was prepared as follows. Methyl hydrogen phthalate[13] (18 g.) was converted to the acyl chloride with thionyl chloride.[13] The acyl chloride was dissolved in 100 ml. of anhydrous ether and dry ammonia was bubbled through the solution for 1 hr. at 0°. The white precipitate was recovered by filtration and dissolved in 50 ml. of chloroform. After discarding the insoluble material, the chloroform was removed by evaporation under reduced pressure. The resulting residue was recrystallized from ether to yield methyl phthalamate, m.p. 102–104°, lit.[11] m.p. 98–99°.

Anal. Calcd.: C, 59.88; H, 5.06; N, 7.90. Found: C, 60.33; H, 5.06; N, 7.82.

Infrared analysis (CHCl$_3$) revealed strong bands at 1680 and 1700 cm.$^{-1}$; n.m.r. spectrum (Varian A 60, deuterioacetone, tetramethylsilane as internal standard) revealed a complex multiplet centered at 7.05, a broad band near 6.6, and a sharp singlet at 3.3 p.p.m. (approximate integrated intensities are in the ratio 4:2:3, respectively).[13] Other materials were obtained commercially and recrystallized or redistilled before use. Distilled water was employed throughout.

Kinetic measurements were carried out spectrophotometrically with a Zeiss PMQ II spectrophotometer equipped with a thermostatted cell carriage as previously described.[14] All reactions were carried out at 25° in aqueous solution at ionic strength 0.5 (adjusted with potassium chloride). Dilute phosphate, borate, or carbonate buffers were employed in appropriate pH regions. For the studies of imide formation from methyl phthalamate, infinite time readings were determined artificially by immediately neutralizing strongly basic solutions of this substrate with hydrochloric acid. This procedure was necessary since the hydrolysis of the imide product was sufficiently rapid to introduce appreciable errors into the observed infinite time readings.[2b] Measurements of pH were obtained with the glass electrode and a Radiometer PHM 4c pH meter.

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[13] We are indebted to Mr. D. P. Cords for recording the n.m.r. spectrum.

[14] W. P. Jencks, *J. Am. Chem. Soc.*, **81**, 475 (1959).

The Acetylation of Biferrocenyl[1,2]

M. D. RAUSCH

Monsanto Chemical Company, Central Research Department, St. Louis, Missouri, and the Department of Chemistry, University of Massachusetts, Amherst, Massachusetts

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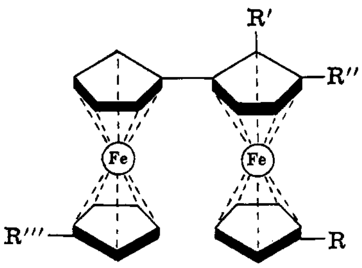
The development of suitable synthetic procedures for biferrocenyl (I)[3-5] has enabled a general study concerning various ring-substitution reactions of this metallocene to be undertaken. The ability of biferrocenyl to undergo acylation and metalation reactions, as well as the isomerism of substituted biferrocenyls, has been discussed in previous communications.[1,6,7] In this paper, details concerning the acetylation of biferrocenyl and the configuration of various acetylated biferrocenyls are presented.

Three positional isomers are possible for a monoacetylated biferrocenyl: (1) isomer II, in which the acetyl group is attached to a cyclopentadienyl ring opposite the two rings joining the two ferrocenyl nuclei; (2) isomer III, in which the acetyl group is located at a position α to a bridging carbon atom; (3) isomer IV, in which the acetyl group is similarly β disposed.



I, R, R′, R″, R‴ = H
II, R = CO–CH$_3$; R′, R″, R‴ = H
III, R′ = CO–CH$_3$; R, R″, R‴ = H
IV, R″ = CO–CH$_3$; R, R′, R‴ = H
V, R, R‴ = CO–CH$_3$; R′, R″ = H

