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# UNSYMMETRICALLY DISUBSTITUTED FERROCENES
# II*. THE ADDITION OF *o*- AND *p*-QUINONES TO [(DIMETHYLAMINO)METHYL]FERROCENE THROUGH LITHIATION

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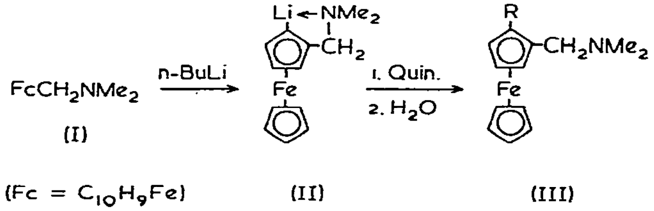
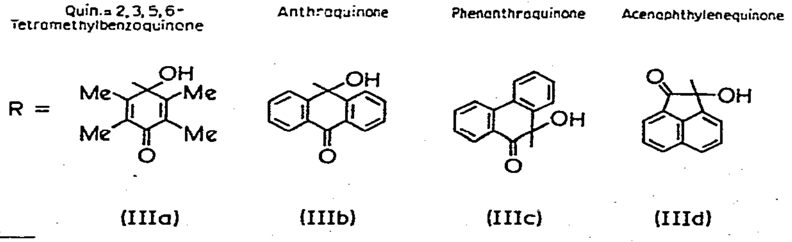
We have observed that the reactions of [(dialkylamino)methyl]ferrocenes with n-butyllithium afforded the corresponding 2-lithio-amines[1,2], thus the amine (I) gave the lithio-amine (II) and this intermediate was condensed with ketones, cyanides, and isocyanates to give the corresponding 1,2-disubstituted ferrocenes[1]. The lithio-amine (II) was also converted to 2-chloro-1-[(dimethylamino)methyl]ferrocene by reaction with hexachloroethane[3] and to other 2-haloferrocenes through 2-[(dimethylamino)methyl]ferroceneboronic acid[4].

To further demonstrate the synthetic versatility of the lithio-amine (II) we now describe its reactions with some *o*- and *p*-quinones. Thus the amine (I) was metallated with n-butyllithium and the lithio intermediate, presumably (II), was allowed to react at room temperature with 2,3,5,6-tetramethylbenzoquinone and anthraquinone to give the hydroxy-amino-ketones (IIIa,b) in yields of 42 and 64% respectively, (Scheme A). The structures proposed for these products were supported by their elemental analyses and by their infrared and PMR absorption spectra. The products were also characterised as their picrate and methiodide derivatives. Similarly,



Scheme A



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* For Part I see ref. 2.

the hydroxy-amino-ketones (IIIc,d) were prepared by reaction of the lithio-amine with phenanthraquinone and acenaphthylenequinone in yields of 21 and 10% respectively. The yields from these additions were much lower than those obtained from the reactions with *p*-quinones, or from aromatic and aliphatic ketones[1] and the reasons for these differences are not clear.

In each of the reactions examined a two-fold excess of the appropriate quinone was used and the quinone was added to the lithiated amine. Under these conditions no evidence for the addition of two molecules of the lithio-amine (II) to the quinone was obtained. The addition of Grignard reagents to quinones normally afford mixtures of the products of carbonyl addition, of 1,4-addition and of reduction[5], thus it was surprising that in each of the reactions of the lithio-amine (II) with quinones exclusively carbonyl addition was observed. This may be due in part to the tendency of lithio reagents to favour 1,2- rather than 1,4-addition[6] and in the case of 2,3,5,6-tetramethylbenzoquinone to steric hindrance at the 4-position. Also 1,4-addition to the three tricyclic quinones would require the loss of aromaticity from one of the benzenoid rings in each case and this is unusual in Grignard addition reactions.

The reactions between ferrocenyllithium and quinones have not been reported and would be expected to be more complicated than the reactions observed here. This is because ferrocene is converted in only poor yield to ferrocenyllithium (FcLi) by a small excess of n-butyllithium[7], the use of a large excess of the metallating agent leads to a mixture of mono- and di-lithiated products[8]. In each case the metallation mixture contains excess n-butyllithium which would react preferentially with the quinone. Preliminary experiments[9] have shown that the reactions between ferrocenyllithium and either phenanthraquinone or acenaphthylenequinone each afforded several products.

