

REDUCTION OF FERROCENYLMETHYL QUATERNARY AMMONIUM IODIDES: SYNTHESIS OF METHYLFERROCENES

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Summary

A series of *N*-(2-substituted ferrocenylmethyl)-*N,N,N*-trimethylammonium iodides was reduced via sodium/ammonia and Emde reduction techniques to the corresponding 2-substituted methylferrocenes in order to examine the comparative utility of these two methods. Reduction of a series of *N*-(*p*-substituted benzyl)-*N*-ferrocenylmethyl-*N,N*-dimethylammonium halides demonstrated that both reductions apparently proceed through anionic intermediates.

Introduction

Previously, we have described the synthesis of methylferrocene (I) by the reduction of *N*-ferrocenylmethyl-*N,N,N*-trimethylammonium iodide (Ia) with sodium in liquid ammonia [1], the utility of this reaction being demonstrated by the preparation of the isomeric dimethylferrocenes [2]. The ability of the sodium/ammonia system to effect reduction of the quaternary salt was not surprising in the light of reported behavior of other quaternary ammonium salts under such conditions [3]. It was, however, noteworthy that the ferrocene system remained intact under these strenuous conditions, ferrocene itself [4] and some disubstituted ferrocenes [5] having been reported to be reduced by sodium ammonia or similar alkali metal/amine solutions to Fe^0 and cyclopentadienide anions.

The purpose of this work was to investigate the general utility of the sodium ammonia reduction for the synthesis of methylferrocenes by determining the ability of various substituents to withstand sodium/ammonia conditions. A representative series of 2-substituted dimethylaminomethylferrocenes was prepared by the directed metalation procedure [6] and these amines were transformed into their respective quaternary ammonium salts. This series of compounds was reduced by both the sodium/ammonia technique and the Emde reduction method which has also been employed for the preparation of methylferrocene [7]. A

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comparison of the utility of these two methods was thus rendered possible.

Of mechanistic interest was the question of whether these reductions occurred by way of a one- or two-electron transfer. Reductions in similar systems have been mostly of the two-electron transfer variety; the ratio of cleavage products in such instances has been shown to be electronically controlled [8]. The reduction of *N*-ferrocenylmethyl-*N*-benzyl-*N,N*-dimethylammonium halides with appropriate *p*-phenyl substitution provided some insight into the answering of this question.

Results

Results of the sodium/ammonia and the Emde reductions are summarized in Table 1. Both of these techniques proved quite capable of accomplishing the reduction of a variety of substituted ferrocene quaternary ammonium salts to the corresponding substituted methylferrocene. However, the success of each reduction was dependent upon the ability of the particular substituent to withstand the reaction conditions. For example, the Emde reduction of methiodide Xa resulted in reduction of not only the methiodide moiety but also the benzoyl substituent to give alcohol Xb (Scheme 1). Sodium/ammonia reduction of this compound proceeded with little difficulty to ketone X and the product of this reduction could also be converted to alcohol Xb by sodium amalgam. This last transformation was somewhat unexpected in view of the fact that benzoylferrocene itself is not reduced in this manner by sodium amalgam [9].

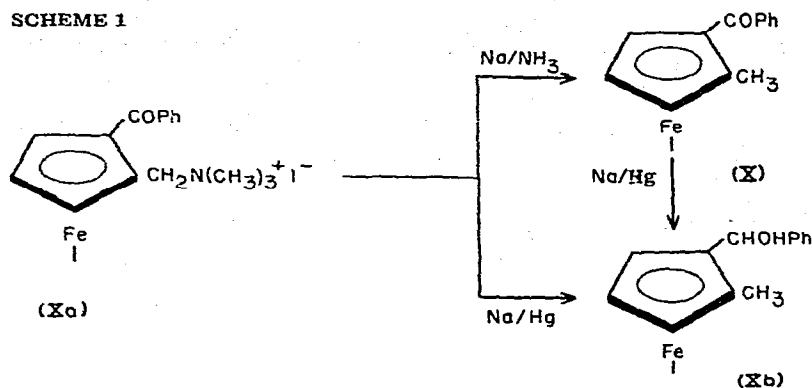
Two compounds were apparently incapable of being reduced by the sodium amalgam reaction, namely *N*-(ferrocenylethyl)-*N,N,N*-trimethylammonium iodide IIa and *N*-[2,1'-bis(diphenylhydroxymethyl)ferrocenylmethyl]-*N,N,N*-trimethylammonium iodide (XIIa), the former providing no evidence of reaction of any kind, the latter affording only a small yield of a cyclization product (XIIb) (see Experimental). The reduction of both these compounds proceeded satisfactorily with the sodium/ammonia system.

