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ORGANOMETALLIC π-COMPLEXES
XXI*. VILSMEIER FORMYLATION OF BIFERROCENE

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SUMMARY

Biferrocene undergoes the Vilsmeier formylation reaction to produce a mixture of many formylated biferrocenes. Both 1'-formyl and 1',1'''-diformylbiferrocene have been isolated and characterized, and certain reactions of these substances have been investigated.

INTRODUCTION

Although the chemistry of ferrocene has been extensively developed since its discovery in 1951, the chemistry of biferrocene (I)** has been only briefly investigated. Following the development of a facile route to (I)[6-8], several groups of investigators[6,9-12] studied the Friedel–Crafts acetylation of this compound. A variety of mono- and diacetylated derivatives were formed, depending on the reaction conditions. In the present paper, we describe studies on the Vilsmeier formylation of (I). Some additional reactions of the resulting formyl derivatives are also briefly discussed.

RESULTS AND DISCUSSION

Treatment of (I) with an excess of *N*-methylformanilide and phosphorus oxychloride produced low yields of 1'-formylbiferrocene (II), 1',1'''-diformylbiferrocene (III), as well as many other formylated products. The various formylated biferrocenes were separated by column chromatography on alumina, and were further purified by recrystallization. Structural assignments on (II) and (III) have been made on the basis of NMR and IR data. The monoformyl derivatives appeared to separate readily from the diformyl products, but further purification of isomers in each group proved to be very difficult.

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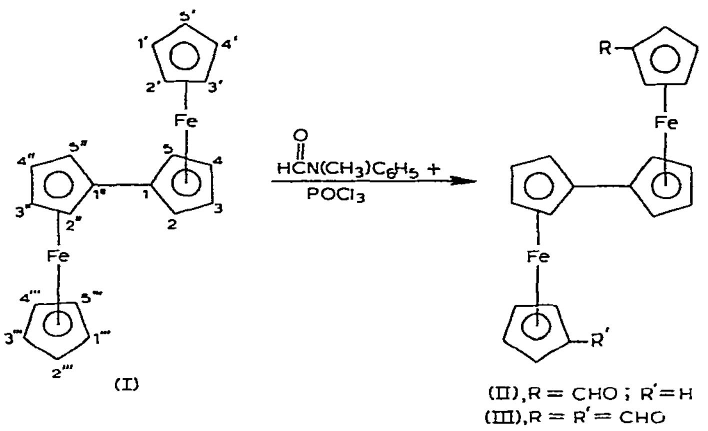
* For Part XX see ref. 1.

** Biferrocene (I) has been shown by X-ray crystallographic studies[2-4] to exist in a *trans*-configuration, and this configuration has been assumed in the present study. The nomenclature and numbering system used is that followed by Chemical Abstracts[5a] and is illustrated in structure (I).



(I)

(II), R = CHO ; R' = H
(III), R = R' = CHO

The first band to be eluted after (I) was shown by NMR to be a mixture of mono-formylated biferrocenes. 1'-Formylbiferrocene (II) was purified by fractional recrystallization of this mixture. Its NMR spectrum ($CDCl_3$) exhibited a singlet at τ 5.99, indicative of an unsubstituted cyclopentadienyl ring, a multiplet centered at τ 5.66 [connected-ring protons H(2)–H(5) and H(2'')–H(5'') and protons H(3') and H(4')], a triplet at τ 5.38 [protons H(2') and H(5')], and a singlet at τ 0.09 (formyl proton). The intensity ratio of these signals was 5/10/2/1, consistent with the proposed structure. The NMR spectrum in the biferrocene region is very similar to the spectrum of 1'-acetylbiferrocene[9,10]. Such a result might be anticipated, since both formyl and acetyl substituents are known to have similar deshielding effects on ferrocenyl ring protons[13]. The IR spectrum of (II) ($CDCl_3$) exhibited strong absorptions near 1000 and 1100 cm^{-1}, indicative of an unsubstituted cyclopentadienyl ring, and a strong carbonyl absorption at 1670 cm^{-1}.

The second band to be eluted after (I) was shown by NMR to be a mixture of di- and possibly higher formylated biferrocenes. Fractional crystallization of the mixture produced a dark red compound which has been shown to be 1',1'''-diformylbiferrocene (III) on the basis of elemental analysis and its NMR spectrum. The latter ($CDCl_3$) exhibited a multiplet centered at τ 5.65 [connected-ring protons H(2)–H(5) and H(2'')–H(5'') as well as protons H(3'), H(4'), H(3''') and H(4''')], a triplet at τ 5.45 [protons H(2'), H(5'), H(2''') and H(5''')], and a singlet at τ 0.53 (formyl protons). The integrated intensities were 12/4/2, respectively. As in the spectrum of 1',1'''-diacetylbiferrocene[9,10] it is significant that no resonance peak was present near τ 6.0, which would be characteristic of an unsubstituted cyclopentadienyl ring. The IR spectrum of (III) ($CDCl_3$) exhibited a strong carbonyl stretching frequency at 1660 cm^{-1}; absorptions near 1000 and 1100 cm^{-1} were virtually absent.

