134. *Ferrocene Derivatives. Part VII.*[1] *Some Sulphur Derivatives.*

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Ferrocenesulphonic acid has been obtained by an improved method and converted *via* the sulphonyl chloride into ferrocenethiol. The latter has been characterised as its *S*-methyl and *S*-allyl ether, as its *S*-carboxymethyl and *S*-acetyl derivative, and as the corresponding disulphide.

AFTER the demonstration by Woodward *et al.*[2] that ferrocene can undergo Friedel–Crafts acylation, numerous studies have amply demonstrated that it behaves as a typical aromatic system towards electrophilic substitution in general. On the one hand, its reactivity has been shown to be comparable with that of highly activated benzene derivatives.[1, 3, 4] On the other, its reactions are limited by the ease of oxidation of ferrocene to the ferricinium ion, preventing, *e.g.*, direct halogenation or nitration. However, the investigation of directive influences within the five-membered ring still awaits the preparation of suitably substituted ferrocenes, and the present study is intended as a contribution in this direction. Hitherto only the alkylferrocenes have received attention from this point of view. Rosenblum [5] showed that a single ethyl group exerts insufficient activating influence to direct exclusively or even predominantly into the same ring (cf. also Nesmeyanov and Vol'kenau [6]). Recently Rinehart and his collaborators [7] have further shown that 1 : 1'-dimethylferrocene is substituted to roughly equal degree in the 2- and the 3-position in Friedel–Crafts acetylation. The preference for the latter position in the case of 1 : 1'-di*iso*propylferrocene is therefore probably attributable largely to steric hindrance of attack at the 2-position.[7]

If any significant difference in reactivity exists between these positions it should be

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[1] Part VI, *J.*, 1958, 656.

[2] Woodward, Rosenblum, and Whiting, *J. Amer. Chem. Soc.*, 1952, **74**, 3458.

[3] Part V, *J.*, 1958, 650.

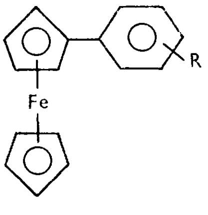
[4] Graham, Lindsey, Parshall, Peterson, and Whitman, *J. Amer. Chem. Soc.*, 1957, **79**, 3416.

[5] Rosenblum, Thesis, Harvard, 1953.

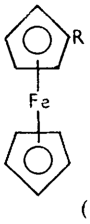
[6] Nesmeyanov and Vol'kenau, *Doklady Akad. Nauk S.S.S.R.*, 1956, **111**, 605.

[7] Rinehart, Motz, and Moon, *J. Amer. Chem. Soc.*, 1957, **79**, 2748.

more apparent when substituents more strongly activating than alkyl are employed. At the beginning of our work aminoferrocene[8,9] was the only known derivative of this type. Unfortunately it appears unsuitable for the study of further substitution owing to its low stability. This is probably due largely to the ease of oxidation and it appears likely that all electron-donating substituents will be found to facilitate oxidation of the ferrocene nucleus. A study of the factors influencing such oxidation is in progress. The results already obtained[10] on a group of substituted phenylferrocenes (I) show that groups which activate the benzene ring increase the ease of oxidation.



(I)



(II)

Methods employed for the introduction of oxygen atoms into benzene nuclei have not hitherto proved applicable to the preparation of hydroxyferrocene. We therefore turned our attention to its sulphur analogue, ferrocenethiol (II; R = SH) which appeared more accessible and also likely to prove more stable than its oxygen analogue. Its preparation has been achieved in three steps from ferrocene, *viz.*, sulphonation, conversion of the resultant monosulphonic acid (II; R = SO_3H) into the sulphonyl chloride, and reduction with lithium aluminium hydride.