Each of the hydroxy-amines (IIIa-d) contained an unsubstituted cyclopentadienyl ring and, as expected[10], absorbed in the infrared near to 1100 and 1000 $cm^{-1}$. The region around 900 $cm^{-1}$ has been used to distinguish between 1,2- and 1,3-disubstitution in ferrocene[11] and from Table 1 it may be seen that the spectra of the adducts (IIIa–d) exhibited very weak absorptions near to 886 $cm^{-1}$ and in the case of the hydroxy-amine (IIIb) also at 924 $cm^{-1}$. Previously[1,2] we have observed bands near these frequencies for 1,2-disubstituted ferrocenes, although in the present case the bands were too weak and poorly resolved to be diagnostically useful. Also,

TABLE 1

INFRARED ABSORPTION FREQUENCIES ($cm^{-1}$) OF SOME 1,2-DISUBSTITUTED FERROCENES[a]

| *Compound* | *Hydroxyl* | *Carbonyl* | "1100, | 1000 *rule*" | "927, | 895 *rule*" |
|---|---|---|---|---|---|---|
| IIIa | — | 1667(m), 1626(s), [1636(s)][b] | 1104(m), | 1006(s) | — | 882(w) |
| IIIa (MeI) | 3310(s) | 1664(m), 1634(s) | 1108(m), | 1002(w) | 925(sh), | 890(sh) |
| IIIb | — | 1658(s), [1672(s)][c] | 1106(w), | 1008(s) | — | 882(w) |
| IIIb (MeI) | 3420(s) | 1654(s) | 1104(m), | 1004(sh) | 926(w) | 886(sh) |
| IIIc | — | 1682(s), [1674(s)][d] | 1104(m), | 1004 (sh) | 924(sh), | 884(sh) |
| IIId | — | 1717(m), [1715(s)][e], 1644(s) | 1105(m) | — | — | 890(sh) |

[a] s = strong, m = medium, w = weak, sh = shoulder. [b] 2,3,5,6-Tetramethylbenzoquinone. [c] Anthraquinone. [d] Phenanthraquinone. [e] Acenaphthylenequinone.

confusion might arise since the monosubstituted ferrocene (I) absorbs at 930 and weakly at 890 $cm^{-1}$. It has been reported recently[1,2] that 1-(hydroxymethyl)-2-[(dialkylamino)methyl]ferrocenes do not show the expected stretching frequencies in the infrared for intermolecularly hydrogen bonded hydroxyl groups and this was ascribed to intramolecular hydrogen bonding between the hydroxyl and tertiary amino groups[2]. The expected hydroxyl frequencies were also absent from the spectra of the hydroxy-amines (IIIa, b), (See Table 1), conversion of the amines to the corresponding methiodides removed the unshared electron pair on nitrogen and inhibited the OH...N interaction. Thus the spectra of these methiodides showed the normal hydroxyl frequencies (see Table 1). Although the hydroxy-amines (IIIc,d) did not exhibit hydroxyl bands, their absence cannot be unambiguously interpreted in terms of OH...N intramolecular hydrogen bonding since the hydroxyl group might also (and more probably) bond to the adjacent carbonyl group.

The PMR spectra of the hydroxy-amines (IIIa–c), (see *Experimental*) each showed an AB quartet centred near $\tau$ 6.7 and characteristic of methylene protons adjacent to a 2-substituted cyclopentadienyl ring[12]. The aromatic absorption patterns of the hydroxy-ketone residues of the amines (IIIb,c) were less symmetrical than the patterns of the corresponding quinones and in the case of the amine (IIIa) all four methyls in the cyclohexadienone moiety showed different chemical shifts indicating the asymmetry of this group. Surprisingly, the chemical shifts of the protons on the unsubstituted cyclopentadienyl rings of the amines (IIIb,c) were considerably lower than expected, however examination of the appropriate molecular models indicated that these compounds might adopt conformations in which the unsubstituted cyclopentadienyl rings were above the planes of the aromatic rings of the 2-substituents and thereby shielded.

## EXPERIMENTAL

For general direction see Part I[2]. M.p.'s were determined in sealed evacuated capillaries. The PMR spectra of the hydroxy-amines (IIIa,b) were recorded in deuterochloroform with hexamethyldisilane as internal standard* and the spectrum of the hydroxy-amino (IIIc) in carbon tetrachloride with tetramethylsilane as internal standard**.