Treatment of biferrocenyl with equimolar amounts of acetyl chloride and aluminum chloride in methylene chloride solution produced a mixture of products which could be separated by chromatography on alumina. The major product from the reaction, isolated in 14% yield, was a monoacetylbiferrocenyl of m.p. 143°. This product is assigned as acetylbiferrocenyl II on the basis of its proton nuclear magnetic resonance spectrum (Fig. 1).[8] A resonance peak at τ 7.85 representing three protons is noted in the region where the proton peak of an acetyl group attached to ferrocene is known to occur.[2] A singlet representing five protons is present at τ 6.03. The chemical shift of this peak is similar to chemical shifts of peaks representing protons of unsubstituted cyclopentadienyl rings in ferrocene (τ 5.86)[2] and biferrocenyl (τ 6.02).[9] A triplet due to two protons is noted somewhat upfield (τ 5.42) from the triplet representing the α protons in acetylferrocene (τ 5.23).[2] It is known, however, that the two directly bonded ferrocene nuclei in biferrocenyl exert a mutual shielding effect on all protons present.[9] The differential shift ($\Delta\tau$) of the triplet representing the α protons in acetylbiferrocenyl II compared to the unsubstituted ring protons in biferrocenyl is τ 0.60. This value is in good agreement with a $\Delta\tau$ value of τ 0.63 for the corresponding α protons of acetylferrocene compared to ferrocene.[2] Complex absorption in the region centered around *ca.* τ 5.71 accounts for the remaining ten protons in acetylbiferrocenyl II.

A second isomeric acetylbiferrocenyl of melting point 158–159° was isolated in *ca.* 1% yield from the reaction products. The proton n.m.r. spectrum of this product exhibited a singlet at τ 7.59 attributable to three acetyl protons, an apparent singlet at τ 5.98 attributable to ten protons on unsubstituted cyclopentadienyl rings, and complex absorption between τ 5.0 and 5.9 due to seven additional ring protons. Using an expanded (50 c.p.s.) scale, the resonance peak at τ 5.98 was further resolved into two peaks of approximately equal

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[1] Presented in part at the 138th National Meeting of the American Chemical Society, New York, N. Y., Sept. 11, 1960; see Abstracts of Papers, p. 54P.

[2] Part IX of a series "Organometallic π-Complexes."

[3] M. D. Rausch, *ibid.*, **26**, 1802 (1961).

[4] E. G. Perevalova and O. A. Nesmeyanova, *Doklady Akad. Nauk SSSR*, **132**, 1093 (1960).

[5] M. D. Rausch, *Inorg. Chem.*, **1**, 414 (1962).

[6] M. D. Rausch, *J. Am. Chem. Soc.*, **82**, 2080 (1960).

[7] Electrophilic aromatic substitution reactions of biferrocenyl since have been described by other investigators: S. I. Goldberg, J. S. Crowell, and R. L. Matteson, XIX International Congress of Pure and Applied Chemistry, London, England, July 10, 1963; see Abstracts A, p. 184.

[8] Acetylbiferrocenyl II also has been synthesized recently by means of an unambiguous route, *viz.*, mixed Ullmann-type coupling of bromoferrocene and 1-bromo-1′-acetylferrocene [S. I. Goldberg and R. L. Matteson, *J. Org. Chem.*, **29**, 323 (1964)]. These investigators have likewise shown that Ullmann-type coupling of the latter derivative gives rise to diacetylbiferrocenyl V. The proton n.m.r. spectra of acetylbiferrocenyl II and diacetylbiferrocenyl V produced in this manner are identical with the spectra of the corresponding products isolated in the present study.

[9] Analogous results concerning the proton n.m.r. spectrum of biferrocenyl in chloroform solution have been reported previously: S. I. Goldberg, D. W. Mayo, and J. A. Alford, *J. Org. Chem.*, **28**, 1708 (1963).

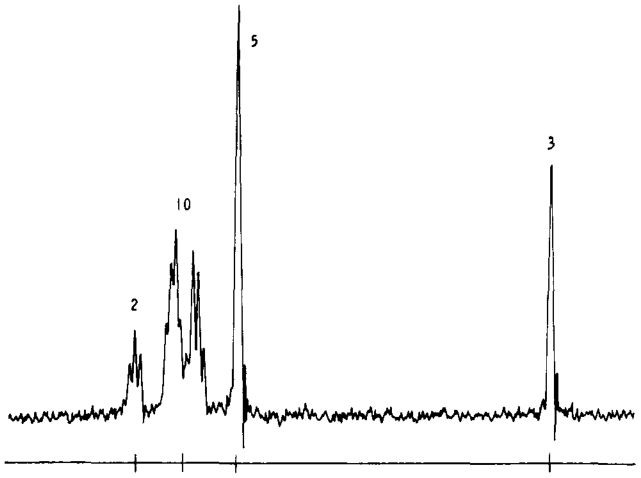
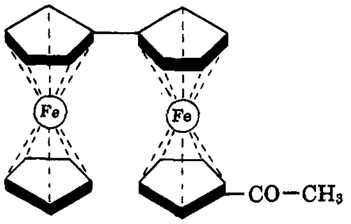


Fig. 1.—Proton n.m.r. spectrum of acetylbiferrocenyl II.



