at 410 mμ was measured in 1-cm. cells with a Cary Model 11 Spectrophotometer. It was found that the absorption of solutions in 92–96% H_2SO_4 increased over a period of hours and then slowly fell. The maximum value of A/c for each solution was in the range $(0.9\text{–}1.2) \times 10^4$ liters/mole. Solutions of II in 86–89% H_2SO_4 absorbed more weakly and the intensity of the 410 mμ band began to decrease immediately, falling to nearly zero over a period of a few hours. The color of a solution in 84% H_2SO_4 was barely discernible, $A/c = 6 \times 10^2$ at 410 mμ. An approximate value of −15 for pK_{R^+} may be calculated from these data. A more precise determination was not attempted due to poor reproducibility. Similar behavior has been reported[12] for other rather unstable carbonium ions.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Certain Alkylations with the Methiodide of *N*,*N*-Dimethylaminomethylferrocene. Synthesis of an α-Amino Acid Having the Ferrocene Group[1]

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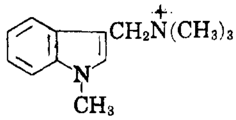
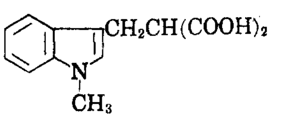
Alkylations of sodio malonic ester and sodio ethyl acetamidocyanoacetate with the methiodide of *N*,*N*-dimethylaminomethylferrocene were effected, and the products hydrolyzed and decarboxylated to form the corresponding monocarboxylic acids. The latter overall reaction produced an α-amino acid having the ferrocene group, which may be regarded as an analogue of phenylalanine.

Certain quaternary ammonium ions have been more available than the corresponding alkyl halides, and have been employed successfully in the alkylations of the sodium derivatives of active hydrogen compounds.[2] For example, quaternary ammonium ion I, which is prepared by the methylation of 1-methylgramine, has been used in the alkylation of sodio malonic ester to form II (after saponification).[3]

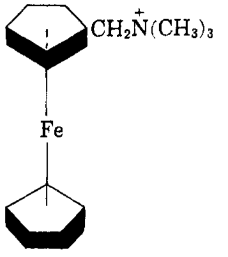


I

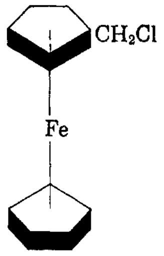


II

In the present investigation quaternary ammonium ion III was employed in the alkylations of sodio malonic ester and sodio ethyl acetamidocyanoacetate. This quaternary ammonium ion was readily prepared by the aminomethylation of ferrocene, followed by the methylation of the resulting tertiary amine.[4] On the other hand attempts to prepare the corresponding chloride (IV) by treatment of hydroxymethylferrocene[4] with thionyl chloride or hydrogen chloride produced material that failed to give the Beilstein test for halogen. Similarly the product from hydroxymethylferrocene and phosphorus tribromide appeared not to contain halogen.



III



IV

The alkylation of sodio malonic ester with quaternary ion III was effected in ethanol, and the resulting alkylation product was saponified to form dicarboxylic acid V in 67% yield. This dicarboxylic acid was decarboxylated to give monocarboxylic acid VI in 85% yield, the overall yield from III being 57%.

Similarly the alkylation of sodio ethyl acetamidocyanoacetate was effected with quaternary ion III, and the alkylation product hydrolyzed and decarboxylated to form amino acid VII in 67% yield. This α-amino acid was isolated as the monohydrate and in the anhydrous condition. It may be considered as an analog of phenylalanine.

It should be mentioned that sodio acetonitrile, prepared by means of sodium amide in a mixture of liquid ammonia and ether, failed to undergo alkylation with quaternary ammonium ion III within one hour in this medium (at −33°). Since the quaternary ammonium salt was recovered, higher temperatures appear to be required for such alkylations.