### *2-Lithio-1-[(dimethylamino)methyl]ferrocene (II)*

This compound was prepared from [(dimethylamino)methyl]ferrocene (I), (2.43 g, 0.01 mole) and a 22% solution of n-butyllithium (5.2 ml, 0.0125 mole) in hexane as previously described[1].

### *Condensation of lithio-amine (II) with 2,3,5,6,-tetramethylbenzoquinone*

To a stirred solution of the lithio-amine (II) prepared as described above, was added dropwise a solution of 2,3,5,6-tetramethylbenzoquinone (3.28 g, 0.02 mole) in

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* We are indebted to Dr. S. McVey, Department of Chemistry, McMaster University, Hamilton, Ontario, for recording these spectra.

** We are indebted to Dr. E. Haws and Dr. G. R. Bedford, Imperial Chemical Industries Ltd., Pharmaceuticals Division, Alderley Park, Macclesfield, for recording this spectrum and the mass spectrum of the condensation product of the lithio-amine (II) with phenanthraquinone.

dry ether (100 ml) and stirring was continued for 1 h. Water was added cautiously and the mixture was extracted with 10% phosphoric acid. The acid extracts were neutralised by slow addition to an excess of a stirred saturated solution of sodium bicarbonate. The mixture was then extracted with ether and the dried ($MgSO_4$) extracts were distilled. The dark brown residual oil was chromatographed on alumina, elution with benzene/ether mixtures afforded the hydroxy-amino-ketone (IIIa), (1.08 g, 42% based on unrecovered starting material) which crystallised from ether/light petroleum as orange granular crystals, m.p. 171.5–174°. (Found: C, 67.55; H, 7.2; Fe, 13.5; N, 3.6. $C_{23}H_{29}FeNO_2$ calcd.: C, 67.8; H, 7.2; Fe, 13.7; N, 3.45%.) The PMR spectrum showed resonances at $\tau$ 8.40 (3 H; *C*-methyl protons), $\tau$ 8.18 (3 H; *C*-methyl protons), $\tau$ 8.02 (3 H; *C*-methyl protons), $\tau$ 7.80 (6 H; *N*-methyl protons), $\tau$ 7.58 (3 H; *C*-methyl protons), all singlets, (2,3,5,6-tetramethylbenzoquinone showed a singlet at $\tau$ 8.10), a doublet centred at $\tau$ 7.25 (1 H; *N*-methylene proton), a multiplet centred at $\tau$ 6.30 (1 H; proton in substituted ring), a singlet at $\tau$ 6.04 (5 H; protons in unsubstituted ring), a singlet at $\tau$ 6.04 ( 5 H; protons in unsubstituted ring), partially obscuring the resonances of two of the protons in the substituted ring, and a doublet centred at $\tau$ 5.96 (1 H; *N*-methylene proton).

The *methiodide* was prepared by reaction of the tertiary amine (IIIa) with excess methyl iodide in methyl cyanide and was precipitated by the addition of dry ether as a yellow-orange microcrystalline solid which did not melt below 250° but slowly darkened from 180°. (Found: C, 52.3; H, 5.9; Fe, 10.1; N, 2.4. $C_{24}H_{32}FeINO_2$ calcd.: C, 52.5; H, 5.9; Fe, 10.1; N, 2.55%.)

The *picrate* was prepared in the usual way and crystallised from ethanol as fluffy yellow needles, m.p. 123° (decomp., with sintering from 110°). (Found: C, 53.1; 53.2; H, 5.05, 5.1; Fe, 8.45; N, 8.6. $C_{29}H_{32}FeN_4O_9$ calcd.: C, 54.7; H, 5.1; Fe, 8.8; N, 8.8%.)

Elution with ether afforded the amine (I), (0.88 g).