II

intensity at τ 5.97 and 5.99. Either acetylbiferrocenyl III or acetylbiferrocenyl IV is consistent with such a spectrum, and further elucidation of the structure of this product is in progress. In acetylation reactions involving a variety of other substituted ferrocenes, the 1,2 isomer was eluted from alumina before the 1,1′ and the 1,3 isomers.[10–12] Further, Rosenblum[13] has shown that the 2-position of aryl-substituted ferrocenes is preferentially attacked by electrophilic reagents. On this basis, the product is tentatively assigned as acetylbiferrocenyl III.

In addition to an appreciable amount of recovered biferrocenyl, a very small amount of acetylferrocene was isolated and characterized by means of its melting point and proton n.m.r. spectrum. Since highly purified biferrocenyl was used as starting material, it is conceivable that acetylferrocene resulted from partial decomposition of biferrocenyl or an acetylated intermediate during the course of the reaction.

The reaction of biferrocenyl with an appreciable molar excess of both acetyl chloride and aluminum chloride produced a variety of acetylated biferrocenyls. The major product of the reaction, isolated in 40% yield, was a diacetylbiferrocenyl of m.p. 191–192°. Although fourteen isomeric diacetylbiferrocenyls are theoretically possible, the product can be assigned as diacetylbiferrocenyl V on the basis of its proton n.m.r. spectrum (Fig. 2).[8] A singlet representing six acetyl protons is found at τ 7.84. A low-field triplet representing four protons occurs at τ 5.43 and is assigned to the four equivalent protons which are α to the two acetyl groups. Absorption due to twelve ring protons occurs as a complex multiplet centered at *ca.* τ 5.67. It is significant that no resonance peak is noted near τ 6.0, where singlets representing unsubstituted cyclopentadienyl ring protons in acetylbiferrocenyls are known to occur. In addition to diacetylbiferrocenyl V, a second isomeric diacetylbiferrocenyl of m.p. 147–147.5° as well as other acetylated biferrocenyls were noted. A detailed investigation of these isomeric products is in progress and will be reported later.

The infrared spectra of acetylbiferrocenyl II and diacetylbiferrocenyl V exhibited strong carbonyl stretching frequencies at 6.0 and absorptions at *ca.* 9.0 μ characteristic of acetylferrocenes.[14] Acetylbiferrocenyl II also exhibited an absorption shoulder at 9.05 and an absorption band at 10.0 μ, in accordance with the presence of an unsubstituted cyclopentadienyl ring.[14]

The recovery of appreciable amounts of biferrocenyl from these and related acylation reactions and the rather low conversions to acylated biferrocenyls are striking in contrast to the facile acylation of ferrocene itself. It is of further interest that a ferrocenyl group appears to deactivate the cyclopentadienyl ring to which it is attached, and preferential acetylation occurs in the unsubstituted ring. A similar deactivating influence of the phenyl group in acetylation reactions of phenylferrocenes previously has been observed.[13,15,16]

Experimental

General.—Biferrocenyl was prepared according to published procedures[3–5] and was repeatedly recrystallized from *n*-heptane before use. Acetyl chloride and anhydrous aluminum chloride were of reagent grade purity and were taken from freshly opened bottles. Methylene chloride was dried over calcium hydride before use. Elemental analyses and molecular weight determinations were performed by the Schwarzkopf Microanalytical Laboratory, Woodside N. Y., and by the analytical section of this laboratory. Melting points are uncorrected. Nuclear magnetic resonance spectra were determined on a Varian Model A-60 spectrometer. Sample concentrations were *ca.* 5 to 10% (w./v.) in deuteriochloroform except for biferrocenyl; the latter was examined as a saturated solution in this solvent. Infrared spectra were obtained on a Beckman Model IR-4 spectrophotometer by means of potassium bromide pellets. Chromatography was performed on columns wrapped with aluminum foil to protect the compounds from light.

Monoacetylation of Biferrocenyl.—A mixture of acetyl chloride (4.93 mmoles, 0.35 ml.) and anhydrous aluminum chloride (6.0 mmoles, 0.80 g.) in 40 ml. of methylene chloride was prepared under nitrogen. The solution of acetylating agent was transferred under nitrogen to a dropping funnel, a glass wool filter being used to separate the undissolved aluminum chloride. The acetylating agent was added dropwise with stirring and under nitrogen to a solution of biferrocenyl (4.93 mmoles, 1.822 g.) in 200 ml. of methylene chloride. The violet-colored reaction mixture was stirred at room temperature for 2 hr. and then hydrolyzed with de-oxygenated water. The organic phase was separated and the methylene chloride washings of the aqueous phase were added to it. The organic solution was washed several times with water and then dried over anhydrous sodium sulfate. The mixture was filtered and the solvent was removed by means of a rotary evaporator at reduced pressure.

