

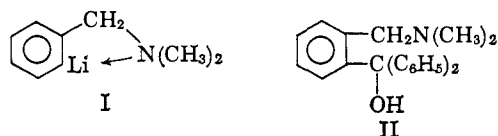
Ring Metalation of Dimethylaminomethylferrocene with Butyllithium and Condensations with Electrophilic Compounds. Synthesis of 1,2-Disubstituted Ferrocenes¹

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N,N-Dimethylaminomethylferrocene (III) was metalated with *n*-butyllithium in ether-hexane, and the resulting monolithioamine was condensed with benzophenone, acetone, benzonitrile, and phenyl isocyanate to form the corresponding 2-derivatives. The methiodide (VI) of the benzophenone adduct was cyclized by means of potassium amide to give the cyclic ether. Methiodide VI was also treated with potassium hydroxide and potassium cyanide to afford the diol and carbinol-nitrile, respectively. Amine III was metalated with excess *n*-butyllithium in THF-hexane and the resulting intermediates were condensed with benzophenone to yield mainly the 2,1'-derivative; also some of the 2- and the 1'-derivatives were formed. These results furnish a route to the synthesis of a number of new 1,2-disubstituted and 1,2,1'-trisubstituted ferrocenes. Amine III underwent lithiation more readily than ferrocene. In THF-hexane, amine III was converted primarily to a dilithioamine. Some infrared and n.m.r. spectral correlations of 1,2-disubstituted ferrocenes are discussed.

Recently,² condensation of electrophilic compounds at the *ortho* position of benzyldimethylamine and related amines was accomplished through an *o*-lithioamine such as I, which was prepared by metalation of the amine with *n*-butyllithium in ether-hexane. For example, I was condensed with benzophenone to form *ortho* derivative II.



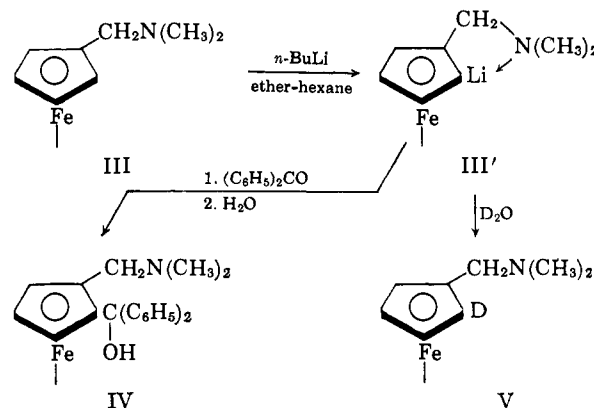
In the present investigation such condensations were similarly effected at the 2-position of *N,N*-dimethylaminomethylferrocene (III). Thus III was lithiated in ether-hexane to form presumably III', which was condensed with benzophenone to give the 2-derivative IV in good yield (65–75%) (*cf.* Table I); the intermediate lithioamine was also deuterated to give a ring derivative, which was tentatively assigned structure V (Scheme A).

That one of the rings of III was lithiated, not the methylene side chain, was supported by the n.m.r. spectrum (CDCl₃) of the deuteration product (*cf.* Scheme A). In agreement with structure V, this spectrum showed the singlet ferrocene proton peak at τ 6.05 reduced in intensity by 70% of one proton

(1) Supported by the Army Research Office (Durham) and the National Science Foundation.

(2) (a) F. N. Jones, M. F. Zinn, and C. R. Hauser, *J. Org. Chem.*, **28**, 663 (1963); (b) F. N. Jones, R. L. Vaulx, and C. R. Hauser, *ibid.*, **28**, 3461 (1963).

Scheme A



relative to the areas of the methylene and methyl protons³ (*cf.* Table IV).

Table I. Metalation of Amine III (A) with *n*-Butyllithium (B) in a Mixture of Hexane and Another Solvent. Condensation with Benzophenone^a

Mole ratio A:B	Other solvent	Lithiation period, hr.	Yield, %		
			IV	VIII	IX
1:1.25	Ether	1	65 ^b
1:1.25	Ether	1	54 ^c , 84 ^d
1:2.5	Ether	1	71 ^b	Trace	...
1:1.25	Ether	5	71 ^e
1:1.25	Ether	16	74 ^e	3 ^f	5 ^f
1:4	THF	1.3 ^g	13 ^c	45 ^c	10 ^c
1:1	THF	0.25 ^g	26 ^c	6 ^c	5 ^c

^a Each condensation period 4 hr. ^b Recrystallized from methanol-ether. ^c Purified by column chromatography. ^d Yield based on unrecovered starting material. ^e Recrystallized from hexane. ^f Recrystallized from 95% ethanol. ^g At reflux temperature of solvent mixture.

Structure IV for the benzophenone adduct was supported by analysis and absorption spectra. The infrared spectrum exhibited 9- and 10- μ bands indicative of an unsubstituted cyclopentadienyl ring (*cf.* Table II).⁴ The n.m.r. spectrum exhibited, for the methyl protons, a singlet at τ 8.03 and, for the methylene protons, an AB quartet centered at 6.85 ($J_{AB} = \sim 13$ c.p.s.).⁵ Ring proton peaks were located at τ 6.05

(3) No information could be gained concerning the site of ring lithiation since resolution of the ferrocene ring protons could not be effected at either expanded scale or by protonation (solvent CF₃COOH).

