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Organometalloidal derivatives of the transition metals

XXXIII *. Reactions of ferrocenylcarboxaldehyde with base and trimethylsilylcyanide. A new high yield reaction for the formation of cyano-amines or silylethers

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Abstract

Treatment of ferrocenecarboxaldehyde with base at 0°C, lithium diisopropylamide (LDA) or n-hutyllithium, followed by the addition of trimethylsilylcyanide, produced 1-(diisopropylamino)cyanomethylferrocene, $FcCH(N(^iPr)_2)(CN)$ (**II**) or 1-trimethylsiloxy-n-pentylferrocene, $FcCH(^nBu)OSiMe_3$ (**IIIa**). The reaction of naphthaldehyde, NpCHO, with LDA/Me_3SiCN led to formation of 1-(diisopropylamino)cyanomethylnaphthalene, $NpCH\{N(^iPr)_2\}(CN)$ suggesting a general new synthesis for cyanoamines. The reaction of ferrocenecarboxaldehyde with Me_3SiCN led to the expected silylether $FcCH(CN)OSiMe_3$ (**I**). An alternative synthesis of ferrocenylmethylsilylethers, $FcCH_2OSiR_3$ (**IV**), involved the reaction of 1-ferrocenylmethanol with R_3SiCl in the presence of pyridine. The basicity of the new silylethers **III** and **IV** is reported.

1. Introduction

The preparation and use of cyanohydrin O-silyl ethers, enol silyl ethers and silyl ethers for chemical transformation of functional groups is an active area of research [2,3]. Studies of α-ferrocenyl derivatives, including stereoselective peptide synthesis, is also an area of broad interest [4].

Aldehydes and ketones react efficiently with trimethylsilyl cyanide to produce the corresponding cyanide O-silyl ether (eqn. (1)).

$$RC(O)R^1 + Me_3SiCN \longrightarrow RC(CN)(R^1)OSiMe_3 \quad (1)$$

This method of protection of the carbonyl group has been used successfully by Hünig and co-workers [2d] to study intramolecular Diels–Alder adducts with furan, and cyanohydrins have also been transformed into unsymmetrically substituted acyloins [2e]. The use of cyanohydrin O-silyl ethers for the preparation of prostaglandin precursors [2h] and the synthesis of cyanohydrin ethers with high optical purity (> 90%) for transformation into a variety of optically active compounds such as cyanohydrins, amino alcohols and α-hydroxy esters [2d,2i], represent examples of the chemical versatility of such systems. Picard and co-workers have also used related chemistry to study enamines of acylsilanes [2g].

The preparation of 1-ferrocenyl-1-cyanomethyl(dimethyl)amine reported using ferrocenecarboxaldehyde, dimethylamine, and potassium cyanide (eqn. (2)) [4a].

$$FcC(H)O + HNMe_2 + KCN \xrightarrow{MeOH} FcCH(CN)NMe_2 \quad (2)$$

This compound is important in the preparation of 1-ferrocenyl-2-methyl-1-propylamine, a good chiral template in the asymmetric synthesis of peptides [4a,b]. The synthesis outlined in eqn. (2) is a form of the well-known Strecker synthesis [5].

We wish to report the reactions between ferrocenylcarboxaldehyde, FcCHO, and the bases lithium diisopropylamide (LDA) and n-butyllithium, followed by

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treatment with trimethylsilylcyanide. These reactions led to differing compounds, namely 1-(diisopropylamino)cyanomethylferrocene, $FcCH(CN)(N\{^iPr\}_2)$, in the former case, and a ferrocenylsilylether, $FcCH(^nBu)(OSiMe_3)$, in the latter case. Spectroscopic analysis of the new compounds, along with base strength studies are also presented. The reaction of ferrocenecarboxaldehyde with Me_3SiCN led to the formation of $FcCH(CN)OSiMe_3$.