Sulphonation of ferrocene was first described by Weinmayr,[11] who showed that concomitant oxidation of ferrocene by sulphuric acid can be minimised by employing acetic anhydride as solvent. The main product was the disulphonic acid, but ferrocenemonosulphonic acid could be isolated (as its ammonium salt) when a substantial excess of ferrocene was employed. Nesmeyanov *et al.*[12] reported the use of the pyridine–sulphur trioxide complex for the preparation of the disulphonic acid and more recently also of the monosulphonic acid;[6] no details of their method are available. We found chlorosulphonic (chlorosulphuric) acid in acetic anhydride to be an efficient reagent for preparation of the monosulphonic acid. We isolated the free acid as its stable, crystalline, ether-soluble dihydrate and characterised it as ammonium salt and methyl ester. The disulphonic acid is formed by the same method when two molecular equivalents of chlorosulphonic acid are employed and has been converted into its (previously unknown) dimethyl ester.

Treatment of the monosulphonic acid with phosphorus pentachloride or thionyl chloride causes extensive oxidative decomposition, but phosphorus trichloride affords the sulphonyl chloride. This is reduced to ferrocenethiol in almost quantitative yield by lithium aluminium hydride in ether. The thiol is low-melting and orange-yellow, but has not been obtained completely pure owing to the extreme ease with which it is oxidised to the disulphide. The latter is readily obtained by passing air through an alkaline solution of the crude reduction product. The reverse process could not be effected with aqueous alkaline glucose or arsenious oxide solutions, but has been brought about by reduction again with lithium aluminium hydride. The thiol thus regenerated has been characterised as its crystalline *S*-allyl and *S*-acetyl derivative. Samples obtained directly from the sulphonyl chloride have also been converted into the liquid methylthio-compound (II; R = Me) and to (ferrocenylthio)acetic acid (II; R = $S{\cdot}CH_2{\cdot}CO_2H$).

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[8] Nesmeyanov, Perevalova, Golovnya, and Shilovtseva, *Doklady Akad. Nauk S.S.S.R.*, 1955, **102**, 535.

[9] Arimoto and Haven, *J. Amer. Chem. Soc.*, 1955, **77**, 6295.

[10] Broadhead, Thesis, Sheffield, 1956.

[11] Weinmayr, *J. Amer. Chem. Soc.*, 1955, **77**, 3009.

[12] (*a*) Nesmeyanov, Abs. XIVth Internat. Congr. Pure Appl. Chem., Zürich, 1955, p. 193; (*b*) Nesmeyanov and Vol'kenau, *Doklady Akad. Nauk S.S.S.R.*, 1956, **107**, 262.

The disulphide was also isolated (but in variable and generally low yield) on catalytic reduction of the sulphonyl chloride: we did not succeed in isolating the expected sulphinic acid from this reaction. We also failed to obtain diferrocenyl sulphone from an attempted Friedel–Crafts reaction between ferrocenesulphonyl chloride and ferrocene: the only identifiable product, isolated in low yield, was again the disulphide, presumably implying reduction of the sulphonyl chloride to the thiol by ferrocene in presence of aluminium chloride.

The sulphonyl chloride reacts smoothly with ammonia, to yield ferrocenesulphonamide.

Positions of the strongest infrared maxima (*cm.*$^{-1}$) *below* 2000 *cm.*$^{-1}$.

(All our measurements refer to KBr discs; those from the literature refer to solutions.)