(4) M. Rosenblum, Ph.D. Thesis, Harvard University, 1953; M. Rosenblum, *Chem. Ind. (London)*, 953 (1958); P. L. Pauson, *Quart. Rev. (London)*, 391 (1955).

(5) Novel features of this n.m.r. spectrum and others described in this paper will be presented in a future publication. *Cf.* G. R. Knox, P. L. Pauson, and G. V. D. Tiers, *Chem. Ind. (London)*, 1046 (1959); also J. C. Randall, J. J. McLeskey, III, P. Smith, and M. E. Hobbs, *J. Am. Chem. Soc.*, **86**, 3229 (1964).

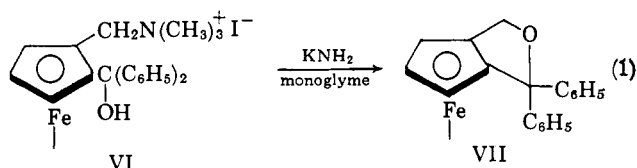
Table II. Characteristic Absorptions of Substituted Ferrocenes (μ)^{a,b}

Compd.	"9-10- μ rule"	"10.8-11.2- μ rule"	Characteristic substituent absorptions
IV	9.03 (m), 10.00 (m)	10.75 (w), 11.12 (m)	
VI	9.05 (s), 10.03 (m)	10.95 (m), 11.15 (w)	2.97 (b) (-OH)
VII	9.06 (s), 10.05 (m)	10.80 (w), 11.10 (w)	
VIII	... 10.00 (w)	... 11.15 (s)	2.96 (b) (-OH)
IX ^c	8.95 (m) ...	10.78 (m), 11.05 (m)	...
XII	9.05 (s), 10.00 (s)
XIII	9.02 (s), 9.98 (m)	10.70 (w), 11.30 (s)	6.07 (s) (-COC ₆ H ₅)
XIV	9.07 (s), 10.02 (s)	... 11.05 (w)	6.01 (s) (-CONHC ₆ H ₅)
XV ^d	9.05 (s), 10.05 (m)	10.82 (m), 11.06 (m)	3.10 (b) (-OH)
XVI	9.04 (m), 10.05 (s)	10.85 (m), 11.20 (m)	4.49 (m) (-CN), 2.87 (sh) (-OH)
XVII	9.05 (s), 9.95 (m)	10.75 (m), 11.15 (m)	5.85 (s) (-COOH), 2.84 (sh) (-OH)

^a Spectra of crystalline compounds determined as Nujol mulls; oils XII and XIII as neat liquid films between sodium chloride plates. Spectra recorded on a Perkin-Elmer Model 237 Infracord spectrometer. ^b s = strong, m = medium, w = weak, b = broad, sh = sharp. ^c Recorded on a Perkin-Elmer Model 137 Infracord spectrometer. ^d Absorptions reported for this compound at 2.9, 9, and 10 μ (R. A. Benkeser, W. P. Fitzgerald, and M. S. Melzer, *J. Org. Chem.*, **26**, 2569 (1961)).

(unsubstituted cyclopentadienyl ring), 6.21 (triplet portion of ABC system), and 5.97 (apparent doublet of ABC system).

Confirmation of the 1,2-relationship of the substituents of IV was secured by cyclization of its methiodide VI to form cyclic ether VII in 79% yield (eq. 1).



Structure VII was established by analysis and absorption spectra. The infrared spectrum exhibited the expected 9- and 10- μ bands (*cf.* Table II). The n.m.r. spectrum displayed, besides the complicated phenyl proton signal lying between τ 2.2 and 3.0, peaks at 6.28 (singlet), 5.80 (multiplet), and 5.41 (AB-type quartet).⁵ These resonances were in the correct intensity ratios (*cf.* Table III).

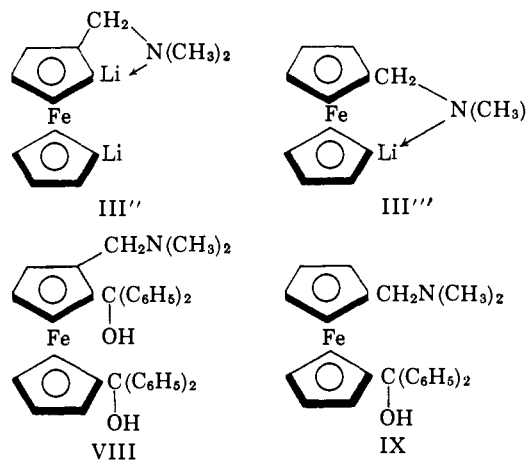
Table III. Chemical Shifts^a of Some Substituted Ferrocenes^b

Compd.	τ_{CH_2} ^c	a-type proton (τ) ^{c,d}	b-type proton (τ) ^{c,e}	c-type proton (τ) ^{c,f}	τ_{CH_3}
IV	6.85 (q)	6.08 (s)	8.03 (s)
VII	5.41 (q)	5.8 (m)	5.8 (m)	6.28 (s)	...
VIII	6.92 (q)	8.08 (s)
IX	7.02 (s)	7.79 (s)
XII	6.68 (q)	6.06 (s)	6.06 (s)	5.92 (s)	7.88 (s)
XIII	6.14 (q)	5.38 (t)	5.57 (m)	5.90 (s)	7.78 (s)
XIV	6.47 (q)	4.96 (t)	5.8 (m)	5.82 (s)	7.73 (s)
XV	5.68 (s)	...
XVI	6.78 (q)	5.67 (s)	...