TABLE 1
REDUCTION OF SUBSTITUTED *N*-FERROCENYLMETHYL-*N,N,N*-TRIMETHYLAMMONIUM IODIDES
 $Y-CH_2N(CH_3)_3I^- \rightarrow Y-CH_3$

Compound	Y	Yield Na/NH ₃ liquid (%)	Yield Na/Hg (%)
Ia	C ₁₀ H ₉ Fe	85 ^a	95
IIa	C ₅ H ₅ FeC ₅ H ₄ CH ₂	22 ^a	0
IIIa	2-D-C ₁₀ H ₈ Fe	81	84
IVa	2-(CPh ₂ OH)C ₁₀ H ₈ Fe	56 ^a	22
Va	2-CH ₃ C ₁₀ H ₈ Fe	78 ^b	89
VIa	1'-CH ₂ N(CH ₃) ₃ I ⁻ -C ₁₀ H ₈ Fe	66 ^{b,c}	53 ^c
VIIa	2-ClC ₁₀ H ₈ Fe	0 ^a	94
VIIIa	2-Si(CH ₃) ₃ C ₁₀ H ₈ Fe	56	78
Xa	2-COPhC ₁₀ H ₈ Fe	52	0 ^d
XIa	2-CONHPhC ₁₀ H ₈ Fe	0 ^d	50
XIIa	2,1'-(CPh ₂ OH) ₂ C ₁₀ H ₇ Fe	90 ^a	0 ^e

^aRef. 1. ^b Ref. 2. ^c Product is 1,1'-dimethylferrocene. ^d Reduction of the substituent occurred. ^e A small yield of cyclization product (XIIb) was obtained.

SCHEME 1



There were some notable failures of the sodium/ammonia system to afford reductions. *N*-(2-Chloroferrocenylmethyl)-*N,N,N*-trimethylammonium iodide (VIIa) was apparently completely decomposed by sodium/ammonia whereas the reduction proceeded quite well under Emde conditions. The 2-bromo analog of VIIa has been found to be unstable even under Emde conditions [10]. Also, *N*-[(2-*N*-phenylcarboxamido)ferrocenylmethyl]-*N,N,N*-trimethylammonium iodide (XIa) was reduced smoothly by the Emde technique to carboxamide XI whereas in sodium/ammonia, none of the expected product was obtained. A moderate yield of 2-(hydroxymethyl)methylferrocene (IX) was obtained from the sodium/ammonia reaction.

The reduction conditions sometimes affected the substituents. When comparable reduction was achieved, the yields by the Emde method were often superior to those from the sodium/ammonia reduction. On the other hand, the sodium/ammonia reductions were much faster and more convenient. One additional advantage of the Emde reduction method was that D₂O could be substituted for H₂O for labeling purposes, i.e., deuterium-labeled alkyl substituents could be synthesized. Table 2 lists the α -deuterated alkylferrocenes prepared by this modification.

Mechanistic considerations

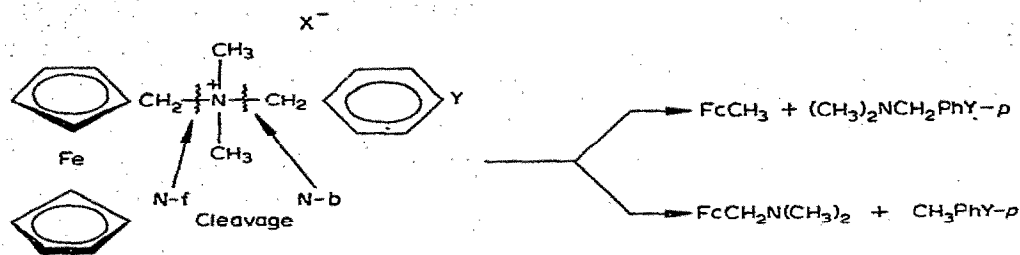
The results of the reduction of a series of *N*-(*para*-substituted benzyl)-*N*-ferrocenylmethyl-*N,N*-dimethylammonium halides are shown in Table 3. Reduction in this series could occur with cleavage of either the ferrocenylmethyl-nitrogen bond or the benzyl-nitrogen bond. Either a one- or two-electron trans-

