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UNSYMMETRICALLY DISUBSTITUTED FERROCENES

XIV*. HOMOANNULAR AND BIFERROCENE DERIVATIVES FROM [(DIMETHYLAMINO)ETHYL] FERROCENE

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Summary

1-Lithio-2-[(dimethylamino)ethyl]ferrocene was treated with tri-n-butyl borate to give the boronic acid and this was converted to the corresponding chloro, bromo and iodo derivatives. A mixture of the *meso* and racemic binuclear diamines was obtained from the same lithioamine with anhydrous cobalt chloride, whilst with paraformaldehyde the hydroxyamine was formed. Oxidation of [(dimethylamino)ethyl]ferrocene gave only vinylferrocene and not the expected ferrocenecarbaldehyde.

Introduction

N-(ferrocenylmethyl)-*N*,*N*,*N*-trimethylammonium iodide underwent a modified Stevens rearrangement to give [(dimethylamino)ethyl]ferrocene (I) [2]. Slocum and his co-workers have recently reported [3] the lithiation of this amine (I) to give a cyclic lithio compound (II), which was treated with benzophenone, benzonitrile, phenyl isocyanate, phenyl isothiocyanate, hexachloroethane and mercury(II) chloride to give the corresponding derivatives (III).

We also investigated independently the reactions of the lithioamine (II) and we have confirmed the results obtained by the present authors and extended the synthetic scope of this reagent to the preparation of the boronic acid (IIIa), the bromo (IIIc), iodo (IIIe) and hydroxymethyl (IIIf) compounds and the biferrocenes (V) and (VI).

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* For Part XIII see ref. 1.

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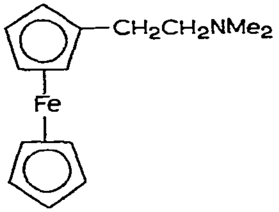
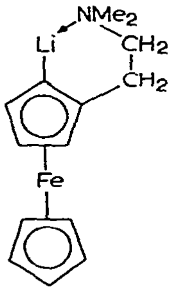


(I)



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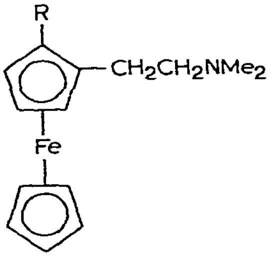
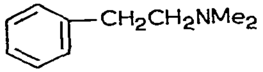


(IIIa) $R = B(OH)_2$;
(IIIb) $R = Cl$;
(IIIc) $R = Br$;
(IIId) $R = HgCl$;
(IIIe) $R = I$
(IIIf) $R = CH_2OH$



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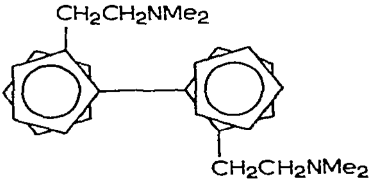

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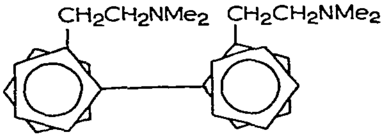

(VI)

Results and discussion

2-[(Dimethylamino)methyl]ferroceneboronic acid [4] has provided a useful route to the 2-halogeno derivatives of the parent amine and we have found that the corresponding boronic acid is a suitable intermediate in the preparation of the analogous compounds of amine (I). In a previous investigation [3] the chloroamine was obtained by treatment of the lithioamine (II) with hexachloroethane, but it was observed that a complete separation of the chloroamine and the unsubstituted amine was very difficult. When the boronic acid

(IIIa) was stirred with copper chloride the chloro derivative (IIIb) was formed in 69% yield, uncontaminated by the parent amine [3]. The same method gave the bromoamine (IIIc) in 58% yield.

Following a report of the preparation of 2-chloromercuri-1-[(dimethylamino)methyl]ferrocene [5] we prepared the analogous derivative (IIId) of [(dimethylamino)ethyl]ferrocene, and this has subsequently been described elsewhere [3]. We have converted this mercuriamine (IIId) to the iodo derivative (IIIe) by stirring it with iodine in xylene solution.

The reaction between paraformaldehyde and the lithioamine (II) gave two isomeric products. One is the hydroxyamine (IIIf) and the other also involves homoannular substitution. The alternative of lithiation in the side chain was excluded by the PMR spectrum although the spectrum did not unambiguously confirm substitution at the 3-position. Side chain lithiation in addition to *ortho*-lithiation was observed previously for *N,N*-dimethyl-β-phenylethylamine [6,7].

When the lithioamine was stirred with anhydrous cobalt chloride [8], two products were obtained and these were separated by repeated chromatography on alumina as the isomeric biferrocenes (V) and (VI). Each of these diamines formed a dimethiodide, while by contrast 2,5′-bis[(dimethylamino)methyl]-biferrocene (VII) gave a monomethiodide [9]. This must be ascribed to the inability of the amine (VII) to give a conformer in which the dimethylamino groups are separated and do not sterically impede one another. The biferrocenes (V) and (VI), with an additional methylene group between each amino group and the metallocene nucleus, suffered little hindrance to quaternization.

