N-Bis(β-chloroethyl)-D-1-glucopyranosylcarbaminate (VI). A 1.0-g. sample of V was dissolved in 50 ml. of chloroform, and 6 ml. of 16% ethanolic hydrochloric acid added (approximately 0.5*N* final hydrochloric acid concentration). After 2 days at room temperature it was evaporated and dried over solid sodium hydroxide. 0.66 g. (100%) of a colorless or slightly yellow, water soluble sirup resulted $[\alpha]_D^{20}$ +79.0° (*c*, 2 methanol).

We attempted chromatography on alumina (neutral, Brockman Grade I) but the urethan was split. After chromatography on silica gel, it could be recovered unchanged, but failed to crystallize.

Anal. Calcd. for $C_{11}H_{19}Cl_2NO_7$: N, 4.02. Found: N, 3.89.

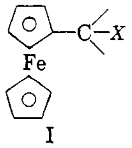
DEPARTMENT OF PHYSIOLOGY
UNIVERSITY OF MONTREAL
MONTREAL, QUEBEC, CAN.

Communications TO THE EDITOR

α-Haloferrocenes. The Synthesis of Ferrocenylacetylene[1]

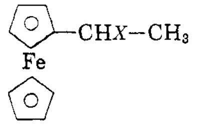
Sir:

Thus far there has been no instance of the successful isolation and characterization of an α-haloferrocene (I), although several unsuccessful attempts to prepare such compounds have been reported.[2] Such compounds should be highly reactive as well as hydrolytically and perhaps even thermally unstable.[2]

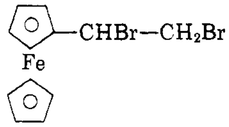


I

We are hereby reporting the successful preparation of α-chloro- and α-bromoethylferrocene (II) as well as α,β-dibromoethylferrocene (III).



X = Cl, Br
II



III

The α-chloroethylferrocene (II. *X* = Cl) was prepared by adding dry hydrogen chloride to vinylferrocene[3] in pentane at −78°. A yellow solid was obtained (94% yield) which, after crystallization from anhydrous ether at −78° melted at 66–68° (dec. above 75°). The infrared spectrum of this material showed a C—Cl band at 14.3–14.4 μ, a CH_3—C compression at 7.3 μ, and ferrocene bands at 9, 10, and 12.2 μ.[4] (*Anal.* Calcd. for $C_{12}H_{13}FeCl$: C, 57.9; H, 5.23; Cl, 14.27. Found: C, 57.3; H, 5.52; Cl, 14.57.)

When this halide was treated at −78° with an ethereal slurry of sodium azide, an 89% yield of an amber liquid (n_D^{20} = 1.6116) was obtained, with infrared bands at 4.80 μ (—N_3) and 9, 10, and 12.2 μ. (lit. value[5] n_D^{20} = 1.6110). (*Anal.* Calcd. for $C_{12}H_{13}FeN_3$: C, 56.5; H, 5.14; Fe, 21.89; N, 16.47. Found: C, 56.3; H, 5.13; Fe, 22.08; N, 16.63.)

The α-chloroethylferrocene was also obtained in 95% yield by treating an ethereal solution of α-hydroxyethylferrocene containing activated alumina with anhydrous hydrogen chloride at −78°. The product thus obtained melted at 66–68°. This melting point was undepressed by a sample of the material prepared directly from vinylferrocene. Both samples had superimposable infrared spectra and formed identical azides.[5]

α-Bromoethylferrocene (II. *X* = Br) formed (93% yield) in a manner similar to the α-chloro compound by adding anhydrous hydrogen bromide to vinylferrocene in pentane at −78° (m.p. 48–50° dec.). The infrared spectrum of this material showed methyl group adsorption at 6.9 and 7.3 μ and bands at 9, 10, and 12.2 μ. (*Anal.* Calcd. for $C_{12}H_{13}FeBr$: C, 49.19; H, 4.47; Br, 27.27; Fe, 19.04. Found: C, 48.76; H, 4.42; Br, 26.92; Fe, 18.92.)