TABLE 2

2-SUBSTITUTED α -DEUTERIOMETHYLFERROCENES PREPARED BY REDUCTION WITH Na/Hg, D₂O

Reduced methiodide	2-Substituent in product	Yield (%)
Ia	H	80
Va	CH ₃	38
VIIa	Cl	54
VIIIa	Si(CH ₃) ₃	86

TABLE 3

REDUCTION OF *N*-(*p*-SUBSTITUTED BENZYL)-*N*-FERROCENYLMETHYL-*N,N*-DIMETHYLAMMONIUM HALIDES

Compound	Y	X	$\frac{N-f}{N-b}$ (Na/NH ₃) ^a	$\frac{N-f}{N-b}$ (Na/Hg) ^a
XIIIa	H	Cl	—	17/81
XIIIb	H	Br	17/77 ^b	—
XIIIc	H	I	13/67	0/0 ^b
XIV	CH ₃	Br	25(57)/11	14(15)/13
XVa	OCH ₃	Br	19(34)/0	53/6
XVb	OCH ₃	I	17/0	19/0

^a Except where indicated by parentheses, values represent yields of methylferrocene and dimethylamino-methylferrocene, respectively. Values in parentheses represent yields of the *para*-substituted dimethylbenzylamine, as determined by NMR. Recorded yields of methylferrocene should be considered as a lower limit since some of this material was invariably lost during isolation due to its high volatility. ^b A 25% yield of hydroxymethylferrocene was obtained.

fer to the quaternary nitrogen could be involved accompanied by the homolytic or heterolytic cleavage, respectively, of the carbon–nitrogen bond. The ferrocenyl methyl or benzyl free radical/carbanion thereby formed could then accept hydrogen or a proton from the solvent. Thus, the effect of the *p*-substituent on the product ratios should be an indication of whether the intermediate were anionic or free radical in nature.

For the sodium/ammonia reduction, the results (Table 3) showed that the methoxy substituent had a profound influence on the benzyl–nitrogen cleavage, i.e., complete suppression of this cleavage was observed, whereas it was the favored reaction in the unsubstituted benzyl derivative. This decided change in reactivity of the benzyl–nitrogen bond upon addition of an electron-donating group is indicative of an anionic transition state resulting from a two-electron transfer. For the Emde reduction of these compounds, the results were similar. Furthermore, if such reductions are truly electronically controlled, these results allow assessment of the electronic effect of ferrocene as a substituent as intermediate between that of the phenyl and *p*-tolyl groups. Previously, the electronic effect of the ferrocene substituent had been estimated as falling between those of the methyl and methoxy groups [11].

The effect of the halide ion on the Emde reduction in the benzyl system can be explained by assuming that at least the chloride and perhaps the bromide salt exists as a tight ion pair in aqueous solution while the iodide salt exists as either a relatively polarized ion pair or is dissociated altogether. This would allow the most dissociated salt to be most susceptible to a nucleophilic substitution process as observed.

TABLE 4
NMR SPECTRA OF FERROCENYLMETHYL QUATERNARY AMMONIUM HALIDES IN CDCl_3

Compound ^a	Chemical shifts (Hz vs. internal TMS)				
	Ferrocene ring position				
	2 ^c	3	1'	CH ₂	CH ₃
$(\text{FcCH}_2\text{NMe}_2\text{CH}_2\text{Ph})^+\text{Cl}^-$	275	258	253	300 ^b , 300 ^b	184
$(\text{FcCH}_2\text{NMe}_2\text{CH}_2\text{Ph})^+\text{I}^-$	280	257	257	308 ^b , 299 ^b	183.5
$(\text{FcCH}_2\text{NMe}_3)^+\text{Cl}^-$	271.5	256.5	256.5	282.5	197
$(\text{FcCH}_2\text{NMe}_3)^+\text{Br}^-$	275.5	259	259	291	199
$(\text{FcCH}_2\text{NMe}_3)^+\text{I}^-$	278.5	259.5	259.5	298	200

