Notes A department for short papers of immediate interest.

The Ferrocene Reduction of the Triphenylmethyl Carbonium Ion[1]

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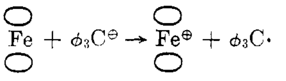
Due to the extreme ease with which ferrocene enters into one-electron transfer redox reactions,[2] it was of interest to briefly investigate the possible reduction of carbonium ions to stable free radicals through the agency of ferrocene. Triphenylmethyl chloride in nitromethane solution was chosen as a source of the model triphenylmethyl carbonium ion since the reversible equilibrium has been well estab-

$$\phi_3CCl \leftrightarrows \phi_3C^{\oplus} + Cl^{\ominus}$$

lished[3] in this solvent. The addition of a slight excess of ferrocene to these nitromethane solutions in the presence of oxygen immediately produced the green coloration of the ferricinium ion and a mild exotherm. Oxygen was absorbed by the solution and the immediate precipitation of di(triphenylmethyl)-peroxide occurred. The latter material was isolated in only 16% yield and no significant quantity of ferrocene was recovered thus indicating the occurrence of side reactions such as attack of triphenylmethyl or the corresponding carbonium ion on ferrocene or the ferricinium ion. The only material isolated in addition to the peroxide was a mixture of solids which was not characterized.

A similar experiment was conducted in benzene solution and it was observed that no oxidation of the ferrocene occurred until a small quantity of phenol was added to the solution. The phenol presumably functioned as an electrophilic catalyst for the ionization of triphenylmethyl chloride.

It is thus established, in principle at least, that



$$Fe + \phi_3C^{\ominus} \rightarrow Fe^{\oplus} + \phi_3C\cdot$$

the reaction will occur in polar, non-functional solvents.

EXPERIMENTAL

Pure triphenylmethyl chloride (800 mg., 2.9 × 10^{-3} mole, m.p. 110–111°) and 800 mg. of pure ferrocene (4.3 × 10^{-3} mole) were placed in a 50-ml. round-bottomed flask and 20 ml. of pure dry nitromethane was added while the flask was flushed with dry oxygen. The flask was immediately stoppered and shaken for one-half hour. On adding the solvent a mild exotherm occurred along with the green coloration of the ferricinium cation and the immediate precipitation of di(triphenylmethyl)peroxide. On opening the flask a considerable decrease in internal pressure was found to have occurred. Methylene chloride (100 ml.) was added and the organic layer was washed copiously with water to remove the intensely blue ferricinium salt. The organic layer was dried over sodium sulfate and was evaporated to dryness under a vacuum. The residual solid was extracted with pentane (which gave 150 mg. of ferrocene on evaporation), heated to boiling with acetone, and the white crystalline product was removed by filtration, yield 120 mg. (2.32 × 10^{-4} mole or 16%), m.p. 176–177°. The crude product was recrystallized from methylene chloride-pentane to a constant melting point of 184–185°[4] and gave a positive test for peroxide by treatment with sodium iodide after decomposition in concentrated sulfuric acid followed by dilution with water.

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[1] This research was carried out under Army Ordnance Contract W-01-021-ORD-334.

[2] See Woodward, Roseblum, and Whiting, *J. Am. Chem. Soc.*, **74**, 3458 (1952) for several examples.

[3] Smith and Leffler, *J. Am. Chem. Soc.*, **77**, 1700 (1955).

[4] Gomberg, *J. Am. Chem. Soc.*, **22**, 757 (1900), reports a melting point of 185–186° for di(triphenylmethyl)peroxide.

The Preparation of Phthalyl Glycyl *dl*-β-(3,4-Dihydroxyphenyl)alanine Methyl Ester

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It was of interest to us to prepare peptides containing *dl*-β-(3,4-dihydroxyphenyl)alanine (Dopa). No peptides containing this amino acid have been reported in the literature. The synthesis methods of Bergmann,[1] Cook, *et al.*,[2] and of Sheehan and Frank[3] were explored. Only the method of Sheehan and Frank was successful in our hands.