2. Results and discussion

The reaction between ferrocenecarboxaldehyde and trimethylsilylcyanide produced the expected addition product $FcCH(CN)OSiMe_3$ (**I**) in good yield (eqn. (3)). The reaction between ferrocenecarboxaldehyde and LDA at 0°C, followed by the addition of trimethylsilyl cyanide produced 1-(diisopropylamino)cyanomethylferrocene (**II**) in excellent yield as the only isolable product (eqn. (4)).

$$FcCHO + Me_3SiCN \longrightarrow \underset{\textbf{(I)}}{FcCH(CN)OSiMe_3} \quad (3)$$

$$FcCHO + LDA + Me_3SiCN \xrightarrow{THF} \underset{\textbf{(II)}}{FcCH(CN)(N\{^iPr\}_2)} \quad (4)$$

The spectral characterizations of the new complexes are presented in Table 1 and are in accord with the proposed structures. The formation of **II** was unexpected but presumably results from the scheme outlined below in which secondary nucleophilic attack by cyanide upon the initially formed silylether results in displacement of the Me_3SiO^- group.

$$FcCHO + \xrightarrow[TMSCl]{LDA} [FcCH(OTMS)(N\{^iPr\}_2)] \xrightarrow[-OTMS]{CN^-} [FcCH(CN)(N\{^iPr\}_2)]$$

To verify this proposal, ferrocenecarboxaldehyde was treated with LDA followed by Me_3SiCl and this mixture transferred to a flask containing KCN and 18-C-6 in THF. After column chromatography, **II** was isolated, consistent with the pathway illustrated. The reason for the facility of the siloxy group displacement is due to two distinctive factors: (a) the effect of the amino group in donating electrons to an incipient carbocation formed upon loss of the $[OSiMe_3]^-$ group; (b) the well-established stability of α-ferrocenyl carbocations. In a separate experiment, we used naphthaldehyde as the aldehyde substrate to investigate the generality of this interesting transformation, and isolated, in poor

TABLE 1. Yield, melting point, analytical and spectroscopic data for new complexes [a,b]

$FcCH(CN)(N\{^iPr\}_2)$ **(II)** 83%, m.p. 85–86°C
Analysis C, 66.66(66.03); H, 7.40(7.52); N, 8.64(8.33)%
IR (cm^{-1}) 3098, 2965, 2931, 2871, 2254, 1463, 1398, 1367
^1H 4.71 (s); 4.42 (bd, s); 4.14 (bd, s); 3.17 (h, $CH(CH_3)_2$; $J\{^1H-^1H\}$ 6.64 Hz); 1.14 (d, $CH(CH_3)$, $J = 6.64$ Hz); 0.8 (d, $CH(CH_3)$, $J = 6.64$ Hz)
^{13}C 121.3 (s, CN), 84.5 (s, C-CN), 69.2 (C_5H_5), 68.9, 68.2, 67.7 (C_5H_4); 47.5 (d, N-CH), 46.0 (d, N-CH), 23.3 (q, N-C-CH_3), 19.8 (q, N-C-CH_3)

$FcCH_2OSiMe_3$ **(IVa)** 50%, m.p. 60°C
Analysis C, 58.34(58.18); H, 6.99(6.94)%
^1H 4.5 (s, CH_2); 4.2, 3.0 (m, C_5H_4); 4.0 (s, C_5H_5); 0.2 (s, $SiMe_3$)
^{13}C 68.7 (C_5H_5); 68.9, 68.2, 68.3 (C_5H_4); 61.3 (CH_2); −0.06 ($SiMe_3$)
^{29}Si 16.1

$FcCH_2OSiMe_2Ph$ **(IVb)** 40%, m.p. 56°C
Analysis C, 65.17(65.30); H, 6.29(6.41)%
^1H 8.0 (m, SiPh); 4.8 (s, CH_2); 4.4 (s, Fc); 0.4 (s, $SiMe_2$)
^{13}C 134.0, 130.0 (SiPh); 69.0 (C_5H_5); 68.6, 69.1 (C_5H_4); 62.0 (CH_2); −0.9($SiMe_2$)
^{29}Si 7.2

$FcCH_2OSiMePh_2$ **(IVc)** 45%
Analysis C, 69.93(69.43); H, 5.83(5.99)%
^1H 7.9 (m, $SiPh_2$); 4.9 (s, CH_2); 4.4 (s, Fc); 0.7 (s, SiMe)
^{13}C 135.0, 130.0 ($SiPh_2$); 68.7 (C_5H_5); 68.3 (C_5H_4); 62.1 (CH_2); −2.42 (SiMe)
^{29}Si −2.7