^a Fc = $\text{C}_5\text{H}_5\text{FeC}_5\text{H}_4$. ^b Two methylene proton signals. ^c Assignment was made to the 2-position protons of the ferrocene ring system as being furthest downfield of the ring system protons. This was verified for one compound by synthesis of 2-deuteriodimethylaminomethylferrocene [6] and preparation of the quaternary ammonium iodide therefrom. The signal at 278.5 Hz was attenuated.

Such a hypothesis is supported by an NMR study of the salts with the data being recorded in Table 4. The chemical shifts in deuteriochloroform of the methylene and the 2-position protons of the ferrocene rings shift upfield as the halogen is changed from $\text{Cl} \rightarrow \text{Br} \rightarrow \text{I}$. Less shielding by the halide ion is clearly indicated and this can be attributed to an increasing looseness of the ion pair. Since apparently only the ferrocene methylenes and the 2-position protons are affected, it is suggested that the halide ion is mainly associated with the ferrocene side of the quaternary nitrogen.

Experimental

General

NMR spectra were run on a Varian A 56/60 spectrometer at ambient temperature. Elemental analyses were performed by Galbraith Laboratories, Nashville, Tenn., or by Alfred Bernhardt Laboratory, Mulheim, West Germany. IR spectra were run on a Perkin-Elmer Infracord 137 instrument as either smears or Nujol mulls. Mass spectra were obtained on a Consolidated Electrodynamics 21-104 spectrometer, with a 70 volt ionizing potential, a 200° inlet temperature and a 240° source temperature.

Each quaternary ammonium salt was prepared by adding the appropriate alkyl halide to an ether solution of the appropriately substituted dimethylaminomethylferrocene. The precipitated ammonium salt was then filtered and reprecipitated from methanol/ether.

Except where noted, the sodium/liquid ammonia reductions were carried out by the general procedure which follows. The quaternary ammonium salt (0.35 to 10 mmoles) was placed in a 250 or 500 ml round bottom flask equipped with a magnetic stirrer. Ammonia was then introduced until the flask was about half full. Sodium, typically in approximately a 12/1 molar excess was added as small chunks or pea size spheres at a rate sufficiently slow to avoid excessive bumping. After 15-30 min, solid NH_4Cl was added to quench the reaction. The crude reaction mixture was worked up by evaporation of the ammonia, followed by addition of water, extraction with ether and evaporation of the combined ether extracts. The crude product was isolated by column chromatography on alumina, vapor phase chromatography or vacuum distillation.

The Emde reductions were carried out by a modification of the procedure described by Nesmeyanov et al. [7]; that is, by adding the ammonium salt (0.8 to 10 mmoles) to a mixture of water and benzene followed by the addition of 5-10% sodium amalgam (usually 10/1 excess). The reaction mixture was then placed on a steam bath and heated at reflux for approximately 1 h, after which time it was stirred at room temperature until the amber color had been transferred from the water layer to the benzene layer. The benzene layer was separated and stripped to give a crude product which was purified by chromatography on alumina, vacuum distillation or vacuum sublimation.

Analytical data for these products are recorded in Table 5 while summaries of the experimental conditions used for each reduction are to be found in Table 6.