^a s = singlet, t = triplet, q = quartet, m = multiplet. ^b All spectra were run in CDCl₃ using tetramethylsilane as internal standard. ^c Average chemical shift. ^d Proton α to substituent introduced into III. ^e Protons β to substituent introduced into III. ^f Protons on unsubstituted cyclopentadienyl ring.

The lithiation of amine III in ether-hexane (*cf.* Scheme A) was nearly complete within 1 hr. whereas that of benzylidimethylamine to give I required about 16 hr.² Treatment of III with *n*-butyllithium in ether-hexane for 16 hr. afforded not only the monolithioamine III' but

also some of the dilithioamine III'' and apparently the monolithioamine III'''. Thus subsequent addition of benzophenone to the lithiation mixture afforded the 2-derivative IV, 2,1'-derivative VIII, and 1'-derivative IX in yields of 74, 3, and 5%, respectively (*cf.* Table I).



Elemental analysis indicated that VIII contained two diphenylhydroxymethyl groups per molecule. Infrared with the absence of absorption in the 9- and 10- μ region and n.m.r. with no five-proton singlet around τ 5.9 disclosed that both rings carried substituents. The methyl singlet at τ 8.08 and the methylene AB quartet centered at 6.92 possessed an integrated intensity ratio of 3:1, thereby demonstrating that neither methyl nor methylene protons had been substituted (*cf.* Table III). Proof of the 1,2-disposition of the substituents on the disubstituted ring was demonstrated by lithiation of carbinol-amine IV and condensation of the resulting dilithio intermediate with benzophenone. A 33% yield of VIII was obtained along with 35% of recovered IV.

By essentially the same but simpler arguments as those in the preceding paragraph, the product IX was assigned a 1,1'-structure. Elemental analysis and n.m.r. indicated the presence of only one diphenylhydroxymethyl substituent and both infrared⁶ and n.m.r. provided evidence that this substituent had

(6) The infrared spectrum of IX possessed absorption at 8.95 and a shoulder at 9.95 μ which were sufficiently close to positions corresponding to the "9-10- μ rule" to cause some confusion.

entered the unsubstituted ring of III (*cf.* Tables II and III).

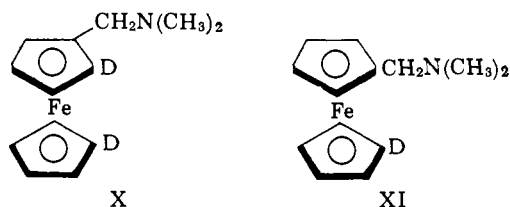
Interestingly, the yields of the disubstitution product VIII and monosubstituted product IX were increased at the expense of monosubstituted product IV by effecting the lithiation of amine III in refluxing THF-hexane for 1 hr. Subsequent addition of benzophenone afforded VIII, IX, and IV in yields of 45, 10, and 13%, respectively.⁷ When this lithiation was repeated and the mixture was neutralized with deuterium oxide, the recovered deuterated amine was indicated by n.m.r. to contain 1.6 atoms of deuterium per molecule (*cf.* Table IV). This n.m.r. verified that substitution of

Table IV. N.m.r. Spectra^a of Deuterated Dimethylaminomethylferrocene

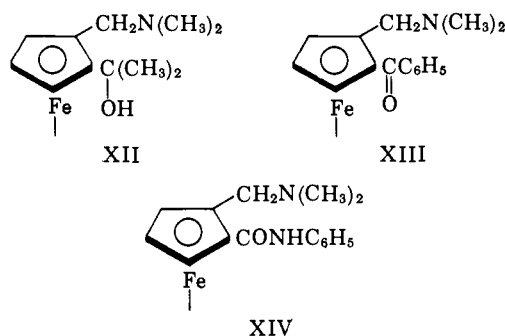
Compd.	τ_{CH_2}	τ_{CH_3}	$\tau_{\text{ferrocene}}^b$	Relative intensities	D atoms
III ^c	6.83 (s)	7.94 (s)	5.98(s)	2:6:9	0.0
V ^d	6.84 (s)	7.92 (s)	6.05 (s)	2.1:6:8.3	0.7
X ^{d,e}	6.73 (s)	7.85 (s)	5.90 (s)	2.1:5.8:7.4	1.6

^a s = singlet. ^b In each case the ferrocene ring protons all had the same chemical shift under the conditions cited. ^c Neat sample. ^d Solvent CDCl_3 with tetramethylsilane as internal standard. ^e Mixture of V, XI, and primarily X.

only ring protons had taken place. The deuterated product was presumably a mixture of V, X, and XI which would be derived from lithio intermediates III', III'', and III'''.