It has been reported [10] that the oxidation of [(dimethylamino)methyl]ferrocene by "active" manganese dioxide gave ferrocenecarbaldehyde in low yield. The oxidation of the amine (I) with manganese dioxide gave only vinylferrocene, identified by its melting point and infrared spectrum, in isolatable quantities, indicating that the elimination of dimethylamine had occurred. This unexpected result was not achieved with the analogous benzene compound which gave benzaldehyde on stirring with manganese dioxide in chloroform for four days. Elimination, rather than substitution, has been observed on the hydrolysis of 2-substituted [(dimethylamino)ethyl]ferrocenes [3]. Nesmeyanov and his co-workers [11] observed oxidative elimination to give 1,2-diferrocenylethylene when 1,2-diferrocenylethane was stirred with manganese dioxide, although some carbonyl compounds were obtained.

The hydrolysis of 2-substituted dimethylaminoethylferrocene methiodides has been described previously [3] and we found that the boronic acid (IIIa) gives vinylferrocene on heating with alkali. Displacement of a boronic acid group on hydrolysis has been reported previously [12].

Experimental

For general directions see Part I [13] of this series.

2-[(Dimethylamino)ethyl] ferroceneboronic acid (IIIa)

The lithioamine (II) was prepared as previously described [3]. A solution of the lithioamine (0.065 mol) in dry ether was cooled to − 78°. Tri-n-butyl borate (30.25 g, 0.13 mol) in ether (120 ml) was added over 45 min to the amine, and stirring was continued for 3 h. The solution was allowed to warm up to room temperature and then water (10 ml) was added. The mixture was extracted with ether and the dried ethereal layer ($MgSO_4$) was evaporated under reduced pressure. The residue was chromatographed on alumina. Ether eluted [(dimethylamino)ethyl] ferrocene (I) and 10% methanol in ether eluted the boronic acid (IIIa) (12 g, 50%). The boronic acid (IIIa) was a viscous oil which did not solidify. The PMR spectrum ($CDCl_3$) showed resonance at δ 2.28, doublet (6H, NMe_2); 2.78, multiplet (4H, CH_2CH_2N); 4.02 singlet (5H, unsubstituted cyclopentadienyl ring protons); 4.02, 4.34 ppm, multiplets (3H, substituted cyclopentadienyl ring protons). The acid (IIIa) formed a methiodide when treated with iodomethane. The product was recrystallized from acetonitrile solution by the addition of dry ether to give a yellow powder, m.p. above 250°. (Found: Fe, 12.58. $C_{15}H_{23}BFeINO_2$ calcd.: Fe, 12.61%.)

2-Chloro[(dimethylamino)ethyl] ferrocene (IIIb)

The boronic acid (IIIa) (3.0 g, 0.01 mol) was added to water (80 ml) and this mixture was added to a stirred solution of copper (II) chloride dihydrate (3.8 g, 0.02 mol) in water (60 ml). The mixture was heated to 50° for one hour. After cooling, the solution was made alkaline with sodium hydroxide and then extracted with ether. The ethereal solution was dried ($MgSO_4$) and then evaporated. The residue was chromatographed on alumina, ether—benzene mixtures eluted the chloride (IIIb) (2.05 g, 69%) as an oil which was characterized as its methiodide. The PMR spectrum of the chloroamine showed resonances at δ 2.25, singlet (6H, NMe_2); 2.46, multiplet (4H, CH_2CH_2N); 3.95, 4.28, multiplets (3H, substituted cyclopentadienyl ring protons) partly overlapping the resonance at 4.08 ppm, singlet (5H, unsubstituted cyclopentadienyl ring protons). The methiodide was recrystallized from acetonitrile—ether as yellow crystals, m.p. 235°. (Found: Fe, 12.96. $C_{15}H_{21}ClFeIN$ calcd.: Fe, 12.89%)

2-Bromo[(dimethylamino)ethyl] ferrocene (IIIc)

The boronic acid (IIIa) (3.0 g, 0.01 mol) was treated with copper(II) bromide (4.5 g, 0.04 mol) by the method described for the chloroamine (IIIb). Chromatography yielded the bromoamine (IIIc) as an oil (1.95 g, 58%) which was characterized as the methiodide and picrate. The PMR spectrum of the bromoamine showed resonances at δ 2.24, doublet (6H, NMe_2); 2.45, multiplet (4H, CH_2CH_2N); 4.02, 4.09, multiplets (3H, substituted cyclopentadienyl ring protons); 4.07 ppm, singlet (5H unsubstituted cyclopentadienyl ring protons).

The methiodide was recrystallized from acetonitrile—ether and formed a yellow microcrystalline material, m.p. above 250°. (Found: Fe, 11.36; N, 2.94. $C_{15}H_{21}BrFeIN$ calcd.: Fe, 11.69; N, 2.93%.) The picrate formed orange crystals from methanol, m.p. 152 - 153°. (Found: C, 42.76; H, 3.76; N, 9.90. $C_{20}H_{21}BrFeN_4O_7$ calcd.: C, 42.50; H, 3.75; N, 9.92%.)