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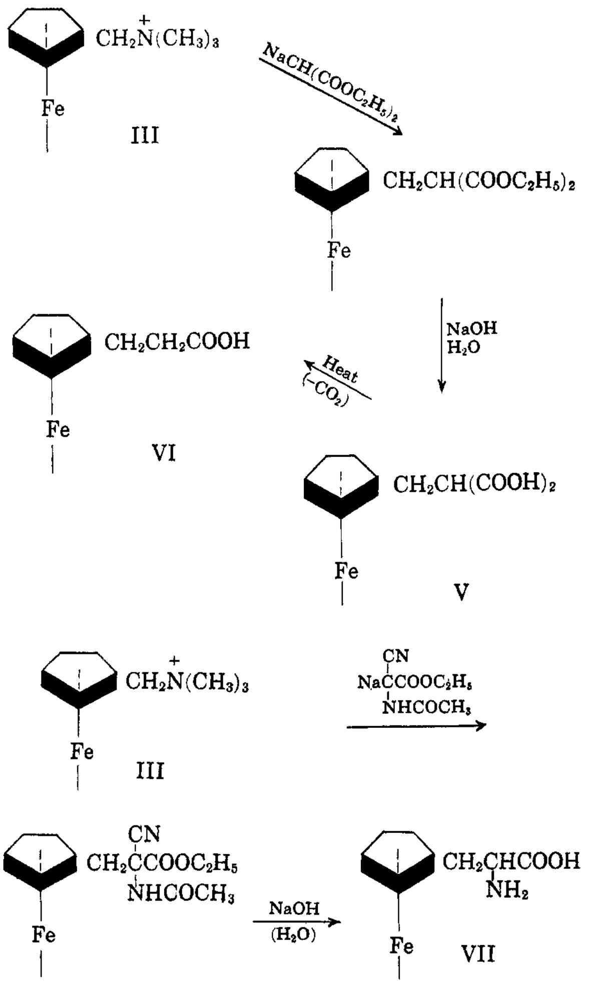
(1) Supported by the Office of Ordnance Research, U. S. Army.

(2) See H. R. Snyder, C. W. Smith, and J. M. Stewart, *J. Am. Chem. Soc.*, **66**, 200 (1944).

(3) H. R. Snyder and E. L. Eliel, *J. Am. Chem. Soc.*, **71**, 663 (1949); *see also, Org. Reactions*, **VII**, 99 (1953).

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



EXPERIMENTAL[5]

Alkylation of malonic ester with quaternary ion III. Dicarboxylic acid V and monocarboxylic acid VI. The methiodide of *N*,*N*-dimethylaminomethylferrocene (III) was prepared as described previously[4] by the aminomethylation of ferrocene (dicyclopentadienyliron)[6] with formaldehyde and dimethylamine, followed by the methylation of the resulting tertiary amine with methyl iodide.

A solution of sodium ethoxide was prepared under nitrogen from 2.3 g. (0.1 mole) of freshly cut sodium and 100 ml. of absolute ethanol, and a solution of 16.0 g. (0.1 mole) of redistilled diethyl malonate in 20 ml. of absolute ethanol was added.

To the resulting sodio malonic ester (0.1 mole) was added, with stirring, 38.5 g. (0.1 mole) of the solid methiodide (III), and the solution stirred and refluxed for 43 hr. The odor of trimethylamine was detected at the top of the condenser. After cooling, the reaction mixture was poured onto crushed ice, acidified carefully with 1*N* hydrochloric acid, and extracted three times with ether. The combined ethereal extract was washed with saturated sodium bicarbonate solution and dried over magnesium sulfate. After filtering, the solvent was removed to leave 34 g. of the alkylation product as a clear amber oil which crystallized slowly.

To 30.0 g. of this crude alkylation product was added 10 ml. of 95% ethanol and 50 ml. of 30% potassium hydroxide solution, and the resulting mixture was refluxed for 8 hr. After cooling, diluting with four volumes of water, and extracting with ether, the alkaline solution was acidified carefully with 6*N* hydrochloric acid to precipitate dicarboxylic acid V which was collected on a funnel, washed with water, and dried. This acid (18 g., 67%) melted at 130–133° (dec.). A sample of the solid acid was boiled with water, and the resulting emulsion was filtered and cooled rapidly to produce fine golden plates m.p. 133–134° (dec.) (sample immersed in the melting point bath at 120°).