$FcCH_2OSiPh_3$ **(IVd)** 30%, m.p. 138°C
Analysis C, 73.41(73.46); H, 5.52(5.66)%
^1H 7.3 (m, $SiPh_3$); 4.5 (s, CH_2); 3.9 (s, Fc)
^{13}C 136.0, 130.0 ($SiPh_3$); 68.7 (C_5H_5); 68.3 (C_5H_4); 62.6 (CH_2)
^{29}Si −12.2

$FcCH_2OSiMe_2SiMe_3$ **(IVe)** 35%
Analysis C,55.36(56.11); H, 6.76(7.49)%
^1H 4.7 (s, CH_2); 4.4 (s, Fc); 0.2 ($SiMe_2$); 0.1 (s, $SiMe_3$)
^{13}C 68.8 (C_5H_5); 68.6, 68.2 (C_5H_4); 62.0 (CH_2); −0.4 ($SiMe_2$); −1.9 ($SiMe_3$)
^{29}Si −21.8, 14.8

$FcCH_2OSiMe_2SiMe_2SiMe_3$ **(IVf)** 38%
^1H 4.3 (s, CH_2); 4.0, 3.7 (m, C_5H_4); 3.8 (s, C_5H_5); −0.1 (s, $OSiMe_2$); −0.25 (s, $SiMe_2$); −0.3 (s, $SiMe_3$)
^{13}C 68.7 (C_5H_5); 68.2 (C_5H_4); 62.0 (CH_2); 0.55 ($OSiMe_2$); −1.44 ($SiMe_2$), −6.56 ($SiMe_3$)
^{29}Si −16.2, −50.8, 17.3

$FcCH_2OSiMe(SiMe_3)_2$ **(IVg)** 35%
^1H 4.3 (s, CH_2); 4.0 and 3.7 (m, C_5H_4); 3.8 (s, C_5H_5); −0.5 (s, SiMe); −0.3 (s, $SiMe_3$)
^{13}C 68.7 (C_5H_4); 68.1 (C_5H_5); 63.9 (CH_2); −1.06 (SiMe); −2.82 ($SiMe_3$)
^{29}Si −19.6, 10.6

$FcCH(^nBu)OSiMe_3$ **(IIIa)** 76%
^1H 4.5 (H), 4.1 (Fc), 1.7–0.9 (^nBu); 0.08 ($SiMe_3$)
^{13}C 92.9, 71.0–65.0, 37.6, 28.3, 22.8, 0.5
^{29}Si 14.5

TABLE 1 (continued)