TABLE 5
ANALYTICAL DATA FOR 2-SUBSTITUTED METHYLFERROCENES^a

Compound	NMR (δ) ^b	Elemental analysis	Mass spectrum
α -D-methylferrocene	1.92 (2.0 protons, t, J (H-D) 2 Hz), 3.92-4.09 (9.0 protons, m)		201 (mol. ion), 135, 134, 121, 82, 81, 56
2-D-methylferrocene	1.95 (3.0 protons, s), 4.03 (8.1 protons, m).		202, 201 (mol. ion), 200, 136, 135, 121, 82, 81, 56 ^c
IV	1.64 (2.6 protons, s), 3.39 (0.8 protons, m), 3.65 (0.9 protons, s), 4.09 (7.03 protons, unresolved), 7.09 (10.5 protons, unresolved)		
2-methyl- α -D-methylferrocene	1.92 (1.9 protons, t, J (H-D) 2.2 Hz), 1.93 (3.0 protons, s), 4.00 (8.0 protons, m)		215 (mol. ion), 200, 199, 149, 148, 121, 92, 91, 82, 81, 56
2-chloro- α -D-methylferrocene	2.03 (2.0 protons, t, J (H-D) 2 Hz), 4.12 (8.0 protons, m)		
2-trimethylsilyl- α -D-methylferrocene	0.26 (9.0 protons, s), 1.97 (3.0 protons, s), 4.00 (8.1 protons, m)	C ₁₄ H ₂₀ FeSi Found (calcd.) C, 61.99 (61.77) H, 7.36 (7.41) Si, 10.21 (10.32)	
X	(CCl ₄) 2.32 (3.0 protons, s), 4.02 (5.4 protons, s), 4.15 (1.0 proton, m), 4.32 (2.0 protons, m), 7.16-7.87 (4.8 protons, m)	C ₁₈ H ₁₆ FeO Found (calcd.) C, 70.96 (71.08) H, 5.48 (5.30) Fe, 18.26 (18.36)	
XI	2.30 (3.0 protons, s), 4.00-4.27 (7.0 protons, m), 4.55 (0.9 protons, m), 6.79-7.82 (6.2 protons, m)	C ₁₃ H ₁₇ ONFe Found (calcd.) C, 68.32 (67.72) H, 5.28 (5.33) N, 4.18 (4.39) Fe, 15.80 (17.6)	
XII	3.20-4.80 (8.8 protons, unresolved), 6.31 (1.2 protons, s), 7.00-7.80 (20.2 protons, unresolved)	C ₃₇ H ₃₀ FeO ₂ Found (calcd.) C, 78.72 (79.00) H, 5.42 (5.37) Fe, 9.57 (9.93)	

^a All compounds were found to exhibit 9 and 10 μ bands in their respective IR spectra [13]. ^c Spectra run in CDCl₃ unless otherwise noted; s = singlet; t = triplet, m = multiplet. ^c The 202 peak is due to a small amount of 2,5-dideuteriomethylferrocene present.

TABLE 6
REDUCTIONS OF 2-SUBSTITUTED DIMETHYLAMINOMETHYLFERROCENE METHIODIDES; EXPERIMENTAL CONDITIONS

Methiodide	Weight (g)	mmoles	Na/Hg (g/%)	Na (g)	Yield (g) ^a	Product ^c
Ia	3.85	10.0	200/10		1.89	I ^d
Ia	1.92	5.0	100/10		0.40	α -D-methylferrocene
IIIa	2.00	5.2		3	0.85	III ^e
IIIa	3.86	10.0	175/7		1.6	III ^e
IVa	0.67	1.2	25/10		0.10	IV ^f
Va	3.99	10.0	175/7		1.9	V ^g
Va	1.5	5.0	67/10		0.30	2-methyl- α -D-methylferrocene
VIa	1.6	2.7	144/6		0.31	VI ^g
VIIa	2.1	5.0	175/7		1.09	VII ^{g,h}
VIIa	2.1	5.0	175/7		0.64	2-chloro- α -D-methylferrocene
VIIIa	0.16	0.35		0.5	0.55	VIII ⁱ
VIIIa	4.56	10.0	175/7		2.13	VIII ⁱ
VIIIa	0.35	0.8	144/7		0.18	2-trimethylsilyl- α -D-methylferrocene
Xa	0.31	0.6		0.29	0.10	X
Xa	1.28	2.7	26/10		0.31	Xb
XIa	0.96	1.9	40/20		0.3	XI
XIa	0.35	0.7		1.5	0.095	IX ^j
XIIa	0.69	0.9	20.8/10		0.120	XIIb ^k

^a Yield (%) recorded in Table 1. ^b Attempted Na/NH₃ reduction of this system resulted in decomposition. ^c α -Deuterio compounds synthesized via use of D₂O in the Emde reduction (Table 2). ^d Properties were identical to those described for this compound in ref. 1. ^e Starting material 2-deuteriodimethylaminomethylferrocene prepared as described in ref. 6. ^f Properties were identical to those described for this compound in ref. 12. ^g Properties were identical to those described for this compound in ref. 2. ^h Properties were identical to those communicated to us by Professors Marr and Rockett [10]. ⁱ Starting material *N*-(2-trimethylsilyl)-*N,N,N*-trimethylammonium iodide prepared as described in ref. 14. ^j Properties were identical to those of the compound prepared according to ref. 15. ^k Successful synthesis of XII via the Na/NH₃ technique is recorded in ref. 1.