Compound	Positions of maxima in wave numbers (cm.$^{-1}$).													
$C_{10}H_9Fe{\cdot}SO_3^-$ Fe^{++} salt	1656	—	—	1190 [c]	—	1112 [d]	1065	1031	1021	1010 [d]	843	822	—	—
NH_4^+ salt	1641	—	1413 [b]	1180 [c]	—	1112 [d]	1055	1030	1020	1006 [d]	823	819	—	—
p-$C_6H_4Me{\cdot}SO_3^-NH_4^+$ ...	1484	1448	1420	1190 [c]	1138	—	1044	1018	—	—	819	—	687	—
$C_{10}H_9Fe{\cdot}SO_3Me$	—	—	1360	1209	1159	1112 [d]	1039	1025	—	1006 [e]	988	844	831	771
1 : 1′-$C_{10}H_8Fe(SO_3Me)_2$	—	1465	1367	1211	1158	—	1042	1030	—	—	988	878	838	773
p-$C_6H_4Me{\cdot}SO_3Me$ [13]	—	—	1375	1185	1100	—	—	—	—	—	—	—	—	—
$C_{10}H_9Fe{\cdot}SO_2Cl$	—	—	1377	1210	1149	1116 [d]	1036	1020	—	1008 [d]	836	823	—	—
$Ph{\cdot}SO_2Cl$ [a, 13]	—	—	1390	1185	1120	—	—	—	—	—	—	—	—	—
$(C_{10}H_9FeS{\cdot})_2$	—	—	1411 [d]	1171	—	1111	1054 [d]	1030	—	1005	890	834	821	807
Ph_2S_2 [13]	—	—	—	1201	—	—	*ca.* 1070 [f]	—	—	—	—	—	—	—

[a] Bellamy [14] gives 1366 and 1166 for *p*-$C_6H_4Me{\cdot}SO_2Cl$. [b] Due to NH_4^+ (cf., *e.g.*, ref. 14). [c] Broad band; exact location doubtful owing to lack of resolution. [d] Weaker than the other maxima listed. [e] Shoulder. [f] Approx., as judged from published curve.

The infrared spectra of some of the products are collected in the Table and compared with those of corresponding benzene derivatives.[13, 14] The bands which have been considered as characteristic of the functional groups show good agreement in the two series. In addition, the ferrocene derivatives which bear a single substituent all possess the bands near 1005 and 1110 cm.$^{-1}$ which have previously been found to be associated with the presence of an unsubstituted *cyclo*pentadiene ring in ferrocene derivatives.[5, 15]

EXPERIMENTAL

M. p.s were determined in evacuated capillaries. Ligroin refers to the solvent of b. p. 60—80°. Alumina was Spence's grade H which had been exposed to air for 6 hr.

Ferrocenesulphonic Acid.—Ferrocene (8 g., 0·043 mole) was dissolved in acetic anhydride (60 ml.) at 23° and technical chlorosulphonic (chlorosulphuric) acid (5 g., 0·043 mole) added from a capillary tube to the rapidly stirred solution during 10 min. The solution immediately darkened, hydrogen chloride was evolved, and the temperature rose to 27°. After 24 hr. at room temperature, the solution was filtered (Caution; explosion) into cold water (75 ml.) and the mixture, which had reached 87°, cooled by addition of further ice-water (25 ml.). The precipitated ferrocene (1·1 g., 14%) was filtered off and the filtrate evaporated to dryness. The residue was extracted with ether, yielding *ferrocenesulphonic acid dihydrate* (7·37 g.; 66% based on unrecovered ferrocene), m. p. 88—92°, as brown prisms. Recrystallisation from benzene afforded yellow plates, m. p. 103—104° [Found: C, 39·8; H, 4·6; H_2O (by Karl Fischer titration), 12·7, 11·7, 11·8, 11·3%; equiv. wt., 296. $C_{10}H_{10}O_3SFe,2H_2O$ requires C, 39·7; H, 4·6; H_2O, 11·9%; equiv. wt., 302]. The ether-insoluble residue was extracted with absolute methanol, yielding a brown solid (2·5 g.; 30%) for which analysis suggested the constitution $(C_{10}H_9FeSO_3^-)_2Fe^{++},4H_2O$. It thus resembles the product isolated by Weinmayr [11] on disulphonation of ferrocene. This *product* crystallised from methanol or glacial acetic acid as a khaki powder [Found: C, 36·75, 36·3, 36·4; H, 4·3, 4·3, 4·2; H_2O (by Karl Fischer titration), 10·3, 11·0. $C_{20}H_{18}O_6S_2Fe_3,4H_2O$ requires C, 36·5; H, 4·0; H_2O, 10·9%]. Addition of concentrated ammonia solution to its methanol solution gave a brown precipitate (presumably a mixture of ferrous and ferric hydroxide) and, on evaporation of the filtrate, the ammonium salt of ferrocenesulphonic acid crystallised as yellow plates. After being dried in a vacuum desiccator ($CaCl_2$) for 24 hr. this was a monohydrate (Found: C, 39·5; H, 5·2. Calc. for $C_{10}H_{15}O_4NSFe$: C, 39·7; H, 5·0%).