By a minor modification of the Sheehan and Frank method, phthalyl glycyl Dopa methyl ester, and its diacetate were successfully prepared. The presence of Dopa with both hydroxyl groups free in the final peptide was confirmed by the Arnow test.[4]

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[1] Bergmann and Zervas, *Ber.*, **65**, 1192 (1932).

[2] Cook, Heilbron, and Levy, *J. Chem. Soc.*, 205 (1948).

[3] Sheehan and Frank, *J. Am. Chem. Soc.*, **71**, 1860 (1949).

[4] Arnow, *J. Biol. Chem.*, **118**, 531 (1937).

EXPERIMENTAL

dl-β-(3,4-Dihydroxyphenyl)alanine methyl ester hydrochloride. The compound, prepared according to the general method of Fischer,[5] was obtained as a crystalline product melting at 180–181°; yield 93%.

Anal. Calc'd for $C_{10}H_{13}NO_4 \cdot HCl$: C, 48.4; H, 5.6; N, 5.6. Found: C, 48.2; H, 5.44; N, 5.6.

dl-β-(3,4-Dihydroxyphenyl)alanine methyl ester. The ester hydrochloride (14 g.) was suspended in 50 ml. of chloroform and an equal volume of chloroform saturated with ammonia was added. After vigorous shaking and filtration to remove ammonium chloride, the chloroform was concentrated and petroleum ether was added; whereupon the ester crystallized at room temperature in quantitative yield. The ester melted at 126°, and was soluble in chloroform and carbon tetrachloride, but insoluble in petroleum ether, cold ethyl acetate, and water.

Anal. Calc'd for $C_{10}H_{13}NO_4$: C, 56.9; H, 6.1; N, 6.6. Found: C, 56.3; H, 5.8; N, 6.5.

Phthalyl glycine. This substance was prepared by the method of Sheehan and Frank[3] with one modification, which led to an increased yield. The modified procedure is as follows: Glycine (3.0 g.) and phthalic anhydride (5.9 g.) were suspended in *para*-cymene and the mixture was refluxed in an apparatus equipped with a Dean and Stark trap. When the theoretical amount of water had been collected, the *para*-cymene was removed under reduced pressure, and the residue was crystallized from water-alcohol. The product was obtained as fine needles (m.p. 192–194°) (reported 191–192°) in 90% yield after recrystallization from water-ethanol.

Phthalyl glycyl dl-β-(3,4-dihydroxyphenyl)alanine methyl ester. A slurry of 4.95 g. of Dopa methyl ester hydrochloride (0.02 mole) and 4.09 g. of triethylamine was mixed with 4.46 g. of phthalyl glycyl chloride[3] (0.02 mole) in chloroform. After stirring for three hours, the mixture was washed with water and the chloroform layer was dried over sodium sulfate. Evaporation of the solvent yielded a syrup which crystallized from chloroform and gave 4 g. (50%) of a compound melting at 196–197° (decomp.). This material gave a positive Arnow test indicating that both hydroxyl groups were free.

Anal. Calc'd for $C_{20}H_{18}N_2O_7$: C, 60.3; H, 4.6; N, 7.05. Found: C, 59.8; H, 4.7; N, 7.0.

Phthalyl glycyl dl-β-(3,4-dihydroxyphenyl)alanine methyl ester di-acetate. The diacetate of the above compound was prepared with acetic anhydride and glacial acetic acid according to the standard procedure. The product crystallized from methanol-water and melted at 174°. This substance gave a negative Arnow test (*loc. sit.*).

Anal. Calc'd for $C_{24}H_{22}N_2O_9$: C, 59.7; H, 4.6; N, 5.8. Found: C, 59.5; H, 4.7; N, 5.7.