Preparation of *N*-(2-deuterioferrocenylmethyl)-*N,N,N*-trimethylammonium iodide (IIIa)

Dimethylaminomethylferrocene (2.08g, 8.55 mmoles), anhydrous ether (about 200 ml), and *n*-butyllithium (10 ml, 1.6 M, 16 mmoles) in hexane were mixed in a 500 ml flask for 1.5 h followed by addition of excess deuterium oxide (about 5 ml). Mass spectral analysis of an evaporated aliquot of this amine solution indicated the incorporation of about 0.80 deuterium atom/molecule [6]. After an additional 30 min, the mixture was filtered. Excess methyl iodide was added, yielding a yellow precipitate. The precipitate was filtered, dissolved in methanol, reprecipitated with ether and filtered again. The solid was washed with ether and air dried, yielding *N*-(2-deuterioferrocenylmethyl)-*N,N,N*-trimethylammonium iodide (IIIa) (2.25 g, 69%), dec. 181°.

Emde reduction of *N*-(2-benzoylferrocenylmethyl)-*N,N,N*-trimethylammonium iodide (Xa)

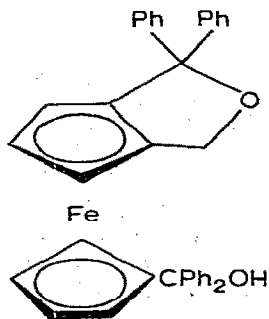
Ammonium salt (Xa) (1.28 g, 2.66 mmoles), 10% sodium amalgam (26 g, 11 mmoles), 140 ml of water and 100 ml of benzene in a 250 ml flask reacted overnight at room temperature. The benzene layer was combined with an ether extraction layer, stripped of solvent and chromatographed on Alumina III. Ben-

zene eluted 2-(phenylhydroxymethyl)methylferrocene (Xb) (0.31 g, 38%) as an oil. Anal. Found: C, 70.28; H, 6.05. $C_{18}H_{16}FeO$ calcd.: C, 70.61; H, 5.93%. NMR (δ , CCl_4): 1.96 (9.0 protons, singlet), 2.21 (1.1 protons, broad singlet), 3.75-4.17 (8.0 protons, multiplet), 5.45 (0.9 proton, broad singlet), 7.12-7.50 (5.0 protons, multiplet). IR (μ): 2.95 (O-H), 9.09 and 10.04 (9, 10 μ bands) [13].

An attempt to detect 2-(benzoyl)methylferrocene as an intermediate in this reaction by stopping the reaction after 30 min was unsuccessful, only the above mentioned alcohol being detected. The above alcohol was actually a mixture of the 2-diastereomeric pairs of enantiomers. Enrichment in small amounts of each isomer was possible by careful chromatography, but complete separation was not accomplished.

Emde reduction of N-[2,1'-bis(diphenylhydroxymethyl)ferrocenylmethyl]-N,N,N-trimethylammonium iodide (XIIa)

Ammonium salt XIIa (0.69 g, 0.89 mmole) was combined with 10% sodium amalgam (20.8 g, 90 mmoles), 100 ml of water and about 50 ml of benzene. The mixture was heated to reflux for 3 h, then left at room temperature for two days. The benzene layer was taken, stripped and chromatographed on Alumina III. The eluant was stripped of solvent and washed with petroleum ether to yield a yellow solid (dec. 220°). Chromatography of the combined petroleum ether washings brought more of the high melting solid (total 0.12 g) and a small amount of an oily material. That the solid product was not the expected reduction product was evidence by the lack of a methyl resonance in the NMR spectrum of the material, but most likely a nucleophilic substitution/cyclization product, XIIb. Anal. Found: C, 78.72; H, 5.42; Fe, 9.57. $C_{37}H_{30}FeO$ calcd.: C, 79.00; H, 5.37; Fe, 9.93%. NMR (δ , $CDCl_3$): 3.20-4.80 (8.8 protons, unresolved resonances), 6.31 (1.2 protons, singlet), 7.00-7.80 (20.2 protons, unresolved resonances).



