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ORGANOMETALLIC DERIVATIVES

V*. THE LITHIATION OF FERROCENYLMETHYL CYANIDE**

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SUMMARY

Ferrocenylmethyl cyanide has been dilithiated with n-butyllithium and condensation of the lithiated intermediate with benzyl chloride gave α,α-dibenzylferrocenylmethyl cyanide. The lithioferrocene was also condensed with methyl iodide, butyl bromide and 1,2-dichloroethane to give the corresponding α-disubstituted ferrocenylmethyl cyanides. The reactions of these α-disubstituted ferrocenylmethyl cyanides with n-butyllithium and lithium aluminium hydride have been investigated.

RESULTS AND DISCUSSION

Recently we reported the dilithiation of ferrocenylmethyl phenyl sulphone with n-butyllithium[1]. The condensation of this lithiated intermediate with electrophiles gave α-substituted ferrocenylmethyl phenyl sulphones. We now report the lithiation of ferrocenylmethyl cyanide (I) to give the dilithiated intermediate (II). The deep red lithioferrocene (II) was formed rapidly at room temperature by the treatment of the ferrocenyl cyanide (I) with n-butyllithium (Scheme 1). When the lithiated intermediate (II) was quenched with deuterium oxide the PMR spectrum of the deuterated ferrocene indicated that both the α-hydrogens had been removed by lithium. The ease of formation of the carbanion was consistent with the protons on the α-carbon being quite acidic. Presumably the carbanion intermediate was stabilized by charge delocalization onto the ferrocenyl group and also onto the electronegative cyanide.

Condensation of the lithioferrocene (II) with benzyl chloride gave the α,α-disubstituted ferrocenylmethane (VII) (70%) and the (ferrocenylmethyl)imine (IV) (5%). Presumably the imine (IV) was formed by condensation of the lithiated intermediate (II) with one molecule of benzyl chloride and one of ferrocenylmethyl cyanide. The lithioferrocene (II) was condensed with methyl iodide, butyl bromide and 1,2-dichloroethane to give the α,α-disubstituted ferrocenes [(III); R=Me, (III); R=Bu] and the cyclopropane [(V); R=CN] respectively.

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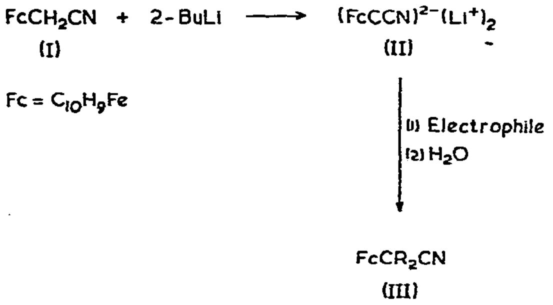
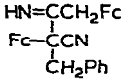
* For Part IV see ref. 1.

** Some of these results have been presented in a preliminary form[2].

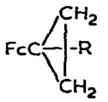


(1)

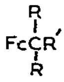


$HN{=}\overset{}{C}CH_2Fc$ / $Fc{-}\underset{CH_2Ph}{C}CN$

(IV)



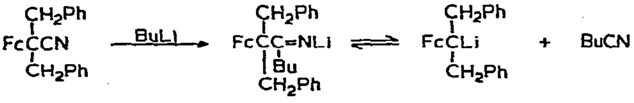
(V)



$Fc\overset{R}{\underset{R}{C}}R'$

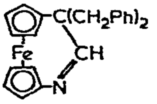
(VI)

The benzylferrocene (VII) was treated with butyllithium but the expected ketone [(VI); $R{=}CH_2Ph$, $R'{=}COBu$] was not isolated. Hydrolysis of the lithiation mixture gave the ferrocenylpropane [(VI); $R{=}CH_2Ph$, $R'{=}H$]. When this lithiation mixture was quenched with D_2O initially no deuterium was introduced but when the experiment was repeated some deuterium (11.5%, estimated by mass spectrometry[3]) was introduced[2]. We proposed that the displacement of cyanide proceeded via a four centre mechanism but the subsequent isolation of some deuterated product contradicted this proposal. It has recently been suggested that the addition of organolithium reagents to cyanides is reversible[4] and it is possible that the displacement of cyanide could proceed via such a mechanism [(2)]*, to give the lithiated intermediate (VIII). When the methyl and cyclopropyl ferrocenyl cyanides [(III); $R{=}Me$] and [(V); $R{=}CN$] were treated with n-butyllithium the expected ferrocenylmethyl ketones [(VI); $R{=}Me$, $R'{=}COBu$] and [(V); $R{=}COBu$] respectively were obtained. The treatment of the ferrocenyl cyanide (VII) with tert-butyllithium gave the ferrocenylpropane [(VI); $R{=}CH_2Ph$, $R'{=}H$] and the cyclic ketimine (IX). This ketimine was formed presumably by heteroannular lithiation of the ferrocenyl cyanide (VII) and intramolecular attack of the lithiated intermediate on the cyanide group.