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[13] Schreiber, *Analyt. Chem.*, 1949, **21**, 1168.
[14] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen & Co., Ltd., London, 1954.
[15] Part I, *J. Amer. Chem. Soc.*, 1954, **76**, 2187.

Methyl Ferrocenesulphonate.—Ethereal diazomethane [from *N*-nitrosomethylurea (1 g.)] was added to a solution of the sulphonic acid (0·1 g.) in ether (10 ml.). After the evolution of nitrogen had ceased, the solvent was evaporated, leaving *methyl ferrocenesulphonate* as an orange oil (90 mg., 95%) which crystallised from ligroin as yellow rods, m. p. 54—55° (Found: C, 47·3; H, 4·4. $C_{11}H_{12}O_3SFe$ requires C, 47·2; H, 4·3%).

Disulphonation.—Chlorosulphonic acid (5·8 g., 0·05 mole) was added dropwise in 3 min. to a rapidly stirred solution of ferrocene (4·6 g., 0·025 mole) in acetic anhydride (75 ml.), causing the temperature to rise from 25° to 40°. After the mixture had been stirred for 16 hr. and set aside for a further 6 hr. the precipitated ferrocenedisulphonic acid was filtered off and washed with acetic anhydride (15 ml.). It was converted into the diammonium salt (5·0 g., 52·6%) by dissolution in concentrated aqueous ammonia, evaporation to dryness, and crystallisation from ethanol–benzene. The acetic anhydride mother-liquors, worked up as described above, yielded the monosulphonic acid (0·8 g., 10·6%) and its ferrous salt (1·75 g., 32%).

The free disulphonic acid is extremely hygroscopic and rapidly becomes blue on exposure to air; but it has been stored under anhydrous ether for several months without decomposition. *Dimethyl ferrocene*-1 : 1′-*disulphonate* was prepared like the above monosulphonic ester, from an ether suspension of the disulphonic acid and excess of diazomethane. It crystallised from ether as golden-yellow plates, m. p. 142—143° (Found: C, 38·1; H, 4·1. $C_{12}H_{14}O_6S_2Fe$ requires C, 38·4; H, 4·0%).

Ferrocenesulphonyl chloride.—Crude ferrocenesulphonic acid (62 g., 0·2 mole) was added in portions to phosphorus trichloride (210 ml., 2·4 moles), preheated to 50°, at such a rate as to maintain gentle refluxing. The mixture was then heated on a water-bath until evolution of hydrogen chloride ceased (approx. 6 hr.), diluted with boiling ligroin (50 ml.), and filtered. The orange filtrate was evaporated under reduced pressure and the residual solid (50 g.) crystallised from ligroin, giving *ferrocenesulphonyl chloride* (48·1 g., 82%) as crimson needles, m. p. 100°, which darkened rapidly in moist air (Found: C, 42·6; H, 3·4. $C_{10}H_9O_2SClFe$ requires C, 42·2; H, 3·2%).

Ferrocenethiol and Diferrocenyl Disulphide.—To a stirred solution of lithium aluminium hydride (3·8 g., 0·1 mole) in ether (150 ml.) under nitrogen, the sulphonyl chloride (7·11 g., 0·025 mole) in the same solvent (100 ml.) was added during 35 min. After 18 hours' refluxing, ethyl acetate (5 ml.) was added dropwise, followed by wet ether (50 ml.) and then 3·5N-sulphuric acid (300 ml.). The ether layer was separated, dried, and evaporated, yielding ferrocenethiol as a foul-smelling oil, b. p. 110°/0·005 mm., which at −70° formed orange crystals.