Condensations of Lithioamine III' with Other Electrophilic Compounds. Lithioamine III', prepared in ether-hexane, was condensed with acetone, benzonitrile, and phenyl isocyanate to form the 2-derivatives XII, XIII, and XIV, respectively. A crystalline



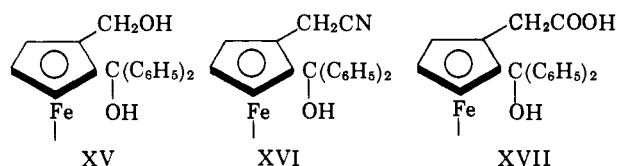
monopicate was prepared of the oils XII and XIII. Each of the isolated products gave an infrared spectrum

(7) Of incidental interest is the order of elution of these compounds from an alumina I column, namely, 1,2- > 1,2,1'- > 1,1'- which is the same order observed for a series of alkyl and aryl ferrocenes. M. Rosenblum, *J. Am. Chem. Soc.*, **81**, 4530 (1959), actually reported the elution order 1,2- > 1,1'- > 1,3- and 1,2,1'- > 1,3,1'-. No comparison between di- and trisubstitution types seems previously to have been made.

which possessed absorptions at 9 and 10 μ (*cf.* Table II).

The n.m.r. spectra of XIII and XIV were especially meaningful; in contrast to spectra of our other compounds they demonstrated unequivocally the 1,2-nature of the substituents of these two compounds. Recent studies⁸ have assigned the protons in certain carbonyl-substituted ferrocenes shifted farthest downfield from about τ 5.9 (unsubstituted ferrocene peak)⁹ to the *ortho* or α -protons; those shifted downfield to a lesser extent to the β -protons. Loss of intensity corresponding to one proton from the downfield ferrocene signal of the n.m.r. spectra of both XIII and XIV demonstrated in each case that these carbonyl compounds contained a substituent in the 2-position (*cf.* Table III).

Reactions of Methiodide VI with Anions. This methiodide reacted with potassium hydroxide and potassium cyanide to form diol XV and carbinol-nitrile XVI in yields of 50 and 75%, respectively.¹⁰ The latter compound was hydrolysed to give hydroxy acid XVII in 71% yield. Surprisingly XVII failed to afford the lactone under the usual conditions.



Structures XV, XVI, XVII for the methiodide substitution products were supported by analyses and infrared spectra which showed not only bands at 9 and 10 μ but also strong absorption for the CN, OH, and COOH groups, respectively (*cf.* Table II). The strong OH band for the diol XV contrasts significantly with the absence of this band in IV.

Discussion

On the basis of the present results, it appears that amine III is first lithiated at the 2-position to form monolithioamine III', followed by lithiation of the unsubstituted ring to give dilithioamine III''. Such a contention is supported by a comparison of the yields of IV for the last two runs of Table I; the 15-min. experiment actually produced a large predominance of the monosubstitution product.¹¹ The second lithiation may be similar to that of ferrocene itself which undergoes lithiation less readily than amine III.¹² Condensation of intermediates III' and III'' with benzophenone would then account for the formation of the

(8) (a) M. D. Rausch and V. Mark, *J. Org. Chem.*, **28**, 3225 (1963); (b) Y. Nagai, J. Hooz, and R. A. Benkeser, *Bull. Chem. Soc. Japan*, **37**, 53 (1964); (c) K. L. Rinehart, Jr., D. E. Bublitz, and D. H. Gustafson, *J. Am. Chem. Soc.*, **85**, 970 (1963); (d) M. I. Levenberg and J. H. Richards, *ibid.*, **86**, 2634 (1964).

(9) A dimethylaminomethyl group apparently does not significantly affect the chemical shift of the ring protons in III relative to that for the ring protons in ferrocene itself (*cf.* Table IV).

(10) The reactions of VI are analogous to previously observed substitutions of the methiodide of amine III with these reagents and with other anions. *Cf.* J. K. Lindsay and C. R. Hauser, *J. Org. Chem.*, **22**, 355 (1957), and D. Lednicer, J. K. Lindsay, and C. R. Hauser, *ibid.*, **23**, 653 (1958).

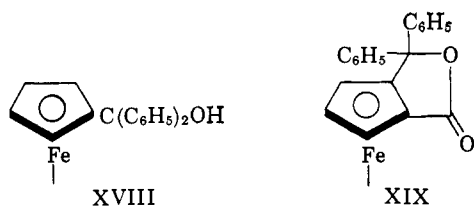
(11) Evidently solvent, temperature, and metalation period play an important role in such lithiations. A further study of these is contemplated.

(12) Whereas maximum lithiation of amine III appears to occur within 1 hr., that of ferrocene itself has been reported to require 5-6 hr. as determined by carbonation. *Cf.* S. I. Goldberg, L. H. Keith, and T. S. Prokopov, *J. Org. Chem.*, **28**, 850 (1963).