$$Fc\overset{CH_2Ph}{\underset{CH_2Ph}{C}}CN \xrightarrow{BuLi} Fc\overset{CH_2Ph}{\underset{CH_2Ph}{C}}\underset{Bu}{C}{=}NLi \rightleftharpoons Fc\overset{CH_2Ph}{\underset{CH_2Ph}{C}}Li + BuCN \qquad (2)$$

(VII) (VIII)



(IX)

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* This mechanism was suggested by Dr. B. J. Wakefield, The University of Salford.

When the ferrocenyl cyanide (VII) was treated with lithium aluminium hydride it resisted reduction whilst under the same conditions the methyl-, butyl- and cyclopropylferrocenes [(III); R=Me, (III); R=Bu and (V); R=CN] were reduced to the corresponding amines [(VI); R=Me, R′=CH_2NH_2; (VI); R=Bu, R′=CH_2NH_2 and (V); R=CH_2NH_2]. The dimethylamine [(VI); R=Me, R′=CH_2NH_2] was characterized as the picrate and on reaction with methyl iodide it gave the quaternary ammonium salt [(VI); R=Me, R′=$CH_2\overset{+}{N}Me_3\bar{I}$]. Treatment of the butylamine [(VI); R=Bu, R′=CH_2NH_2] with methyl iodide gave the salt [(VI); R=Bu, R′=$CH_2\overset{+}{N}HMe_2\bar{I}$].

EXPERIMENTAL

For general directions see Part I[5].

Lithiation and deuteration of ferrocenylmethyl cyanide

n-Butyllithium (0.005 mole) was added to a yellow solution of ferrocenylmethyl cyanide (0.56 g, 0.0025 mole) in ether (25 ml), the colour of the solution immediately turned deep red. The mixture was stirred at room temperature for 15 min and then quenched by the addition of deuterium oxide, extracted with ether and the dried ($MgSO_4$) ether extracts were evaporated to leave a red oil. The oil was chromatographed on alumina and ether eluted the deuterated ferrocenyl cyanide [(VI); R=D, R′=CN] (0.32 g, 57%). The PMR spectrum ($CDCl_3$) showed a resonance at τ 5.85, singlet, the PMR spectrum ($CDCl_3$) of the undeuterated ferrocenylmethyl cyanide (I)[6] showed resonances at τ 5.82, singlet (9H, substituted and unsubstituted ring protons); 6.14, singlet (2H, methylene protons).

α,α-Dibenzylferrocenylmethyl cyanide (VII)

The lithioferrocene (II) was prepared from ferrocenylmethyl cyanide (1.13 g, 0.005 mole) and n-butyllithium (0.01 mole) as described above. A solution of benzyl chloride (5.06 g, 0.04 mole) in ether (50 ml) was added quickly. The resultant mixture was heated under reflux for 15 min, hydrolysed, extracted with ether and the dried ($MgSO_4$) ether extracts were evaporated to leave a red oil. The oil was chromatographed on alumina, ether eluted the product (VII) (1.4 g, 70%) which crystallized from ether/light petroleum as orange-yellow crystals, m.p. 178–180°. (Found: C, 76.72; H, 5.66; Fe, 13.87; Mol.wt., 405 by mass spectrometry. $C_{26}H_{23}FeN$ calcd.: C, 77.04; H, 5.72; Fe, 13.79%; Mol.wt. 405). Ether eluted the ketimine (IV) (0.133 g, 5%) which crystallized from ether as a yellow microcrystalline solid, m.p. 226–227°. (Found: C, 68.91; H, 5.24; Fe, 19.88; N, 5.31. $C_{31}H_{28}Fe_2N_2$ calcd.: C, 68.66; H, 5.21; Fe, 20.61; N, 5.17%).