A stream of air was passed for 18 hr. through a solution of the crude thiol in ethanol (100 ml.), water (250 ml.), and ammonia (100 ml.; *d* 0·88). During this period *diferrocenyl disulphide* (5·21 g., 96%) was precipitated as a pale yellow powder, m. p. 188°. Chromatography on alumina and crystallisation from benzene afforded golden-yellow plates, m. p. 192° (Found: C, 55·1; H, 4·0. $C_{20}H_{18}S_2Fe_2$ requires C, 55·35; H, 4·2%). In only one of several such experiments chromatography yielded a small by-product of unknown structure. This crystallised from ligroin as yellow plates, m. p. 54° (Found: C, 57·2; H, 5·6%).

The disulphide was reduced back to the thiol by lithium aluminium hydride, by the method described above except that the reflux period was 1·5 hr. and tetrahydrofuran was used to dissolve the disulphide.

Catalytic Hydrogenation of the Sulphonyl Chloride.—This was attempted with 10% palladium–charcoal and ether. Both the rate of hydrogen uptake and the yields of products were very variable. The only products isolated after extraction with water and chromatography of the residue from evaporation of the ether layer were the sulphonic acid from the aqueous extract and the disulphide from the chromatogram.

Ferrocenyl Thiolacetate (II; R = S·COMe).—To crude ferrocenethiol, prepared from the disulphide (1·08 g., 0·0025 mole), acetyl chloride (7 ml., 0·1 mole) was added and the mixture heated on a water-bath for 1 hr., then kept overnight. Water (100 ml.) was added, the mixture extracted with ether, and the ether layer washed with sodium hydrogen carbonate solution and with water, and dried (Na_2SO_4). Removal of the ether left a brown oil (0·7 g.) which yielded yellow needles of *ferrocenyl thiolacetate*, m. p. 56—57° (from ligroin at −78°) (Found: C, 55·6; H, 4·7. $C_{12}H_{12}OSFe$ requires C, 55·4; H, 4·65%). Diferrocenyl disulphide (0·35 g., 32% recovery) was obtained by chloroform-extraction of the aqueous suspension remaining after the above ether extraction.

Methylthioferrocene.—To crude thiol, prepared from the sulphonyl chloride (7·11 g.), sodium hydroxide (4 g., 0·1 mole) in deaerated water (50 ml.) was added. Cooling of the resultant solution caused the separation of the sodium salt of the thiol as yellow crystals. Freshly distilled dimethyl sulphate (3·15 g., 0·025 mole) was added in three portions, in an atmosphere of nitrogen, stoppered, and shaken for 15 min. after each addition. The mixture was finally warmed to 60° for a further 15 min., cooled, and extracted with chloroform (4 × 50 ml.). On being washed with water, dried, and evaporated, the extract afforded a red oil (5·9 g.) which was chromatographed in ligroin on alumina. The main band yielded the *sulphide* (5·17 g., 89%) followed by some of the disulphide (0·45 g., 8%) which was eluted with benzene. Methylthioferrocene was obtained as an unpleasant-smelling orange-red liquid, b. p. 97·5—98°/0·1 mm., n_D^{25} 1·6488 (Found: C, 56·9; H, 5·2. $C_{11}H_{12}SFe$ requires C, 56·9; H, 5·2%). No methylation took place when a solution of the thiol in ether was treated with excess of diazomethane: only the disulphide was recovered on chromatography of the product.