Several reactions of formylated biferrocenes (II) and (III) were subsequently investigated. Treatment of 1'-formylbiferrocene (II) with methyllithium proceeded in a normal fashion to produce 1'-(1-hydroxyethyl)biferrocene. This same product could also be obtained from the reduction of 1'-acetylbiferrocene by lithium aluminum hydride. In a manner analogous to formylferrocene[14–16], treatment of (II) with malonic acid in pyridine containing a trace of piperidine produced the condensation product 3-(1'-biferrocenyl)acrylic acid (IV) in good yield. The IR spectrum of (IV)

(KBr) exhibited a strong carbonyl stretching frequency at 1680 cm^{-1} and C=C absorption at 1610 cm^{-1}. 1',1'''-Dimethylbiferrocene (VI) was also prepared in 64% yield by a reaction between (III) and lithium aluminum hydride/aluminum chloride.

EXPERIMENTAL

Proton NMR spectra were recorded on a Varian A-60 spectrometer, and IR spectra were obtained on either Beckman IR-5 or IR-10 spectrophotometers. Melting points are uncorrected. Elemental analyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside, New York. Biferrocene was prepared in yields of 90–98% by means of a literature procedure[7].

Formylation of biferrocene (I)

Biferrocene (10.0 g, 0.027 mole), phosphorus oxychloride (6.87 g, 0.045 mole), and 35 ml of heptane were added to a 250-ml 3-necked flask fitted with condenser, addition funnel, mechanical stirrer, and nitrogen inlet. The reaction mixture was heated with stirring to 50°, and freshly distilled *N*-methylformanilide (9.72 g, 0.072 mole) was added dropwise over a 20 min period. The contents turned black after ca. 5 min following the start of the addition. The reaction mixture was heated at 50–60° for an additional ½ h, cooled to 0°, and a solution of 22.5 g of sodium acetate in 110 ml of water was added slowly, the temperature being maintained below 10°. The mixture was allowed to hydrolyze overnight with stirring, extracted with benzene, and the extracts were washed with satd. sodium carbonate, then satd. sodium chloride solution. The benzene was removed by evaporation, and the dark semi-crystalline residue was extracted with 20 ml of ethyl ether to remove unreacted *N*-methylformanilide; an orange solid remained. Concentration of the ether extract afforded additional solid which was combined with that obtained above. The ethereal solution was worked up separately (*vide infra*).

The combined solids were dissolved in benzene and chromatographed on alumina. Due to the large volume of solution, several columns were used, and corresponding bands were subsequently combined. Elution with benzene afforded 6.7 g of biferrocene (I). A second band was eluted with benzene/ethyl ether (9/1). Evaporation of the solvent and recrystallization of the resulting red solid produced 250 mg of 1'-formylbiferrocene (II), m.p. 170–171°. (Found: C, 63.32; H, 4.68; Fe, 27.97. $C_{21}H_{18}Fe_2O$ calcd.: C, 63.38; H, 4.52; Fe, 28.07%.)

Continued elution with benzene/ethyl ether (1/1) and recrystallization of the product from benzene/hexane (1/1) yielded 100 mg of a red solid, identified as 1',1'''-diformylbiferrocene (III). After several recrystallizations, an analytically pure sample of (III), m.p. 175–176.5°, was obtained. (Found: C, 62.29; H, 4.32; Fe, 25.86. $C_{22}H_{18}Fe_2O_2$ calcd.: C, 62.01; H, 4.32; Fe, 26.22%.)

The ether extract of the original formylation product was stirred vigorously with satd. sodium bisulfite solution, first briefly at ice temperature, then overnight at room temperature. The yellow product was collected by filtration, washed thoroughly with ethyl ether, and dried in the air. After powdering, the solid was stirred with 50 ml of 2 *N* sodium hydroxide for ½ h. The resulting precipitate was separated, dried, and chromatographed on alumina to produce three main bands. The first band produced a small amount of biferrocene (I), while the second band afforded 97 mg of 1'-formylbiferrocene (II), after recrystallization of the product from hexane. The total yield of (II) was therefore 347 mg (3.2%). A third band produced 115 mg of 1',1'''-diformylbiferrocene (III), for a total yield of (II) of 215 mg (2.2%).

The mother liquors from the recrystallization of (II) were combined and chromatographed on alumina. The principal band was eluted with benzene/hexane (1/1) and appeared by NMR to consist of a mixture of (II) and another formylated biferrocene, tentatively assigned as 3-formylbiferrocene[17]. The two products could not be separated by column chromatography, preparative thin-layer chromatography, nor by fractional recrystallization. Combination and chromatography of the mother liquors from the recrystallization of (III) produced at least five other products, but the yield of any one of these was too small to allow meaningful characterization.

When the formylation reaction was carried out using a three-fold excess of biferrocene to formylating agent, the yields of formylation products were even lower, and biferrocene was largely recovered. Complicated mixtures of various formylation products were still obtained, even under these conditions.