(XII b)

Emde reduction of 2-(benzoyl)methylferrocene (X)

2-(Benzoyl)methylferrocene (X) (0.04 g, 0.13 mmole), 10% sodium amalgam (14.16 g, 62 mmoles), 75 ml of water and about 50 ml of benzene were mixed in a 250 ml round bottom flask equipped with a magnetic stirrer. The mixture was stirred (rapidly enough to mix the phases well) for one day. The benzene layer was then combined with an ether extract and the combined solution evaporated. The resulting oil was chromatographed on Alumina III. Two

bands were collected. A small pink band was first collected yielding 12 mg of an unidentified material. A yellow fraction was then collected and evaporated, yielding 2-(phenylhydroxymethyl)methylferrocene (Xb) (0.010 g, 20%) identified by comparison of its IR and NMR spectra with those of the material prepared by the Emde reduction of methiodide Xa.

Sodium/liquid ammonia reduction of N-[2-(N-phenylcarboxamido)ferrocenylmethyl]-N,N,N-trimethylammonium iodide (XIa)

Ammonium salt XIa (0.350 g, 0.695 mmole) was suspended in 125 ml of liquid ammonia. An excess (approximately 1.5 g, 66 mmoles) of sodium spheres was then added. After the solution had turned blue (10 min), ammonium chloride was added. Water was added and the mixture was extracted three times with ether. The ether layers were dried over magnesium sulfate, stripped of solvent, and chromatographed on activated alumina. The main band was eluted with benzene and was stripped of solvent. The resulting oil was identified as 2-(hydroxymethyl)methylferrocene (IX) (0.0948 g, 59%) by its mass spectrum (molecular ion at m/e 230) and by comparison of its NMR spectrum to that of an authentic sample prepared by literature procedures [15]. NMR (δ , CCl_4) 1.33 (1.1 protons, broad singlet), 2.02 (3.0 protons, singlet), 4.07 (8.0 protons, broad singlet), 4.30 (1.9 protons, singlet).

Emde reduction of N-benzyl-N-ferrocenylmethyl-N,N-dimethylammonium chloride (XIIIa) [16]

Ammonium salt XIIIa (4.48 g, 12.2 mmoles), 20% sodium amalgam (124 g), water (90 ml) and benzene (100 ml) were refluxed in a 250 ml flask for 1 h. The benzene layer was combined with the benzene extracts and the solvent was evaporated. Chromatography of the residue on Alumina I yielded methylferrocene (0.401 g, 16.5%) and dimethylaminomethylferrocene (2.4 g, 81%), identified by comparison of their respective NMR spectra with those of authentic samples.

Sodium/liquid ammonia reduction of N-benzyl-N-ferrocenylmethyl-N,N-dimethylammonium bromide (XIIIb)

Quaternary ammonium salt XIIIb (3.87 g, 9.4 mmoles) was dissolved in ammonia and sodium pellets (8.0 g, 350 mmoles) were added with stirring. After 12 min, NH_4Cl was added. Addition of water and ether followed. The combined ether extracts were dried over MgSO_4 , stripped of solvent and chromatographed on Alumina I, yielding methylferrocene (0.32 g, 17.1%) and dimethylaminomethylferrocene (1.76 g, 77.3%).

Reduction of N-benzyl-N-ferrocenylmethyl-N,N-dimethylammonium iodide (XIIIc)

1. *Sodium/liquid ammonia reduction.* A procedure similar to that for salt XIIIb was followed utilizing 1.92 g (4.14 mmoles) of ammonium salt XIIIc. Chromatography of the evaporated ether extracts yielded methylferrocene [0.10 g, 12% (13% based on unrecovered starting material)] and dimethylaminomethylferrocene [0.60 g, 60% (67% based on unrecovered starting material)]. Chloroform extraction of the reaction mixture yielded 0.2 g (10%) of starting material.