α,α-Dimethylferrocenylmethyl cyanide (III); R=Me

The lithioferrocene (II) prepared from ferrocenylmethyl cyanide (1.13 g, 0.005 mole) was condensed with excess methyl iodide and heated under reflux for 6 h. The work-up was as described above. Ether/light petroleum eluted the product [(III); R=Me] (0.76 g, 60%) which crystallized from light petroleum as pale yellow needles, m.p. 55.5–56°. (Found: C, 66.47; H, 5.97; Fe, 21.98; Mol.wt. 253 by mass spectrometry. $C_{14}H_{15}FeN$ calcd.: C, 66.43; H, 5.58; Fe, 22.08%; Mol.wt., 253).

α,α-Dibutylferrocenylmethyl cyanide (III); R = Bu

The lithioferrocene (II) (0.005 mole) was condensed with excess butyl bromide (13.7 g, 0.1 mole), heated under reflux for 2 h and the work-up was as described above. Ether eluted the product [(III); R = Bu] (0.943 g, 56%) which crystallized from light petroleum as yellow crystals, m.p. 33–34°. (Found: C, 71.09; H, 8.14; Fe, 16.64; Mol.wt., 337 by mass spectrometry. $C_{20}H_{27}FeN$ calcd.: C, 71.22; H, 8.07; Fe, 16.56%; Mol.wt., 337).

1-Ferrocenyl-1-cyanocyclopropane (V); R = CN

The lithioferrocene (II) (0.005 mole) was condensed with excess dichloroethane (9.9 g, 0.1 mole), heated under reflux for 30 min and the work-up was as described above. Ether/light petroleum eluted the product [(V); R = CN] (0.67 g, 53%) which crystallized from ether/light petroleum as orange-yellow needles, m.p. 47–48°. (Found: C, 67.05; H, 5.07; Fe, 22.08; Mol. wt., 251 by mass spectrometry. $C_{14}H_{13}FeN$ calcd.: C, 66.96; H, 5.22; Fe, 22.24%; Mol.wt., 251).

The treatment of α,α-dibenzylferrocenylmethyl cyanide (VII) with n-butyllithium

n-Butyllithium (0.006 mole) was added to a solution of the cyanide (VII) (0.202 g, 0.0005 mole) in ether (50 ml) and after approximately 10 min the yellow solution slowly turned red. The mixture was stirred at room temperature for 17 h, hydrolysed, extracted with ether and the dried ($MgSO_4$) ether extracts were evaporated to give an orange oil which was chromatographed on alumina. Ether/light petroleum eluted the ferrocenylpropane [(VI); R = CH_2Ph, R′ = H] (0.133 g, 70%) which crystallized from light petroleum as yellow needles, m.p. 112–115°. (Found: C, 78.52; H, 6.40; Fe, 15.03; Mol.wt., 380, by mass spectrometry. $C_{25}H_{24}Fe$ calcd.: C, 78.85; H, 6.37 Fe, 14.79%; Mol.wt. 380).

2-Ferrocenyl-2-methylheptan-3-one (VI); R = Me, R′ = COBu

n-Butyllithium (0.008 mole) was added to a solution of the cyanide [(III); R = Me] (0.396 g, 0.0016 mole) in ether (30 ml) and stirred at room temperature for 24 h. The work up was as described above. Ether/light petroleum eluted the starting cyanide [(III); R = Me] (0.07 g). Ether/light petroleum then eluted the ketone [(VI); R = Me, R = COBu] (0.055 g, 14%)* which crystallized from light petroleum as yellow plates, m.p. 39–39.5°. (Found: C, 69.80; H, 7.51; Fe, 18.30. $C_{18}H_{24}FeO$ calcd.: C, 69.29; H, 7.75; Fe, 17.90%).

1-Ferrocenyl-1-pentanoylcyclopropane (V); R = COBu

The reaction between n-butyllithium (0.008 mole) and the cyanide [(V); R = CN] (0.20 g, 0.0008 mole) was carried out as described above. The product [(V); R = COBu] (0.20 g, 81%) crystallized from light petroleum as yellow needles, m.p. 79–80.5° (Found: C, 69.65; H, 7.22; Fe, 17.94. $C_{18}H_{22}FeO$ calcd.: C, 69.70; H, 7.15; Fe, 18.01%).

The treatment of α,α-dibenzylferrocenylmethyl cyanide (VII) with tert-butyllithium

tert-Butyllithium (0.009 mole) was added to a solution of the cyanide (VII)

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* Yields are based on unrecovered starting material.