Anal. Calcd. for $C_{14}H_{14}O_4Fe$: C, 55.66; H, 4.67; Fe, 18.49; Neut. equiv., 151. Found: C, 56.07; H, 4.77; Fe, 18.23; Neut. equiv., 148.

A 7 g. (0.023 mole) sample of dicarboxylic acid V was heated in a flask immersed in an oil bath at 145–150° until frothing ceased (20 min.). The resulting residue was dissolved in 1*N* sodium hydroxide and the solution boiled with decolorizing carbon. After filtering, the solution was cooled and acidified with 6*N* hydrochloric acid to precipitate monocarboxylic acid VI which was collected on a funnel, washed with water, dried, and recrystallized from *n*-heptane. There was obtained 5 g. (84%) of acid VI as fine orange needles, m.p. 116–118°.[7]

Anal.[8] Calcd. for $C_{13}H_{14}O_2Fe$: C, 60.49; H, 5.47; Fe, 21.64. Found: C, 60.50; H, 5.39: Fe, 21.28.

Alkylation of ethyl acetamidocyanoacetate with quaternary ion III. Amino acid VII. This alkylation was carried out in ethanol essentially as described above for malonic ester employing 0.1 mole each of sodium ethoxide, ethyl acetamidocyanoacetate, and the methiodide (III). After stirring and refluxing for 43 hr. (odor of trimethylamine), the reaction mixture was cooled, and the solvent removed partially (water aspirator). Four volumes of water were added, and the mixture extracted three times with ether. The combined ethereal extract was washed with water until neutral to litmus, and dried over magnesium sulfate. After filtering, the solvent was removed to give 30.0 g. of yellow powder, m.p. 172–178°.

This crude alkylation product was hydrolyzed and decarboxylated to form amino acid VII in one step essentially as described by Herz, Dittmer, and Cristol.[9]

To 20.0 g. of the crude alkylation product was added a solution of 20 g. of sodium hydroxide in 200 ml. of water, and the resulting mixture was refluxed for 20 hr. After cooling, and filtering, the reaction mixture was acidified with 1*M* phosphoric acid to *p*H6. The resulting mixture was chilled in an ice bath, and the precipitate collected on a funnel, washed with ice water, and dried. There was obtained 13 g. (67% overall yield calculated as the monohydrate) of crude amino acid VII (yellow powder). It gave the ninhydrin test for α-amino acids. A sample of the yellow powder was recrystallized from a mixture of equal amounts of 95% ethanol and water to give golden plates of the monohydrate of amino acid VII, m.p. 321–333° (dec.).

Anal. Calcd. for $C_{13}H_{17}O_3NFe$: C, 53.63; H, 5.89; N, 4.81; Fe, 19.18. Found: C, 53.66; H, 5.92; N, 4.64; Fe, 19.24.

A sample of the monohydrate was dried at 110° to give yellow plates of anhydrous VII, m.p. 321–333° (dec.).

Anal. Calcd. for $C_{13}H_{15}O_2NFe$: C, 57.17; H, 5.54; N, 5.13; Fe, 20.45. Found: C, 57.29; H, 5.67; N, 5.13; Fe, 20.18.

DURHAM, N. C.

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(5) Melting points are uncorrected. Analyses are by Galbraith Laboratories, Knoxville, Tenn.

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

(7) This melting point was not depressed on admixture with a sample of acid VI kindly furnished by Dr. K. L. Rinehart of the University of Illinois who prepared it by the carbethoxylation of acetylferrocene, followed by hydrogenation and saponification.

(8) Galbraith Laboratories reported that this acid was too insoluble for a neutralization equivalent.

(9) W. Herz, K. Dittmer, and S. J. Cristol, *J. Am. Chem. Soc.*, **70**, 504 (1948).