salt II to produce 47% of VII, as red needles, m.p. 73.5–74° (recrystallized from *n*-hexane). Admixture with a sample of VII from salt II did not depress the melting point.

Cyclization of salt III *with phenylhydrazine to form* VIII. A solution of 1.5 g. of salt III, 1.5 g. of phenylhydrazine, in 10 ml. each of absolute ethanol and glacial acetic acid was refluxed for 6 hr. On standing overnight at room temperature the red solution deposited orange needles, which were collected on a funnel and recrystallized from absolute ethanol to give 0.7 g. (49%) of 1-phenyl-3-ferrocenylpyrazoline (VIII), (orange plates), m.p. 142–144°.

Anal.[12] Calcd. for $C_{19}H_{18}FeN_2$: C, 69.1; H, 5.5; Fe, 16.9; N, 8.5. Found: C, 68.9, 69.1; H, 5.8, 6.0; Fe, 16.6, 16.8; N, 8.6, 8.7.

Infrared bands: 6.25, 6.64, 7.72, 9.04, 9.96, and 14.5 μ.

DURHAM, N. C.
SOUTH CHARLESTON, W. VA.

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(9) See ref. 6, p. 286.

(10) Melting points are uncorrected. Infrared spectra were obtained on Perkin-Elmer Model 21 recording infrared spectrophotometer.

(11) A. A. Pavlic and H. Adkins, *J. Am. Chem. Soc.*, 68, 1471.

(12) Analysis by Galbraith Laboratory, Knoxville, Tenn.

(13) The values for iron and chlorine were low by 1.5 and 0.73% but high in another determination by 0.63 and 0.46%, respectively.