### *Condensation of lithio-amine (II) with anthraquinone*

To a stirred solution of the lithio-amine (II) prepared as described above was added a suspension of anthraquinone (4.16 g, 0.02 mole) in dry benzene (200 ml) and stirring was continued for 1 h. The reaction mixture was worked up as described in the preceding experiment and the residue chromatographed on alumina. Ether eluted the hydroxy-amino-ketone (IIIb) (1.19 g, 64%) which crystallised from large volumes of ether as bright red granular crystals, m.p. 190–194°. (Found: C, 72.0; H, 5.5; Fe, 12.0. $C_{27}H_{25}FeNO_2$ calcd.: C, 71.85; H, 5.6; Fe, 12.4%.) The PMR spectrum showed a singlet resonance at $\tau$ 7.70 (6 H; *N*-methyl protons), a doublet centred at $\tau$ 7.32 (1 H; *N*-methylene proton), multiplets at $\tau$ 7.08, 6.34, 6.20 (each 1 H; protons in substituted ring), a singlet at $\tau$ 6.58 (5 H; protons in unsubstituted ring), a doublet centred at $\tau$ 5.83 and a broad multiplet at $\tau$ 2.86–1.66 (8 H; protons in anthraquinone residue).

The *methiodide* was prepared as described above as a yellow microcrystalline powder which did not melt below 250° but darkened slowly from 180°. (Found: C, 56.1; H, 4.35; Fe, 9.4; N, 2.8. $C_{28}H_{28}FeINO_2$ calcd.: C, 56.7; H, 4.75; Fe, 9.4; N, 2.35%.)

The *picrate* was prepared in the usual way and crystallised from ethanol as fine orange needles which did not melt below 250° but darkened slowly from 180°.

(Found: C, 58.1; H, 4.1; Fe, 8.65; N, 8.1. $C_{33}H_{28}FeN_4O_9$ calcd.: C, 58.25; H, 4.15; Fe, 8.2; N, 8.25%.)

Methanol ether then eluted the amine (I), (1.42 g).

### *Condensation of lithio-amine (II) with phenanthraquinone*

To a stirred solution of the lithio-amine (II) prepared as described above was added a solution of phenanthraquinone (4.16 g, 0.02 mole) in dry benzene (400 ml) and stirring was continued for 42 h. The reaction mixture was worked up as described above and the residue chromatographed on alumina. Benzene/light petroleum mixtures eluted the amine (I), (1.73 g) and ether then eluted the hydroxy-amino-ketone (IIIc) (0.27 g, 21%) which crystallised from light petroleum as bright orange granular crystals, m.p. 185.5–188° with darkening from 170°. (Found: C, 71.9; H, 5.7; Fe, 12.2; N, 2.95; mol. wt. by mass spectrometry, 451. $C_{27}H_{25}FeNO_2$ calcd.: C, 71.85; H, 5.6; Fe, 12.4; N, 3.1%; mol. wt., 451.) The PMR spectrum showed a singlet resonance at $\tau$ 7.64 (6 H; *N*-methyl protons), a doublet centred at $\tau$ 7.30 (1 H; *N*-methylene proton), a multiplet at $\tau$ 7.04 (1 H; proton in substituted ring), a singlet at $\tau$ 6.60 (5 H; protons in unsubstituted ring), a multiplet at $\tau$ 6.37–5.99 (protons in substituted ring) a doublet centred at *ca.* $\tau$ 5.95 and partially obscured by the ring proton resonances (1 H; *N*-methylene proton), and a multiplet at $\tau$ 2.82–1.65 (8 H; protons in phenanthraquinone residue).

### *Condensation of lithio-amine (II) with acenaphthylenequinone*

To a stirred solution of the lithio-amine (II) prepared as described above from amine (I), (4.86 g, 0.02 mole) and n-butyllithium (10.4 ml, 0.025 mole) was added a solution of acenaphthylenequinone in dry bis(2-methoxyethyl) ether (300 ml) and stirring was continued for 14 h. The reaction mixture was worked up as described above and the residue chromatographed on alumina. Benzene/light petroleum mixtures eluted the amine (I), (3.42 g), methanol/ether mixtures then eluted the hydroxy-amino-ketone (IIId), (0.24 g, 10%) which was deposited from light petroleum under nitrogen as a brown powder. It did not melt below 250° but darkened slowly from 120°. Even after repeated reprecipitation the substance failed to give a completely satisfactory elemental analysis. (Found: C, 68.6; H, 5.7; Fe, 13.35; N, 3.2. $C_{25}H_{23}FeNO_2$ calcd.: C, 70.6; H, 5.45; Fe, 13.15; N, 3.3%.)

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## SUMMARY

[(Dimethylamino)methyl]ferrocene has been metallated with n-butyllithium and the resulting monolithioamine condensed with some *o*- and *p*-quinones to afford the corresponding 1,2-disubstituted ferrocenes. The PMR and IR spectra of these products are discussed.

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