FcCH(^{n}Bu)OSiMe$_2$Ph (**IIIb**) 67%	
^{1}H	7.6, 7.40–7.32 (Ph); 4.5 (H); 4.0 (s, Fc); 1.8–0.9 (^{n}Bu); 0.3 (SiMe$_2$)
^{13}C	137.4, 134.9, 129.9 (Ph), 92.6 (OCH), 72.0–66.3 (Fc), 38.2, 28.3, 23.0, 14.4 (^{n}Bu), −1.5 (SiMe$_2$)
^{29}Si	4.3
FcCH(^{n}Bu)OSiMePh$_2$ (**IIIc**) 63%	
Analysis	C, 71.05(71.96); H, 7.01(7.10)%
^{1}H	8.0–7.5 (Ph); 4.5 (t, OCH); 3.9 (s, Fc); 2.0–0.9 (^{n}Bu); 0.5 (SiMe$_3$)
^{13}C	139.0, 135.0, 129.8, 127.7 (Ph); 92.9 (OCH); 38.3, 28.4, 23.0, 14.3 (^{n}Bu); −0.3 (SiMe$_3$)
^{29}Si	−5.7
FcCH(^{n}Bu)OSiPh$_3$ (**IIId**) 55%, m.p. 110–112°C	
Analysis	C, 74.70(74.39); H, 6.46(6.48)%
^{1}H	7.6 and 7.4 (Ph); 4.7, 4.1, 4.0, 1.8, 1.3–1.1, 0.8
^{13}C	135.7, 135.0, 129.8, 127.7 (Ph), 92.1 (OCH), 72.2– 66.0 (Fc), 37.6, 27.8, 22.6, 14.0 (^{n}Bu)
^{29}Si	−14.2
FcCH(Et)OSiMe$_3$ (**IV**) 54%	
Analysis	C, 60.56(60.32); H, 7.94(7.88)%
^{1}H	4.4 (bt); 4.1 (s); 4.0 (bs, Fc); 1.8 (q, CH_2CH$_3$, J = 7.6 Hz); 1.0 (t, CH$_2$CH_3); 0.13 (SiMe)
^{13}C	93.2 (OCH); 72.4, 67.9, 67.7, 67.3, 66.3 (C$_5$H$_4$); 68.8 (C$_5$H$_5$)
^{29}Si	13.8
FcCH(OTMS)CN (**I**) 61%, m.p. 80–81.5°C	
Analysis	C, 57.52(57.21); H, 6.11(5.98)%
IR (cm^{-1})	
(THF)	2189
^{1}H	5.1 (s, CH(CN)); 4.1 (s, C$_5$H$_5$); 4.0 (s); 3.9 (s, C$_5$H$_4$); 0.4 (s, SiMe)
^{13}C	119.3 (CN); 84.1 (C–O); 69.7 (C$_5$H$_5$); 69.4, 69.0, 68.7, 67.7, 61.5 (C$_5$H$_4$)
^{29}Si	21.9
NpCH(N-^{i}Pr$_2$)CN, 11%, m.p. 128–129°C	
Analysis	C, 81.16(81.24); H, 8.32(8.24); N, 10.52(10.78)%
^{1}H	7.6–7.2 (m, Np); 4.58 (s, CH); 2.97 (h, CH(CH$_3$)$_2$, J = 6.6 Hz); 1.13 (d, CH(CH_3)$_2$, J = 6.6 Hz)
^{13}C	134.9, 113.1, 132.9, 128.4, 128.1, 127.6, 126.4, 126.3, 125.0 (Np); 120.9 (CN); 51.1, 46.6 (CH(Me$_2$)); 23.3, 19.5 (CH(CH_3)$_2$)

[a] Recorded in $CDCl_3$. [b] ppm, TMS as reference, s = singlet, d = doublet, h = heptet, m = multiplet.

11% yield, the naphthyl analog of complex **II** (eqn. (5)). No attempt was made to optimize the yield in this reaction; however, it seems to be a general synthetic route to cyanoamine compounds *.

$$\alpha\text{-NpCHO} \xrightarrow[2.\ Me_3SiCN]{1.\ LDA} \alpha\text{-NpCH(CN)}\left(N\{^i Pr\}_2\right) \qquad (5)$$

To determine the need for the diisopropylamino group in activating the loss of the OSiMe$_3$ group, we replaced LDA by n-butyllithium in the initial step of the synthesis of **II**. This reaction led to the formation of only the expected silylether **IIIa** (eqn. (6)).

$$FcCHO \xrightarrow[2.\ Me_3SiCN]{1.\ ^nBuLi} FcCH(^nBu)OSiMe_3 \qquad (6)$$

(IIIa)

Clearly the loss of the siloxy group by nucleophilic attack of CN^- does not occur in the absence of the activating amino group. Several other ferrocenylsilylethers were synthesized in this manner using both cyano- and chlorosilanes (55–76%).

The preparation of related ferrocenylmethyl silylethers, FcCH$_2$OSiR$_3$ (**IV**), was accomplished via the reaction of 1-ferrocenylmethanol with the corresponding chlorosilane (R = SiMe$_3$, SiMe$_2$Ph, SiMePh$_2$, SiPh$_3$, SiMe$_2$SiMe$_3$, SiMe$_2$SiMe$_2$SiMe$_3$, (SiMe$_3$)$_3$Si) and pyridine in ether (eqn. (7)). The products were isolated in good to moderate yields (30–50%). Spectroscopic data are provided in Table 1.