Reaction of 1'-formylbiferrocene (II) with methyllithium

Into a 10-ml flask containing 50 mg (0.13 mmole) of 1'-formylbiferrocene in dry benzene was added 0.60 mmole of methyllithium in ethyl ether. The addition was made under nitrogen and with stirring. The reaction mixture was stirred at room temperature for 2 h, after which time it was hydrolyzed with several ml of dilute hydrochloric acid. After extraction with ethyl ether and removal of the solvent, the residue was taken up in benzene and chromatographed on alumina. The first band was eluted with heptane to afford 35 mg of a yellow solid. This material was further purified by preparative thin-layer chromatography on silica gel and subsequent recrystallization from methanol/water to give 25 mg (48%) of yellow crystals of 1'-(1-hydroxyethyl)biferrocene (IV), m.p. 90–91°. (Found: C, 63.60; H, 5.56. $C_{22}H_{22}Fe_2O$ calcd.: C, 63.82; H, 5.36%.)

The NMR spectrum (CS_2) of (IV) exhibited multiplets at τ 5.73 and 5.88 [connected-ring protons H(2)–H(5) and H(2'')–H(5'') and methine proton]; a singlet at τ 6.12 [unsubstituted cyclopentadienyl ring protons and H(2')–H(5')], a doublet (J 6 Hz) at τ 8.82 (methyl protons) and a broad singlet at τ 7.69 (hydroxyl proton).

A second band, eluted with heptane/benzene (1/1), proved to be a mixture of at least three different compounds, as indicated by TLC. Due to the small amount available, this mixture was not investigated further.

Lithium aluminum hydride reduction of 1'-acetylbiferrocene

1'-Acetylbiferrocene (25 mg, 0.06 mmole) in 5 ml of dry ethyl ether was added to 19 mg (5.0 mmoles) of lithium aluminum hydride in 10 ml of the same solvent. The reaction mixture was stirred at room temperature for 2 h, after which it was poured into 20 ml of ice water. The ether layer was separated from the aqueous layer, and the latter was extracted repeatedly with ethyl ether. The ether solutions were combined, washed twice with satd. sodium bicarbonate solution, and dried over sodium sulfate. Evaporation of the solvent afforded 20 mg (81%) of a yellow solid, which on recrystallization from methanol/water gave yellow crystals of 1'-(1-hydroxyethyl)biferrocene (IV). The NMR spectrum of the product was identical to the spectrum of (IV) prepared from (II) and methyllithium.

3-(1'-*Biferrocenyl)acrylic acid* (*V*)

A mixture of 1'-formylbiferrocene (100 mg, 0.25 mmole), malonic acid (25 mg, 0.25 mmole), 0.20 ml of piperidine and 6 ml of pyridine was heated under nitrogen in a 25-ml flask on a bath of boiling water for 2 h. The reaction mixture was then cooled in an ice bath and diluted with 5 ml of water, whereupon a precipitate formed. The hydrolysate was extracted with chloroform until the extracts were colorless. The combined extracts were washed with dilute hydrochloric acid (4 times), water (3 times), and then extracted with 2 *N* sodium hydroxide solution. Addition of the first drop of sodium hydroxide produced a yellow precipitate, which was collected together with the sodium hydroxide extract. Acidification turned the yellow precipitate into a brickred solid. The latter was taken up in chloroform, and the solvent was evaporated to leave 91 mg of red residue. Recrystallization of the product from benzene produced 72 mg (65%) of a red solid, characterized as 3-(1'-biferrocenyl)acrylic acid (V), dec. >190°. (Found: C, 62.70; H, 4.70. $C_{23}H_{20}Fe_2O_2$ calcd.: C, 62.77; H, 4.58%.) Acid (V) was found to be insoluble in virtually all organic solvents, and an NMR spectrum could not be obtained.

1',1'''-*Dimethylbiferrocene* (*VI*)

To a mixture containing 38 mg (1.0 mmole) of lithium aluminum hydride and 133 mg (1.0 mmole) of aluminum chloride in 25 ml of dry ethyl ether was added 50 mg (0.12 mmole) of 1',1'''-diformylbiferrocene in the same solvent. The mixture was allowed to stir for 10 min, then poured into 30 ml of ice water and extracted with 10 ml portions of ethyl ether until the extracts were colorless. The combined extracts were washed, dried, the ether removed, and the residue was dissolved in hexane and chromatographed on alumina. A yellow band was eluted with hexane and afforded 46 mg of the orange product. Recrystallization of the solid from methanol/water gave 30 mg (64%) of red crystals, m.p. 151–152°, identified as 1',1'''-dimethylbiferrocene (VI). (Found: C, 66.75; H, 5.92; Fe, 27.52. $C_{22}H_{25}Fe_2$ calcd.: C, 66.39; H, 5.57; Fe, 28.07%.)

The NMR spectrum ($CDCl_3$) of (VI) exhibited a multiplet centered at τ 5.72 [connected-ring protons H(2)–H(5) and H(2'')–H(5'')], a singlet at τ 6.12 [H(2')–H(5') and H(2''')–H(5''')] and a singlet at τ 8.25 (methyl protons). The integrated area intensities were 8/8/6, respectively.

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