This bromide reacted almost instantaneously with aqueous sodium carbonate producing α-hydroxyethylferrocene[3] (m.p. 78–79°).

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(1) This research was supported by the United States Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command under contract No. A.F. 49(638)-297. Reproduction in whole or in part is permitted for any purpose of the United States Government.

(2) C. R. Hauser and J. K. Lindsay, *J. Org. Chem.*, **22**, 1246 (1957); K. Schlögl, *Monatsh*, **81**, 601 (1957); P. L. Pauson, *Quart. Revs.*, **9**, 391 (1955).

(3) F. Arimoto and A. Haven, Jr., *J. Am. Chem. Soc.*, **77**, 6295 (1955).

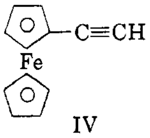
(4) An NMR spectrum of this compound showed a doublet signal at τ = 8.19 which is strong evidence for a formulation having a methyl group adjacent to a carbon atom bonded to only one hydrogen. In addition, the complete absence of peaks with τ values greater than 10 supports a formulation *without* a metal to hydrogen bond. [See T. J. Curphey, J. O. Santer, M. Rosenblum, and J. H. Richards, *J. Am. Chem. Soc.*, **82**, 5249 (1960)].

(5) The properties of this material agreed well with those reported by G. R. Buell, E. McEwen, and J. Kleinberg, *Tetrahedron Letters*, **5**, 16 (1959).

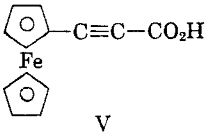
α,β-Dibromoethylferrocene (III) was prepared (74.5% yield) by adding bromine to vinylferrocene in pentane at −78°. The purified yellow solid melted to a yellow liquid at 63–64°. It was completely stable at −78°, but decomposed at room temperature. (*Anal.* Calcd. for $C_{12}H_{12}FeBr_2$: C, 38.78; H, 3.22; Fe, 15.00; Br, 43.00. Found: C, 39.23; H, 3.34; Fe, 15.03; Br, 42.50.)

When a pentane solution of this dibromide was added to potassium amide in liquid ammonia, an amber crystalline solid (29% conversion), melting at 54–55°, was obtained. The infrared spectrum of the amber solid showed a —C≡C—H band at 3.2 μ, a —C≡C— band at 4.8 μ, as well as bands at 9, 10 and 12.2 μ. The spectrum was devoid of olefinic absorption. (*Anal.* Calcd. for $C_{12}H_{10}Fe$: C, 68.56; H, 4.75; Fe, 26.60. Found: C, 68.84; H, 4.92; Fe, 26.41.)

Further evidence that this material was ferrocenylacetylene (IV) was obtained by treating it with methyllithium followed by carbonation with Dry Ice. A dark red crystalline solid was obtained (94% yield) melting with effervescence at 122°.



IV



V

Its infrared spectrum showed a shifted —C≡C— band at 4.65 μ, a carboxyl peak at 6.05 μ, a broad shallow —OH region, and bands at 9, 10, and 12.2 μ, identifying the material as ferrocenylpropiolic acid (V). (*Anal.* Calcd. for $C_{13}H_{10}FeO_2$: C, 61.46; H, 3.97; Fe, 21.98. Found: C, 61.49; H, 4.20; Fe, 21.78.)

Chemical Laboratories
Purdue University
Lafayette, Ind.

Robert A. Benkeser
Walter P. Fitzgerald, Jr.

Received May 26, 1961

Alkoxylation of Steroids with Cupric Bromide: Alcohol

Sir:

The halogenation of ketones with cupric halides has been reported by Kochi[1] and, very recently, by Fort.[2] While attempting to find more specific methods for the halogenation of steroids, we investigated the oxidation of steroids with cupric halides in alcohol in the presence and absence of pyridine. In most cases, 6-alkoxylation of the steroid resulted.