$$FcCH_2OH \xrightarrow{R_3SiCl/pyridine} FcCH_2OSiR_3 \qquad (7)$$

(IV)

(R$_3$Si = a, Me$_3$Si; b, Me$_2$PhSi; c, MePh$_2$Si; d, Ph$_3$Si; e, Me$_3$SiMe$_2$Si; f, Me$_3$SiMe$_2$SiMe$_2$Si; g, (Me$_3$Si)$_3$Si)

2.1. Spectral properties of ferrocenyl silyl ethers

The ferrocenyl derivatives were characterized by means of spectroscopic methods (^{1}H, ^{13}C, ^{29}Si NMR) and the data, summarized in Table 1, are in accord with the structures. For example, the methine H in the ferrocenyl silyl ethers **III**, resonates in the region 4.45–4.71 ppm; the methylene protons of complexes **IV** appear in the region of 4.8 ppm, deshielded due to the inductive effect of the neighboring oxygen and ferrocenyl groups [6].

The ^{29}Si NMR data show a progressive shielding with decreasing number of methyl groups, *e.g.* **IVa**, 16.1 ppm; **IVb**, 7.2 ppm; **IVc**, −2.7 ppm; **IVd**, −12.2 ppm. For the ferrocenylmethyl oligosilyl ethers, **II** ≠ **, f, g**, significant deshielding is observed for α-silicon atoms due to the neighbouring oxygen, *e.g.* FcCH$_2$OSi$_\alpha$Me$_2$ Si$_\beta$Me$_2$Si$_\gamma$Me$_3$, Si$_\alpha$ = 17.3 ppm, CH$_3$Si$_\alpha$Me$_2$Si$_\beta$Me$_2$ Si$_\gamma$Me$_3$, Si$_\alpha$ = −16.0 ppm [7]. The ferrocene group produces a small shielding effect (1.5 ppm) on the α-silicon atoms in the ferrocenyl ethers compared to those of the corresponding methoxysilanes.

* At the suggestion of a referee, we investigated an alternative pathway involving displacement of the siloxy group from **I** by LDA, even though the sequence of events seemed to make this implausible. The reaction between **I** and LDA and quenching with MeI, resulted in much recovered starting material and several compounds that defied isolation and characterization. No evidence for the formation of **II** was observed.

TABLE 2. $\Delta\nu$ and formation constants for silyl ether/phenol complexes

Parent compound: R	$FcCH_2OR$ [a]			CH_3OR		
	$\Delta\nu$ (cm^{-1})	k_1	k_2	$\Delta\nu$ (cm^{-1})	k_1	k_2
Me_3Si	289	5.3	–	278	3.1	–
Me_2PhSi	278, 60	4.4	0.4	270	5.7	–
$MePh_2Si$	267, 60	1.5	1.7	252, 52	4.6	0.3
Ph_3Si	202, 60	1.4	1.3	224, 52	2.0	0.6
$Me_3SiSiMe_2$	295	4.2		–	–	–
$Me_3SiSiMe_2SiMe_2$	288	3.1		–	–	–
$(Me_3Si)_2SiMe$	309	2.2		–	–	–
$FcCH(^nBu)OR$ [b]						
Me_3Si	286, 69	1.45		278	3.1	–
Me_2PhSi	272, 65	1.84		270	5.7	–
$MePh_2Si$	260, 60	1.30		252, 52	4.6	0.3
Ph_3Si	245, 34			224, 52	2.0	0.6

$\Delta\nu$ = –, no detectable association, k_1 = for complex formed by hydrogen bonding through the ether-oxygen, k_2 = for complex formed by hydrogen bonding to the aromatic ring of the ether. [a] In CCl_4, silyl ether (0.1 M) and phenol (0.01 M). [b] In CCl_4, silyl ether (0.5 M) and phenol (0.02 M).