The residue was extracted repeatedly with ethyl ether and the extracts were chromatographed on a 3 cm. × 60 cm. column of

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[10] K. L. Rinehart, Jr., K. L. Motz, and S. Moon, *J. Am. Chem. Soc.*, **79**, 2749 (1957).

[11] M. Rosenblum, W. G. Howells, A. K. Banerjee, and C. Bennett, *ibid.*, **84**, 2726 (1962).

[12] D. W. Hall and J. H. Richards, *J. Org. Chem.*, **28**, 1549 (1963).

[13] M. Rosenblum and W. G. Howells, *J. Am. Chem. Soc.*, **84**, 1167 (1962).

[14] M. Rosenblum, *Chem. Ind.* (London), 953 (1958).

[15] M. Rosenblum, *J. Am. Chem. Soc.*, **81**, 4530 (1959).

[16] A. N. Nesmeyanov, E. G. Perevalova, S. P. Gubin, T. V. Nikitina, A. A. Ponomarenko, and L. S. Shilovtseva, *Doklady Akad. Nauk SSSR*, **139**, 888 (1961).

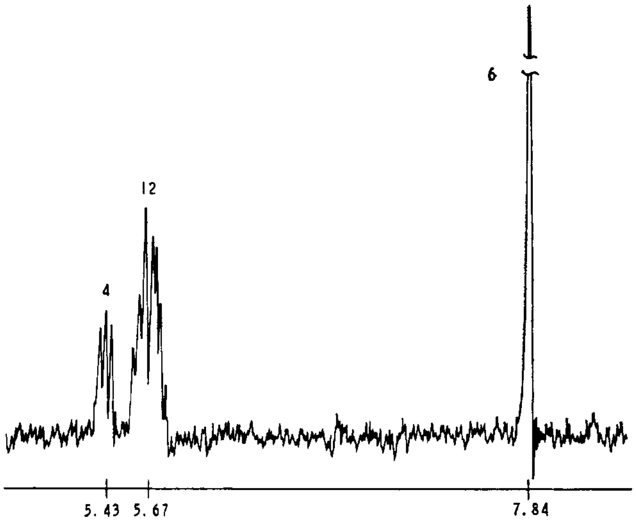
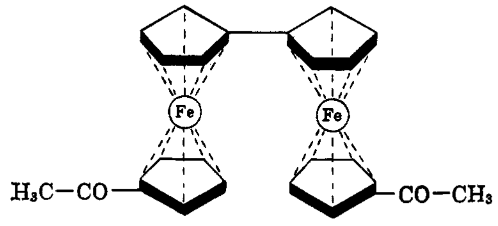


Fig. 2.—Proton n.m.r. spectrum of diacetylbiferrocenyl V.



V

Merck alumina. Elution with ether rapidly removed a broad yellow band from which 1.13 g. of an orange solid was obtained. Recrystallization of the solid produced 0.95 g. of biferrocenyl, m.p. 237–239° (nitrogen). The n.m.r. spectrum of this product exhibited a triplet at τ 5.65 due to four protons, a triplet at 5.83 due to four protons, and a singlet at 6.02 due to ten protons.[9] The n.m.r. and infrared spectra of biferrocenyl obtained from this reaction were identical with the corresponding spectra of an authentic sample. Continued elution with ether removed a faint yellow band; the latter yielded 8 mg. of red crystals, m.p. 83–85°. A mixture melting point determination of this product with acetylferrocene (m.p. 85–86°)[17] was undepressed, and the n.m.r. spectrum of the product was identical with the n.m.r. spectrum of acetylferrocene. Elution with ether next removed a faint red band. There was obtained 23 mg. of an orange solid, m.p. 153–158°. Recrystallization of the solid from *n*-heptane produced 15 mg. (1%) of acetylbiferrocenyl III, m.p. 158–159°.

Anal. Calcd. for $C_{22}H_{20}Fe_2O$: C, 64.12; H, 4.89; mol. wt., 412. Found: C, 63.96; H, 5.11; mol. wt., 417.

Elution of the final band produced 290 mg. (14%) of acetylbiferrocenyl II in the form of red crystals, m.p. 140–141°. Recrystallization of the product raised the melting point to 143°.