Treatment of 4-androstene-3,17-dione with two molar equivalents of cupric bromide and two molar equivalents of pyridine in methanol at reflux for thirty-five minutes yielded 6β-methoxy-4-androstene-3,17-dione, m.p. 164–166°; $\lambda_{max}^{Methanol}$ 233.5 mμ (ε 13,100); $[\alpha]_D$ +123° (chloroform); $\lambda_{max}^{CHCl_3}$ 5.72, 5.92, 6.18, 9.22 μ (found: C, 75.56; H, 8.95; OCH_3, 9.67). This material was identical in all respects with a sample of 6β-methoxy-4-androstene-3,17-dione prepared from 5α,6α-epoxy-3β-hydroxyandrostan-17-one *via* reaction with methanol, oxidation, and very mild dehydration.[3]

To provide evidence for the course of the reaction, a more thorough study was made on testosterone. Treatment of testosterone (I) with two molar equivalents of cupric bromide in methanol at 5° for seven days yielded 6β-methoxytestosterone (III) (35% yield), m.p. 210–214° [4]; $\lambda_{max}^{methanol}$ 235 mμ (ε 13,000); λ_{max}^{KBr} 2.87, 6.01, 9.18 μ $[\alpha]_D$ +45° (chloroform); (found: C, 75.60; H, 9.25). The use of four molar equivalents of cupric bromide with testosterone, under the above conditions yielded 6-methoxy-6-dehydrotestosterone (IV) (60% yield), m.p. 167–168°; $\lambda_{max}^{methanol}$ 248 mμ (ε 7580), 304 mμ (ε 14,900); (found: C, 75.57; H, 9.24; OCH_3, 9.83); 17-acetate, m.p. 161–162°; $\lambda_{max}^{methanol}$ 248.5 mμ (ε 7900), 303 mμ (ε 15,400); (found: C, 74.08; H, 8.27). Acid hydrolysis of IV acetate produced 6-oxotestosterone acetate (V), m.p. 209–211°, $\lambda_{max}^{CHCl_3}$ 5.75, 5.88, 7.94 μ, identical in all respects (mixed melting point and infrared spectra) with an authentic sample.[5] To investigate the possibility that bromination at C-6 could precede the introduction of the methoxy group, 6β-bromotestosterone acetate (IIa)[6] was heated under reflux in methanol with two molar equivalents of cupric bromide and five molar equivalents of pyridine. This reaction gave a 70% yield of 6β-methoxytestosterone acetate (IIIa). When the above reaction was run at room temperature in the absence of pyridine, 6-methoxy-6-dehydrotestosterone (IV) (70% yield) was obtained.

Oxidation of 6α - methyl - 17α - acetoxyprogesterone[7] (VI) with two molar equivalents of cupric bromide in methanol at 2°, produced 6β - methoxy - 6α - methyl - 17α - acetoxyprogesterone (VII) (50% yield), m.p. 207–212°; $\lambda_{max}^{methanol}$ 235.5 mμ (ε 13,500); (found: C, 72.06; H, 8.46). Compound VII was very easily demethoxylated with concentrated hydrochloric acid to the known

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[1] J. K. Kochi, *J. Am. Chem. Soc.*, **77**, 5274 (1955).

[2] A. W. Fort, *J. Org. Chem.*, **26**, 765 (1961).

[3] We are indebted to Dr. Roy Bible of these laboratories for this sample.

[4] E. Kaspar, R. Weichert, and M. Schenck, Deutsches Patentamt Auslegeschrift **1,071,081**, June 20, 1958.

[5] A. Butenandt and B. Riegel, *Ber.*, **69**, 1163 (1936). See C. Amendolla, G. Rosenkranz, and F. Sondheimer [*J. Chem. Soc.*, 1226 (1954)] for the melting point of 6-oxotestosterone.

[6] C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann, and J. Pataki, *J. Am. Chem. Soc.*, **72**, 4534 (1950).

[7] J. C. Babcock, E. S. Gutsell, M. E. Herr, J. A. Hogg, J. C. Stucki, L. E. Barnes, and W. E. Dulin, *J. Am. Chem. Soc.*, **80**, 2904 (1958).