2.2. Base strength study

The relative basicities of the ferrocenyl ethers **III** and **IV** were studied using the procedure reported by West and co-workers involving infrared spectroscopic analysis of the H-bonding interaction between the silyl ether and the hydroxyl group of phenol (eqn. (8)) [8].

$$Ph\text{–}OH + ROR' \longrightarrow [Ph\text{–}OH \cdots ORR'] \quad (8)$$

A measure of the basicity is given by the value of the shift of the phenolic OH stretching frequency between free and H-bonded phenol. For **III** and **IV**, a new OH stretching frequency was observed, along with a second band of weak intensity due to the association between the phenol and the π-system of the ferrocenyl aromatic rings (Table 2).

Ferrocenyl groups are electron-releasing, thus the basicities of **III** and **IV** are higher than those of the corresponding methoxysilanes (Table 2) except for the case of the bulkiest compound (*i.e.* Ph_3SiOR) where the association between the phenol and the ferrocenyl ether oxygen is highly hindered. The data are in accord with the trend of the formation constants since the smallest K_f values correspond to the ferrocenyl silyl ethers with the smallest shifts in phenolic OH stretching frequencies. The basicity of the mono silyl ethers decreases in going from $FcCH_2OSiMe_3$ to $FcCH_2OSiPh_3$ as the electron-density on the oxygen atom decreases in the same order. The same trend was observed in going from $Fc(H)C(^nBu)OSiMe_3$ (**IIIa**) to $Fc(H)C(^nBu)OSiPh_3$ (**IIId**) and these complexes are less basic than **IIa–d** due to the steric effect of the butyl group which acts in a manner similar to the methyl groups responsible for the variation of the solution basicities $NH_3 < NH_2Me < NHMe_2 > NMe_3$ [9]. The oligosilyl ethers exhibit a greater basicity than the monosilyl analogs due to inductive electron-release by extra silyl groups.

2.3. Hydrolytic stability

The stability of ferrocene towards hydrolytic conditions is well known. We have investigated the effect of ferrocene on the hydrolytic stability of the Si–O–C bond silyl ethers, comparing the rate of hydrolysis of such ethers with that of the corresponding methoxysilanes (eqns. (9) and (10)). The study was carried out at 23°C under pseudo-first order reaction conditions in THF, [silylether]/[H_2O] = 1 : 150, and followed by gas chromatography.

$$MeOSiMe_3 + H_2O \xrightarrow[THF]{H_2O} Me_3SiOH + MeOH \quad (9)$$

$$FcCH_2OSiMe_3 + H_2O \xrightarrow[THF]{H_2O} Me_3SiOH + FcCH_2OH \quad (10)$$

Whereas the hydrolysis of Me_3SiOMe was very fast, $k = 7.5 \times 10^{-3}$ min^{-1}, in the case of the ferrocenylsilyl ether there was no hydrolysis even after 3 days. It was necessary to reflux the THF/water solutions for 14 h to achieve complete hydrolysis.

3. Experimental section

Syntheses were performed in a nitrogen atmosphere using dry oxygen-free solvents. Diisopropylamine and trimethylchlorosilane were distilled from calcium hydride prior to use. All the chlorosilanes and trimethylsilylcyanide were purchased from Hüls America/Petrarch Systems Inc, Bristol, PA or prepared according to literature procedures. $FcCH_2OH$ was obtained from Research Organic/Inorganic Chemical Corp., Sun Valley, CA; ^nBuLi (1.6 M in hexane) and FcCHO were purchased from Aldrich Chemical Co, Milwaukee, WI; alumina (80–200 mesh) was purchased from Fisher Scientific, Fair Lawn, NJ; silica gel (60–200 mesh) was purchased from J.T. Baker Chemical Co., Phillipsburg, NJ.

Infrared spectra were recorded on a Perkin–Elmer 580B spectrophotometer and NMR spectra were recorded on an IBM NR 200 FT NMR spectrometer, with chemical shifts reported in ppm using $SiMe_4$ as reference. Elemental analyses were performed by Galbraith Laboratories Inc., Knoxville, TN.

Representative synthetic procedures are presented below.