2. *Emde reduction.* A procedure similar to that for the reduction of XIIIa was followed utilizing 2.51 g (5.43 mmoles) of salt XIIIc. The combined benzene extracts were evaporated and chromatographed yielding hydroxymethylferrocene [0.30 g, 25% (45% based on unrecovered starting material)]. Chloroform extraction of the reaction mixture yielded starting material (1.1 g, 44%).

Reduction of N-p-methylbenzyl-N-ferrocenylmethyl-N,N-dimethylammonium bromide (XIV)

1. *Sodium/liquid ammonia reduction.* A procedure similar to that for reduction of XIIIb was followed utilizing 0.29 g (0.56 mmole) of ammonium salt XIV. The ether extracts were combined, dried over MgSO₄ and evaporated, yielding 0.10 g of crude product. This material was analyzed by NMR showing a ratio of 1.0/0.44/2.2/0.44 for methylferrocene, dimethylaminomethylferrocene, dimethyl-*p*-methylbenzylamine and *p*-xylene, respectively. Chromatography brought an isolated yield of 0.0182 g (18%) for methylferrocene; the amount of dimethylaminomethylferrocene was insufficient for isolation.

2. *Emde reduction.* A procedure similar to that for reduction of XIIIa was followed utilizing 0.20 g (0.46 mmole) of ammonium salt XIV. The benzene layer was combined with ether extracts of the aqueous layer, dried over MgSO₄ and evaporated yielding 52.0 mg of product mixture. NMR analysis showed calculated yields of 13.5, 13.4, 15.4 and 13.4% for methylferrocene, dimethylaminomethylferrocene, *p*-methylbenzyl-*N,N*-dimethylamine and hydroxymethylferrocene, respectively. Chromatography yielded 5 mg (6%) of methylferrocene, and about 25 mg of an unseparated mixture of dimethylaminomethylferrocene and hydroxymethylferrocene.

Reduction of N-(p-methoxybenzyl)-N-(ferrocenylmethyl)-N,N-dimethylammonium bromide (XVa)

1. *Emde reduction.* A procedure similar to that for XIIIa was followed, utilizing 1.33 g (3.0 mmoles) of ammonium salt XVa. The benzene layer was separated, combined with ether extracts of the aqueous layer, dried over MgSO₄ and evaporated. NMR analysis of this oily product showed the presence of methylferrocene and *p*-methoxybenzyl-*N,N*-dimethylamine in a ratio of 0.8/1.0. Other small peaks were also present, possibly attributable to trace amounts of dimethylaminomethylferrocene and *p*-methoxytoluene. Chromatography of this mixture yielded methylferrocene (0.316 g, 53%) and dimethylaminomethylferrocene (0.04 g, 5.5%), both identified by their NMR spectra. No starting material was isolated.

2. *Sodium/liquid ammonia reduction.* A procedure similar to that for salt XIIIb was followed utilizing 0.60 g (1.35 mmoles) of ammonium salt XVa. The combined ether extracts were dried over MgSO₄ and evaporated. This oily product was analyzed by NMR which revealed a 1/1.8 ratio of methylferrocene to *p*-methoxybenzyl-*N,N*-dimethylamine. Chromatography yielded methylferrocene (0.053 g, 19%).

Reduction of N-(p-methoxybenzyl)-N-(ferrocenylmethyl)-N,N-dimethylammonium iodide (XVb)

1. *Emde reduction.* A procedure similar to that for XIIIa was followed

utilizing 2.1 g (4.3 mmoles) of ammonium salt XVb. The benzene extracts were dried over $MgSO_4$ and chromatographed on Alumina I yielding methylferrocene [0.15 g, 18.5% (19.5% based upon unrecovered starting material)], identified by its NMR spectrum. Essentially no dimethylaminomethylferrocene was isolated, and only 0.1 g (5%) of starting material could be recovered.

2. *Sodium/liquid ammonia reduction.* A procedure similar to that for XIIIb was followed utilizing 0.69 g (1.3 mmoles) of ammonium salt XVb. The ether extracts were stripped and chromatographed on Alumina I yielding methylferrocene (0.060 g, 17%), identified by comparison of its NMR spectrum with that of an authentic sample. No dimethylaminomethylferrocene was obtained.

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