2- and 2,1'-derivatives IV and VIII, respectively. However, the manner of formation of the 1'-derivative IX is not entirely clear. This product might have arisen through intermediate III''' as indicated above or through III'' by partial condensation of benzophenone at the lithio function in the lower ring and incomplete reaction of this intermediate with benzophenone.¹³

The above lithiations and condensations furnish a route to a number of new 1,2- and 1,2,1'-derivatives of ferrocene. Not only could lithioamine III' be condensed with other electrophiles, but the 1,2-derivatives could presumably be converted to 1,2,1'-derivatives in which the three substituents could each be varied. This was illustrated by the stepwise condensation of III with benzophenone to form VIII. Other trisubstituted products would be available through dilithio salt III''. Moreover, substitution products of the methiodides of these compounds should be accessible.

All of the compounds described above appear to be new except diol XV which has previously been prepared by lithiation of XVIII followed by carbonation to produce the 2-carboxylic acid; reduction of the corresponding lactone XIX afforded XV.¹⁴



Aside from the lithiation procedure of Benkeser, only a few electrophilic substitution methods have been used to produce 1,2-disubstituted ferrocenes. Among these, the acid-catalyzed cyclization of 2-ferrocylethylamine with formaldehyde and subsequent Hofmann degradation has afforded a series of 2-substituted vinylferrocenes.¹⁵ Other electrophilic substitution procedures have been reported but these usually have led to mixtures from which the 1,2-isomers have been isolated in only small yields.¹⁶ Recently in contrast to our results, Benkeser and Bach¹⁷ have observed that lithiation of monoalkyl ferrocenes occurs primarily at the 3- and 1'-positions in nearly statistical distribution. The 1,2-orientation in our metalations may be ascribed to coordination of the free pair of electrons of the amine with lithium (see structure III').

Finally some comments concerning the infrared data in Table II should be made. Spectra of Nujol mulls of carbinol-amines IV, IX, and XII were noted to lack O-H absorption. A study of the solution spectrum of IV in carbon tetrachloride failed to detect any O-H absorption, even at high concentrations. This is

(13) A referee has pointed out that intermediate III''' need not possess a chelated structure. III''' could also arise from an exchange reaction, viz., III'' + III → III' + III'''. It is possible that part of product IV arose through partial condensation of benzophenone with the lithio function in the upper ring of III'' and incomplete condensation at the lithio function in the lower ring, but this seems less likely.

(14) R. A. Benkeser, W. P. Fitzgerald, and M. S. Melzer, *J. Org. Chem.*, **26**, 2569 (1961).

(15) D. Lednicer and C. R. Hauser, *ibid.*, **24**, 43 (1959).

(16) Cf. for example, (a) D. W. Hall and J. H. Richards, *ibid.*, **28**, 1549 (1963); (b) M. Rosenblum and W. G. Howells, *J. Am. Chem. Soc.*, **84**, 1167 (1962).

(17) R. A. Benkeser and J. L. Bach, *ibid.*, **86**, 890 (1964).

remarkable since three separate O-H modes for hydroxymethylferrocene have been assigned recently.¹⁸ It is to be noted that each of our compounds possessing a single hydroxymethyl group adjacent to the dimethylaminomethyl group gave no absorption; when the dimethylaminomethyl group was absent, or when more than one OH group was present, O-H absorption was observed (cf. Table II).

In accordance with the "9-10- μ rule"⁴ spectra of all compounds possessing an unsubstituted cyclopentadienyl ring were found to exhibit absorptions near 9 and 10 μ (Table II).

A recent rule enunciated by Rosenblum^{16b,19} and modified by Benkeser^{8b} proposes that the region between 10.8 and 11.20 μ be diagnostic of 1,2- and 1,3-disubstituted acylferrocenes. The modified rule states that a 1,3-relationship is signified by two bands in this region, the stronger of which is at the longer wave length, while a 1,2-relationship is shown by a single band or by two bands with the stronger absorption occurring at the shorter wave length. Although this rule applies to our carboxamide XIV and perhaps to certain other compounds (see Table II), it does not apply to ferrocenylphenone XIII.

Experimental²⁰

Lithiation of Dimethylaminomethylferrocene (III) in Ether-Hexane to Form III'. A magnetically stirred solution of 2.44 g. (10 mmoles) of dimethylaminomethylferrocene (III)²¹ in 10 ml. of anhydrous ether under a nitrogen atmosphere was treated dropwise over a period of 10 min. with 16 ml. (25 mmoles) of a 1.5 M solution of *n*-butyllithium in hexane²² (slight exotherm). Metalation was completed by stirring for 1 additional hr. at room temperature and the solution was then employed as described below. Results of the use of other lithiation periods are listed in Table I.

Deuteration of III'. A solution of 4.88 g. (20 mmoles) of III' in ether-hexane was prepared in the same manner as that described above except that 16 ml. (25 mmoles) of *n*-butyllithium was utilized (A:B = 1:1.25; cf. Table I). After stirring for 1 hr., the product solution was hydrolyzed with D₂O. The product oil was extracted with ether and the extracts were combined, dried over anhydrous sodium sulfate, and stripped. Distillation of the oil brought a fraction, b.p. 93-95° at 0.6 mm., 3.5 g. (72%). The n.m.r. spectrum of the oil is summarized in Table IV.