(0.303 g, 0.001 mole) in ether (50 ml) and after approximately 1 min the yellow solution turned red. The mixture was stirred at room temperature for 45 min, hydrolysed, extracted with ether and the dried ($MgSO_4$) ether extracts were evaporated to give a red oil which was chromatographed on alumina. Ether/light petroleum eluted the ferrocenylpropane [(VI); $R=CH_2Ph$, $R=H$] (0.130 g, 54%)* (identical m.p. and IR), ether eluted the starting cyanide (VII) (0.080 g) (identical m.p. and IR) and ether also eluted the ketimine (IX) (0.070 g, 31%)* which crystallized from ether as red crystals, m.p. 203–207°. (Found: C, 77.25; H, 5.63; Fe, 13.73; N, 3.48; Mol.wt., 405 by mass spectrometry. $C_{26}H_{23}FeN$ calcd.: C, 77.23; H, 5.49; Fe, 13.83; N, 3.47%; Mol.wt., 405).

Attempted reduction of α,α-dibenzylferrocenylmethyl cyanide (VII) with lithium aluminium hydride

The cyanide (VII) (0.30 g, 0.00074 mole) was dissolved in ether and lithium aluminium hydride (1 g, 0.026 mole) was added. The mixture was heated under reflux for 4 h and the excess lithium aluminium hydride was destroyed. The mixture was extracted with ether and the dried ($MgSO_4$) ether extracts were evaporated to give a yellow solid which was chromatographed on alumina. Ether eluted the cyanide (VII) (0.218 g, 73%) (identical m.p. and IR spectrum).

1-*Ferrocenyl*-1,1-*dimethylethylamine* (*VI*); $R=Me$, $R'=CH_2NH_2$

The ferrocenyl cyanide [(III); R=Me] (0.109 g, 0.0004 mole) in ether (20 ml) was heated under reflux with lithium aluminium hydride (0.02 g, 0.00053 mole) for 3 h and the work-up was as described above. Evaporation of the ether extracts gave the ferrocenylamine [(VI); R=Me, $R'=CH_2NH_2$] (0.103 g, 94%) as a yellow oil. The picrate was prepared in the usual way and it crystallized as red plates from absolute ethanol, m.p. 185–186°. (Found: C, 49.18; H, 4.22; Fe, 10.64. $C_{20}H_{22}FeN_4O_7$ calcd.: C, 49.40; H, 4.56; Fe, 11.50%).

The amine [(VI); R=Me, $R'=CH_2NH_2$] (0.120 g, 0.00047 mole) in ether (20 ml) was treated with excess methyl iodide and the mixture was kept in the dark for 24 h. The methiodide [(VI); R=Me, $R'=CH_2\overset{+}{N}Me_3\bar{I}$] (0.164 g, 82%) was deposited and it was crystallized from methyl cyanide/ether as dark red plates, m.p. 249–250° (dec.). (Found: C, 48.05; H, 6.22; Fe, 13.12. $C_{17}H_{26}FeIN$ calcd.: C, 47.81; H, 6.14; Fe, 13.09%).

1-*Ferrocenyl*-1,1-*dibutylethylamine* (*VI*); $R=Bu$, $R'=CH_2NH_2$

The ferrocenyl cyanide [(III); R=Bu] (0.455 g, 0.0012 mole) in ether (50 ml) was heated under reflux with lithium aluminium hydride (1.0 g, 0.026 mole) for 1 h and the work-up was as described above. Evaporation of the ether extracts gave the ferrocenylamine [(VI); R=Bu, $R=CH_2NH_2$] (0.326 g, 71%) as a red oil. The oil was dissolved in ether and excess methyl iodide was added, after 48 h the methiodide [(VI); R=Bu, $R'=CH_2\overset{+}{N}HMe_2\bar{I}$] was collected as yellow-orange crystals, m.p. 143–147° (with darkening from 120°). (Found: C, 52.88; H, 7.14; Fe, 11.24. $C_{22}H_{36}FeIN$ calcd.: C, 53.13; H, 7.30; Fe, 11.24%).

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* Yields are based on unrecovered starting material.

1-Ferrocenyl-1-(aminomethyl)cyclopropane [(*V*); *R*=CH_2NH_2]

The ferrocenyl cyanide [(V); R=CN] (0.26 g, 0.00103 mole) in ether (100 ml) was heated under reflux with lithium aluminium hydride (1 g, 0.026 mole) for 90 min and the work-up was as described above. Evaporation of the ether extracts gave the ferrocenylamine [(V); R=CH_2NH_2] (0.26 g, 98%) which crystallized from ether/petroleum ether as yellow needles, m.p. 38.5–40°. (Found: C, 65.67; H, 6.62; Fe, 21.78. $C_{14}H_{17}FeN$ calcd.: C, 65.91; H, 6.72; Fe, 21.89%).

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