Anal. Calcd. for $C_{22}H_{20}Fe_2O$: C, 64.12; H, 4.89; Fe, 27.10; mol. wt., 412. Found: C, 64.04; H, 4.89; Fe, 27.34; mol. wt., 417.

Diacetylation of Biferrocenyl.—A solution of biferrocenyl (1.0 mmole, 0.370 g.) in 30 ml. of methylene chloride was added dropwise with stirring and under nitrogen to a solution of acetyl chloride (3.0 mmoles, 0.22 ml.) and anhydrous aluminum chloride (3.0 mmoles, 0.40 g.) in 20 ml. of the same solvent. Following the addition, the reaction mixture was refluxed for 1 hr. and then hydrolyzed with de-oxygenated water. The phases were separated and the aqueous phase was extracted with methylene chloride. The combined organic phases were washed several times with water and dried over anhydrous sodium sulfate. The mixture was filtered and concentrated to dryness.

The residue was dissolved in *ca.* 15 ml. of methylene chloride–benzene (1:1) and the solution was chromatographed on a 1.5 cm. × 50 cm. column of Merck alumina. Elution with benzene removed a yellow band. Recrystallization of the resulting product from *n*-heptane produced 60 mg. of biferrocenyl, m.p. 237–239° (nitrogen). Further elution removed a salmon-colored band. The product from this band was recrystallized from *n*-heptane to yield 15 mg. of crude acetylbiferrocenyl II, m.p. 137–139°. The infrared spectrum of this product was identical with the spectrum of acetylbiferrocenyl II obtained from the monoacetylation of biferrocenyl. A broad red band was next eluted with methylene chloride. Recrystallization of the resulting product from a mixture of benzene and *n*-hexane produced 180 mg. (40%) of diacetylbiferrocenyl V in the form of deep red crystals, m.p. 191–192°.

Anal. Calcd. for $C_{24}H_{22}Fe_2O_2$: C, 63.48; H, 4.88; Fe, 24.60; mol. wt., 454. Found: C, 63.85; H, 4.98; Fe, 24.20; mol. wt., 454.

A narrow red band was next eluted with 5% methanol in chloroform. The product was rechromatographed in benzene solution and a red band was eluted with mixtures of benzene and chloroform. The resulting product was recrystallized from methanol to yield 20 mg. of red crystals, m.p. 147–147.5°.

Anal. Calcd. for $C_{24}H_{22}Fe_2O_2$: C, 63.48; H, 4.88; Fe, 24.60. Found: C, 63.32; H, 5.10; Fe, 24.68.

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[17] P. J. Graham, R. V. Lindsey, G. W. Parshall, M. L. Peterson, and G. M. Whitman, *J. Am. Chem. Soc.*, **79**, 3416 (1957).

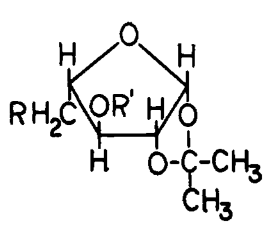
Preparation of Methyl L-Arabinothiapyranoside and Disulfide Derivatives of 5-Mercapto-L-arabinose[1]

Roy L. Whistler and R. M. Rowell

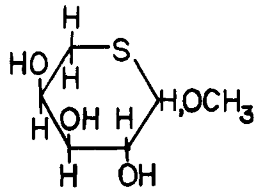
Department of Biochemistry, Purdue University, Lafayette, Indiana

Received September 16, 1963

In the preparation of analogs of natural sugars wherein sulfur replaces the normal ring oxygen, the analog of the common plant sugar, L-arabinose, is now made. As in several previous preparations[2-5] of thia sugars, sulfur is introduced by nucleophilic displacement of the tosyloxy group with the thiobenzylate anion. The starting compound is 1,2-*O*-isopropylidene-5-*O*-tosyl-L-arabinofuranose[6] (I) which is converted to II with the thiobenzylate ion. Reduction with sodium in liquid ammmonia gives 5-deoxy-1,2-*O*-isopropylidene-5-mercapto-L-arabinofuranose (III). Methanolysis produces an anomeric mixture of methyl



I R = OTs, R' = H
II R = $SCH_2\phi$, R' = H
III R = SH, R' = H
IV R = SAc, R' = Ac



V

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[1] Journal Paper No. 2206 of the Purdue Agricultural Experiment Station, Lafayette, Ind. Presented in part at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963.

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[5] V. S. R. Rao, J. F. Foster, and R. L. Whistler, *ibid.*, **28**, 1730 (1963).

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