Condensation of III' with Benzophenone. A solution of 2.43 g. (10 mmoles) of III was lithiated as described above. After 1 hr., an ethereal solution of benzophenone, 7.3 g. (40 mmoles), was added dropwise over 10 min. (moderate refluxing) and the product complex was hydrolyzed by careful addition of water after stirring for 4 hr. Separation of the organic layer was followed by extraction of the remaining aqueous layer with

(18) Cf. D. S. Trifan and R. Bacskai, *ibid.*, **82**, 5010 (1960).

(19) M. Rosenblum, *ibid.*, **81**, 4530 (1959).

(20) Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Melting points were determined on a Hoover melting point apparatus and are corrected. Chromatographies were performed on 28-200 mesh Fisher alumina I. All n.m.r. spectra were run on a Varian A-60 spectrometer using TMS as an internal standard. We are indebted to Mr. James McLeskey for aid in the interpretation of these spectra.

(21) D. Lednicer and C. R. Hauser, *Org. Syn.*, **40**, 31 (1960):

(22) Foote Mineral Company, New Johnsonville, Tenn.

several portions of ether. The organic layers were combined and extracted with 1:10 phosphoric acid and the resulting acid solution was neutralized by slow addition to a large excess of 10% sodium carbonate solution with stirring. A total of 3.9 g. of crude solid was obtained which was chromatographed on a 1 × 20 in. column of alumina. Elution with benzene gave 3.0 g. (71%) of 2-(α,α -diphenylhydroxymethyl)dimethylaminomethylferrocene (IV), m.p. 121–125° after recrystallization from methanol–ether. A second recrystallization gave analytical material, m.p. 126–127.5°.

Anal. Calcd. for $C_{26}H_{27}FeNO$: C, 73.43; H, 6.40; Fe, 13.13; N, 3.29. Found: C, 73.35; H, 6.40; Fe, 13.53; N, 3.13.

Results for other runs which employed different lithiation periods are described in Table I.

The picrate of IV was formed in the usual manner; orange crystals were obtained, m.p. 166–168° dec. after recrystallization from 95% ethanol.

Anal. Calcd. for $C_{32}H_{30}FeN_4O_8$: C, 58.72; H, 4.62; N, 8.56. Found: C, 58.86; H, 4.76; N, 8.35.

Formation of Methiodide VI. The methiodide VI was prepared in 98% yield from IV and excess methyl iodide in acetonitrile at 35°. It melted at 220–225° dec. (darkened at 180°) after recrystallization from acetonitrile–ether.

Anal. Calcd. for $C_{27}H_{30}FeINO$: C, 57.16; H, 5.33; I, 22.38; N, 2.47. Found: C, 57.07; H, 5.20; I, 22.47; N, 2.39.

Reactions of Methiodide VI. A. Formation of Cyclic Ether VII. To a stirred suspension of 15 mmoles of potassium amide in 1500 ml. of liquid ammonia was added rapidly 5.67 g. (10 mmoles) of methiodide VI. After 30 min. the ammonia was removed by heating as 1200 ml. of dry monoglyme was added. The resulting suspension was refluxed until no more trimethylamine was evolved (6 days). The mixture was cooled and water was added cautiously; ether was added and the layers were separated. After three ether extractions of the aqueous layer, the organic layers were combined and stripped to give 4.0 g. of crude orange solid. This was recrystallized from ethanol to give 2.6 g. of orange crystals, m.p. 133.5–135.5°. Chromatography of the stripped filtrate on alumina and elution with benzene gave an additional 0.4 g. of product, m.p. 133–135°. The total yield of (cyclopentadienylo[*c*]-3-1,1-diphenylfuran)(cyclopentadienyl)iron was 79%.

Anal. Calcd. for $C_{24}H_{20}FeO$: C, 75.80; H, 5.30; Fe, 14.69. Found: C, 75.44; H, 5.36; Fe, 15.11.

B. Formation of 2-Diphenylhydroxymethylferrocenylcarbinol (XV). This reaction was effected essentially as described for the preparation of hydroxymethylferrocene.¹⁰ A slurry of 1.19 g. (3 mmoles) of methiodide V in 35 ml. of 1 N potassium hydroxide was refluxed for 30 hr. Filtration at the pump and chromatography on alumina gave 0.6 g. (50%) of light orange crystals, m.p. 149–151°. Recrystallization from cyclohexane–ether gave analytical material, m.p. 150–152° (lit.¹⁴ m.p. 146°).

Anal. Calcd. for $C_{24}H_{26}FeO_2$: C, 72.38; H, 5.57; Fe, 14.03. Found: C, 72.56; H, 5.72; Fe, 14.08.

C. Formation of 2-Diphenylhydroxymethylferrocenylacetonitrile (XVI). This experiment was conducted

essentially as described for the preparation of ferrocenylacetonitrile¹⁰ except that the reaction mixture was refluxed for 10 hr. There was obtained carbinol–nitrile XVI, m.p. 160–162° dec., recrystallized from ethanol; yield 75%.