Allylthioferrocene.—The thiol, prepared from the disulphide (1·085 g., 0·0025 mole), was converted into its sodium salt by sodium hydroxide (0·2 g., 0·005 mole) in water (5 ml.). A solution of allyl bromide (1·2 g.; 0·01 mole) in acetone (50 ml.) was added, causing immediate dissolution of the sodium salt. The mixture was then refluxed for 5·5 hr., the solvent removed under reduced pressure, and the orange residue dissolved in chloroform. The dried chloroform solution was evaporated *in vacuo* and the residue chromatographed in ligroin on alumina. Ligroin eluted the *allylthio-derivative* (0·4 g., 65% based on unrecovered disulphide) which crystallised, on cooling of the concentrated ligroin solution to −70°, as yellow rods, m. p. 32° (Found: C, 60·25; H, 5·7. $C_{13}H_{14}SFe$ requires C, 60·5; H, 5·5%). Benzene eluted unchanged disulphide (0·56 g., 52%) from the chromatogram.

(*Ferrocenylthio*)*acetic acid.*—The crude thiol [from the sulphonyl chloride (2·6 g.; 0·009 mole)] was mixed with potassium hydroxide (0·28 g.), anhydrous potassium carbonate (2·8 g.), chloroacetic acid (0·86 g., 0·009 mole), and acetone (50 ml.). The mixture was refluxed for 3 hr., left overnight, and then evaporated and the residue dissolved in warm (60°) aqueous potassium hydroxide (5 g. in 50 ml.). The solution was aerated for 18 hr., the precipitated disulphide (0·93 g., 47%) filtered off, and the filtrate acidified with dilute hydrochloric acid and extracted with ether (4 × 30 ml.). The extracts were dried (Na_2SO_4) and evaporated under reduced pressure, and the residue crystallised from ligroin containing a little benzene. (*Ferrocenylthio*)*acetic acid* (1·06 g., 42%) formed orange-yellow rods, m. p. 110·5°, and was slightly hygroscopic (Found: C, 52·0; H, 4·4. $C_{12}H_{12}O_2SFe$ requires C, 52·2; H, 4·4%).

Ferrocenesulphonamide.—A solution of ferrocenesulphonyl chloride (1·42 g., 0·005 mole) and ammonia (20 ml.; *d* 0·88) in acetone (20 ml.) was heated on a steam-bath for 1 hr. Most of the solvent was removed by distillation, and water (20 ml.) added. The precipitate was filtered off, washed with water (20 ml.), and recrystallised from ethanol, yielding yellow-brown prisms of *ferrocenesulphonamide* (1 g., 75%), m. p. 175° (Found: C, 45·0; H, 4·5. $C_{10}H_{11}O_2NSFe$ requires C, 45·3; H, 4·2%).

Attempted Friedel–Crafts Reaction between Ferrocene and Ferrocenesulphonyl Chloride.—To a stirred mixture of the sulphonyl chloride (1·74 g., 0·006 mole) and ferrocene (0·57 g., 0·003 mole) in dry, alcohol-free chloroform (75 ml.) under nitrogen at 0°, anhydrous aluminium chloride (1·63 g., 0·024 mole) was added. The mixture was stirred for 16 hr. during which the temperature was allowed to rise gradually (to 23°). Ice (100 g.), concentrated hydrochloric acid (3 ml.), and a little titanous chloride solution were then added. The organic layer was separated, washed, and dried and the chloroform removed *in vacuo*. The residual orange solid (0·675 g.) was chromatographed on alumina (50 g.) with ligroin as solvent. Unchanged ferrocene (0·43 g., 76%) was followed by a band, which on elution with benzene afforded diferrocenyl disulphide (115 mg.), identified by m. p., mixed m. p., and infrared spectrum (Found: C, 55·3; H, 4·3%). A minute amount of a third, unidentified substance was eluted from the column in one of two such experiments and, crystallised from ligroin, had m. p. 65° (Found: C, 48·1; H, 5·4%).

The authors thank Dr. M. Hunt, of E.I. du Pont de Nemours & Co., for generous gifts of ferrocene, and the Department of Scientific and Industrial Research for a maintenance grant (to G. R. K.).

THE UNIVERSITY, SHEFFIELD, 10. [*Received, October 11th*, 1957.]