2-[(Dimethylamino)ethyl] ferrocenemethanol (IIIf)

A solution of paraformaldehyde (0.73 g, 0.024 mol) in dry ether was added over 0.5 h to a stirred solution of the lithioamine (II) (0.02 mol). The mixture was stirred for a further 2.5 h, water was added and the solution was extracted with ether. The dried ethereal solution was evaporated and the residue was chromatographed on alumina. Benzene eluted the alcohol (IIIf) (2.83 g, 49%) as an oil which was characterized as its methiodide. Small orange crystals of the methiodide were obtained from acetonitrile, m.p. above 300°. (Found: C, 45.04; H, 5.64; N, 3.50. $C_{15}H_{24}FeINO$ calcd.: C, 44.78; H, 5.62; N, 3.26%.) Ether eluted an oil (0.78 g, 13%) which was converted to a methiodide. The methiodide was crystallized from acetonitrile as dark yellow crystals, m.p. 225 - 257°. (Found: C, 44.85; H, 5.65; N, 3.42; $C_{15}H_{24}FeINO$ calcd.: C, 44.78; H, 5.62; N, 3.26%.)

2-Iodo[(dimethylamino)ethyl]ferrocene (IIIe)

The chloromercuriamine (IId) was prepared by the reported method [3]. 2-Chloromercuri[(dimethylamino)ethyl]ferrocene (5 g, 0.01 mol) was stirred with iodine (10 g) in xylene solution (100 ml) for 3 h. The reaction mixture was extracted with thiosulphate solution, dried ($MgSO_4$) and evaporated under reduced pressure. Benzene eluted the iodide (IIIe) (1.6 g, 41%) as an oil which was characterized as its red crystalline picrate, m.p. 129 - 131°. (Found: C, 39.45; H, 3.61; N, 9.06. $C_{20}H_{19}FeIN_4O_7$ calcd.: C, 39.23; H, 3.46; N, 9.15%.)

2,2''- and 2,5''-bis[(dimethylamino)ethyl]biferrocene (V) and (VI)

The lithioamine (II) (0.04 mol) in dry ether was stirred at — 78° while anhydrous cobalt(II) chloride (30 g) was added slowly. The mixture was stirred for 2 h and then allowed to warm to room temperature. The dark mixture was made basic with sodium hydrogen carbonate solution and extracted with an ether—benzene mixture. The dried solution ($MgSO_4$) was evaporated and chromatographed. Benzene—ether eluted the 2,5''-biferrocene (VI) which formed brown crystals from petrol, m.p. 87 - 88°. (Found: C, 65.91; H, 7.05; N, 5.61. $C_{28}H_{36}Fe_2N_2$ calcd.: C, 65.63; H, 7.08; N, 5.47%.) The PMR spectrum showed resonances at δ 2.38, singlet (12H, NMe_2); 2.77, multiplet (8H, CH_2CH_2N); 4.14, 4.38, multiplets (6H, substituted cyclopentadienyl ring protons); 3.99 ppm, singlet (10H, unsubstituted cyclopentadienyl ring protons). The amine (VI) formed a yellow dimethiodide which had m.p. above 250° on crystallization from acetonitrile—ether. (Found: C, 44.09; H, 5.18; N, 3.67; I, 31.85. $C_{30}H_{42}Fe_2I_2N_2$ calcd.: C, 45.26; H, 5.32; N, 3.86; I, 31.85%.)

Methanol—ether mixtures eluted the 2,2''-biferrocene (V) as an oil which crystallized with difficulty. It was characterized as the yellow dimethiodide, m.p. 215° (dec.). (Found: C, 45.28; H, 5.41; N, 3.66; I, 31.85%.)

Oxidation of [(dimethylamino)ethyl]ferrocene with manganese dioxide

A solution of [(dimethylamino)ethyl]ferrocene (4 g) in chloroform (150 ml) was stirred with "active" manganese dioxide (20 g) for a week. The mixture was filtered and the filtrate was evaporated to dryness. The residue was chromatographed on alumina. Benzene eluted vinylferrocene (0.25 g, 20%) and ether—benzene mixtures eluted unchanged amine (I). The vinylferrocene was identified by its melting point and infrared spectrum.

Oxidation of N,N-dimethyl-β-phenylethylamine with manganese dioxide

The *N,N*-dimethyl-β-phenylethylamine (5 g) was dissolved in chloroform

(100 ml) and stirred with "active" manganese dioxide (20 g) for four days. The solvent was evaporated off under reduced pressure and the residue treated with 2,4-dinitrophenylhydrazine. The hydrazone (0.2 g, 7%) was crystallized from ethanol and identified as the 2,4-dinitrophenylhydrazone of benzaldehyde, m.p. 235° (lit. [14] 237°).

Hydrolysis of the methiodide of the boronic acid (IIIa)

The methiodide of the boronic acid (IIIa) (0.5 g, 0.001 mol) and 1*M* sodium hydroxide solution (50 ml) were heated under reflux for 24 h. The reaction product was treated with ether, and the dry ethereal product was chromatographed. It was found to be identical with the vinylferrocene obtained from the oxidation of the amine (I).

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