Anal. Calcd. for $C_{25}H_{23}FeNO$: C, 73.72; H, 5.20; N, 3.44. Found: C, 73.52; H, 5.20; N, 3.37.

Hydrolysis of Nitrile–Amine XVI. Hydrolysis of XVI (1 g., 2.6 mmoles) was effected with 1.46 g. (26 mmoles) of potassium hydroxide in 20 ml. of 95% ethanol and 8 ml. of water. The reaction mixture was refluxed under nitrogen for 36 hr., cooled, and 28 ml. of a 5% sodium hydroxide solution was added. After filtering, the well stirred yellow alkaline solution was acidified by dropwise addition of glacial acetic acid to a slight excess. The resulting buff precipitate was collected, washed with water, and dried to give 0.74 g. (71%) of 2-diphenylhydroxymethylferrocenylacetic acid (XVII), m.p. 147–149° and 150–151° after dissolving in 95% ethanol and precipitating with water.

Anal. Calcd. for $C_{25}H_{22}FeO_3$: C, 70.44; H, 5.20; Fe, 13.10. Found: C, 70.36; H, 5.37; Fe, 12.91.

Further Condensations of III' in Ether–Hexane.

A. With Acetone. Synthesis of 2-(α,α -Dimethylhydroxymethyl)dimethylaminomethylferrocene (XII). A solution of III' in 40 ml. of ether was prepared in the usual manner except that 9.8 g. (40 mmoles) of III and 32 ml. (50 mmoles) of *n*-butyllithium in hexane²² were utilized (A:B = 1:1.25; cf. Table I). After stirring for 1 hr. at room temperature under nitrogen, the solution was cooled in ice and 20 ml. (280 mmoles) of dry acetone was added over a period of 30 min. A gel formed after stirring this solution for 2–3 hr. The gel was broken up repeatedly and, after 4 hr., hydrolysed with water. The aqueous layer was separated and extracted three times with ether and the total organic layers were stripped and then distilled. A small colorless forerun was followed by a fraction, b.p. 87–96° at 0.45 mm., 8.15 g. (83%), identified as starting material by comparison of its infrared spectrum with that of an authentic sample. A third fraction was collected, b.p. 113–118° at 0.45 mm., 1.7 g. (14%). Redistillation of this last fraction through a microapparatus produced analytical material, b.p. 116–118° at 0.45 mm., $n^{22.5D}$ 1.5708.

Anal. Calcd. for $C_{16}H_{23}FeNO$: C, 63.80; H, 7.70; Fe, 18.54; N, 4.65. Found: C, 64.27; H, 7.87; Fe, 18.50; N, 4.59.

The red-brown picrate, recrystallized from 95% ethanol, melted at 164–165°.

Anal. Calcd. for $C_{22}H_{26}FeN_4O_8$: C, 49.82; H, 4.94; Fe, 10.53; N, 10.56. Found: C, 49.86; H, 4.81; Fe, 10.50; N, 10.73.

B. With Benzoinitrile. Synthesis of 2-(Dimethylaminomethyl)ferrocenylphenone (XIII). A solution of III' from 2.43 g. (10 mmoles) of III in 20 ml. of ether was prepared as described above. After 1 hr. this was treated with 2.06 g. (20 mmoles) of benzoinitrile over 10 min. and the solution was stirred under nitrogen for 4 hr. Water was then added to hydrolyze the reaction mixture and the product was extracted with several portions of ether. These were combined, dried over anhydrous sodium sulfate, and stripped. Chromatography of the thick, oily residue on a 0.75 × 24 in. column of alumina brought 2.0 g. (58%) of a

thick red oil identified by infrared and n.m.r. spectra as XIII. This oil appeared to be moderately sensitive to light.

Anal. Calcd. for $C_{20}H_{21}FeNO$: C, 69.18; H, 6.10; Fe, 16.08; N, 4.03. Found: C, 69.46; H, 6.00; Fe, 16.21; N, 4.01.

The maroon picrate, recrystallized from 95% ethanol, melted at 152–154°.

Anal. Calcd. for $C_{26}H_{24}FeN_4O_8$: C, 54.19; H, 4.20; Fe, 9.69; N, 9.72. Found: C, 54.27; H, 4.52; Fe, 9.66; N, 9.61.

C. With Phenyl Isocyanate. Synthesis of 2-(Dimethylaminomethyl)-N-phenylferrocenecarboxamide (XIV). A solution of III' from 2.44 g. (10 mmoles) of amine III was prepared as described above; the flask was stoppered and stirred for 1 hr. Treatment with 4.3 ml. of phenyl isocyanate over 20 min. produced a clear solution which began to precipitate solids after stirring for 1 hr. After a total of 4 hr. the reaction was quenched with water, and the crude product was extracted with benzene. The combined organic layers were evaporated on a steam bath and the crude oil was taken up in benzene wherein it was deposited on a 20 × 1 in. column of alumina. Elution with benzene-ether gave a crude fraction which was rechromatographed on the same size alumina column to give 1.11 g. (31%) of XIV as orange crystals, m.p. 121.5–125.5°. Rechromatography of a small sample produced analytical material of m.p. 123.5–125.5°.