The diacetate (2.5 g.) was dissolved in 50 ml. of methanol and was treated with 5 ml. of 2 *N* sodium hydroxide in a nitrogen atmosphere at room temperature. Upon acidification of the mixture, a precipitate which was insoluble in ether, alcohol, and petroleum ether was obtained. This material melted at 198° (decomp.) and showed no depression in melting point when melted mixed with the phthalyl glycyl Dopa methyl ester prepared above.

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(5) Fischer and Suzuki, *Ber.*, **37**, 2842 (1904).

The Acid Cleavage of 1-(3-Alkoxypropyl)-3-Guanidines and Nitroguanidines[1]

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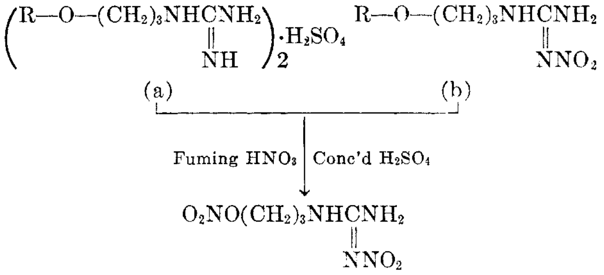
In the nitration of 1-(3-alkoxypropyl)-3-guanidinium sulfate salts and 1-(3-alkoxypropyl)-3-nitroguanidine, a unique ether cleavage occurred giving excellent yields of 1-(3-nitroxypropyl)-3-nitroguanidine. The nitrations were performed at 0–5° with a nitrating mixture consisting of fuming nitric acid and concentrated sulfuric acid.



$$\left(R{-}O{-}(CH_2)_3NH\overset{\displaystyle NH}{\overset{\|}{C}}NH_2\right)_2 \cdot H_2SO_4 \ \text{(a)} \qquad R{-}O{-}(CH_2)_3NH\overset{\displaystyle NNO_2}{\overset{\|}{C}}NH_2 \ \text{(b)} \xrightarrow[\text{Conc'd } H_2SO_4]{\text{Fuming } HNO_3} O_2NO(CH_2)_3NH\overset{\displaystyle NNO_2}{\overset{\|}{C}}NH_2$$

$R = CH_3; (CH_3)_2CH$

The infrared spectra of the product formed from both reactions (a) and (b) were found to be identical with an authentic sample of 1-(3-nitroxypropyl)-3-nitroguanidine prepared earlier by the authors.[2]

The mechanism of this reaction is somewhat obscure in that attempts to nitrate 1-(2-methoxyethyl)-3-guanidinium sulfate under the same conditions failed to give ether cleavage and resulted in the formation of the normal 1-(2-methoxyethyl)-3-nitroguanidine. Attempts to cleave 1-(2-methoxyethyl)-3-nitroguanidine by an analogous nitrating procedure resulted in the recovery of the starting material. The elucidation of the course of this reaction is being investigated.

EXPERIMENTAL[3]

1-(Alkoxyalkyl)-3-guanidinium sulfate salts. 1-(2-Methoxyethyl)-, 1-(3-methoxypropyl)-, and 1-(3-isopropoxypropyl)-3-guanidinium sulfate were prepared according to the procedure of Rathke,[4] utilizing 2-methyl-2-thiopseudouronium sulfate and the corresponding alkoxyalkylamine.

1-(3-Isopropoxypropyl)-3-guanidinium sulfate had m.p. 135–137° after one crystallization from 95% ethanol.

Anal. Calc'd for $C_{14}H_{36}N_6O_6S$: C, 40.38; H, 8.67; N, 20.19. Found: C, 40.30; H, 8.70; N, 20.33.

Picrate, m.p. 178–180° after one crystallization from 95% ethanol.

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(1) Publication approved by the Bureau of Ordnance, Navy Department. The opinions expressed are those of the authors.

(2) Fishbein and Gallaghan, *J. Am. Chem. Soc.*, **76**, 3217 (1954).

(3) All melting points are corrected.

(4) Rathke, *Ber.*, **17**, 297 (1884); Schoeller and Schotte, German Patent 455,682 (June 23, 1931).