Anal. Calcd. for $C_{20}H_{22}FeN_2O$: C, 66.31; H, 6.12; Fe, 15.42; N, 7.73. Found: C, 66.51; H, 6.37; Fe, 15.08; N, 7.58.

The orange picrate, recrystallized from an ethanol-acetonitrile mixture, did not melt below 300° but decomposed slowly from 130°.

Anal. Calcd. for $C_{27}H_{26}FeN_5O_8$: C, 52.79; H, 4.26; N, 11.84. Found: C, 53.14; H, 4.39; N, 11.64.

Lithiation of Dimethylaminomethylferrocene (III) in THF. *n*-Butyllithium²² (26 ml., 40 mmoles) was dripped into a refluxing solution of 2.43 g. (10 mmoles) of III in 15 ml. of THF over a 10-min. period (nitrogen atmosphere). The dark solution was refluxed for 1 hr. and 20 min. The solution was then employed as described below.

Deuteration of III in THF. A solution of 4.86 g. (20 mmoles) of III in 35 ml. of refluxing THF was treated cautiously over 30 min. with 52 ml. (80 mmoles) of *n*-butyllithium in hexane²² (nitrogen atmosphere). After refluxing for 1 hr., the dark solution was hydrolyzed with 4 ml. of D₂O. This addition caused rapid reflux and considerable precipitate. The system was allowed to stand and then was shaken with 20 ml. of water wherein the precipitate dissolved. The aqueous layer was separated and extracted once with ether. The combined organic layer was stripped and distilled through a microapparatus; the fraction was collected, b.p. 95–100° at 0.45 mm., 4.1 g. (84%). The n.m.r. spectrum of this oil is summarized in Table IV.

Synthesis of 2,1'-Di(α,α-diphenylhydroxymethyl)dimethylaminomethylferrocene (VIII) and 1'-(α,α-

Diphenylhydroxymethyl)dimethylaminomethylferrocene (IX). A solution of 7.3 g. (40 mmoles) of benzophenone in 10 ml. of THF was added over 20 min. to a 4:1 mixture of *n*-butyllithium and amine III (see above). This solution was stirred for 4 hr., undergoing during this period a color change from nearly black to orange with suspended solids. The solution was hydrolyzed with water and the resulting two layers were separated. Two additional extractions of the aqueous layer with benzene, combination of the organic extracts, stripping, and trituration with acetone gave a yellow powder, VIII, which was isolated on a Büchner funnel and air dried, yielding 3.1 g. The filtrate was stripped and the residue was chromatographed on a 1.25 × 13 in. alumina column. Fraction 1 (benzene) was found to be contaminated with benzophenone; it was extracted with dilute HCl and neutralized and the resulting oil was taken up in benzene. The benzene was stripped and the oil was induced to crystallize by the addition of a small amount of methanol. Orange crystals were isolated and air-dried on a Hirsh funnel yielding 0.5 g., m.p. 123.5–126.5°, and identified as IV (13%). Fraction 2 (benzene-ether) contained 0.4 g. of additional aminediol (VIII). Fraction 4 (ether-acetone) was crystallized from benzene-hexane to give 0.4 g. (10%) of IX, m.p. 137–147°. Recrystallization from 95% ethanol afforded yellow crystals, m.p. 153–154°.

Anal. Calcd. for $C_{26}H_{27}FeNO$: C, 73.43; H, 6.40; Fe, 13.13. Found: C, 73.24; H, 6.53; Fe, 12.84.

The total crude VIII, 3.5 g., was recrystallized from acetone to give 2.7 g. (45%) of VIII, m.p. 191.5–196.5°; 195–196.5° after further recrystallization from acetone.

Anal. Calcd. for $C_{39}H_{37}FeNO_2$: C, 77.09; H, 6.14; Fe, 9.19; N, 2.31. Found: C, 76.80; H, 6.32; Fe, 9.60; N, 2.30.

The results of a second run utilizing a 1:1 ratio of A to B are noted in Table I.

Lithiation of Carbinol-Amine IV. Condensation with Benzophenone to Produce VIII. A solution of 0.85 g. (2 mmoles) of IV in 5 ml. of refluxing THF was treated dropwise over 5 min. with 2.6 ml. (4 mmoles) of *n*-butyllithium in hexane²² (nitrogen atmosphere). After refluxing for 1 hr., the solution was cooled and 1.1 g. (6 mmoles) of benzophenone in 5 ml. of THF was added over 10 min. The clear amber solution was left stoppered for 4 hr. with stirring and hydrolyzed with water and the layers were separated. Extraction of the aqueous layer with ether was followed by stripping of the combined organic layers. The oily product was chromatographed on a 1 × 20 in. column of alumina. Fraction 1 was eluted with benzene-ether; fraction 2 was eluted with ether-acetone. The former gave 0.3 g. (35%) of orange crystals when triturated with methanol, m.p. 124–126°; this was identified as starting material IV. The second fraction was recrystallized from a small volume of acetone to give 0.4 g. (33%) of orange crystals, m.p. 190–194°. This material was identified as VIII by melting point and by comparison of its infrared spectrum with that of an authentic sample.