3.1. Preparation of 1-(diisopropylamino)cyanomethyl ferrocene (II)

Into a 250-ml side arm round-bottomed flask equipped with magnetic stirring bar and gas-tight septa was placed 10 ml of THF. The solution was cooled to 0°C and 0.7 ml (4.8 mmol) of diisopropylamine was added, followed by dropwise addition of 3 ml of a 1.6 M n-butyllithium solution (4.8 mmol). After stirring for 30 min, 1 g (4.67 mmol) of ferrocenecarboxaldehyde in 8 ml of THF was added. The reaction was monitored by IR spectra and after 6 h the carbonyl absorption had disappeared. At this stage, 0.64 ml (4.8 mmol) of trimethylsilylcyanide was added. After 1 h at 0°C the reaction mixture was allowed to reach room temperature, the solvent was removed and 30 ml of dry hexane was added. After precipitation of the salts, the solution was transferred under nitrogen to another flask and the solution concentrated to 50% of the original volume. The title compound crystallized to give an initial crop of orange-yellow material, 1.25 g (3.86 mmol, 83%). The product was further purified for analytical purposes by column chromatography on neutral alumina using hexane/dichloromethane (75:25, 150 ml), and a 1×25 cm^2 column under a nitrogen atmosphere.

3.2. Preparation of 1-(n-butyl)trimethylsiloxymethylferrocene (IIIa)

Into a 50-ml 2-neck round-bottomed flask equipped with magnetic stirring bar and gas-tight septa was placed 1.07 g (5 mmol) of ferrocenecarboxaldehyde in 5 ml of THF. The solution was cooled to 0°C and 3.1 ml (5 mmol) of n-butyllithium was added and after stirring for 1.5 h, when the carbonyl stretching frequency disappeared, trimethylchlorosilane (0.64 ml, 5 mmol) was added and the solution allowed to warm, with stirring, to room temperature over 3 h. The solvent was removed and 100 ml of hexane was added to facilitate precipitation of the salts. Subsequent to filtration through 7.5 cm of neutral alumina in a Schlenk apparatus and removal of the solvent, the residue was purified by column chromatography using alumina (1×25 cm^2 column) eluting with a 1:2 dichloromethane/hexane solvent system to produce **IIIa** (1.30 g, 3.8 mmol, 76%). The same product was isolated in 50% yield upon addition of trimethylsilyl cyanide instead of trimethylchlorosilane (5 mmol scale, same conditions).

3.3. Reaction of ferrocenecarboxaldehyde with LDA, Me_3SiCl, followed by KCN

To a 50-ml round-bottomed flask with a side arm charged with 5 ml of THF and cooled to 0°C, was added 0.84 ml (6 mmol) of diisopropylamine and 3.75 ml (6 mmol) of n-butyllithium. After stirring for 30 min, ferrocenecarboxaldehyde (1.28 g, 6 mmol) was added in 3 ml of THF, and the mixture stirred for 6 h. When all FcCHO had been consumed, 0.65 g (6 mmol) of trimethylchlorosilane was added and the mixture stirred for 2 h. This solution was transferred by syringe to a flask containing 0.33 g (5.07 mmol) of potassium cyanide and 0.58 g (3 mmol) of 18-crown-6 and stirred overnight. The solvent was removed *in vacuo* and the crude material was purified by column chromatography on a (1×25 cm^2) column of neutral alumina using hexane/dichloromethane (75:25) to yield **I** (0.14 g, 0.42 mmol, 7%).

3.4. Synthesis of trimethylsiloxymethylferrocene (IVa)

A 500-ml side-arm flask was charged with $FcCH_2OH$ (0.25 g, 1.2 mmol), pyridine (0.2 ml, 2.4 mmol) and 10 ml of diethyl ether and, with stirring, a solution of Me_3SiCl (0.15 ml, 1.2 mmol) in 3 ml of diethyl ether was added dropwise. A white precipitate of pyridinium hydrochloride was formed immediately. The mixture was stirred for 10 min, filtered, and the solvent removed under vacuum. The residual yellow solid was sublimed overnight (0.05 mmHg) to yield 0.17 g (0.6 mmol, 50%) of **IVa**.

3.5. Synthesis of 1-trimethylsiloxy-cyanomethylferrocene (I)

Into a 50-ml 2-neck round-bottomed flask equipped with a magnetic stirring bar and gas-tight septa was placed 2.14 g (10 mmol) of ferrocenecarboxaldehyde, 1.40 ml (10.38 mmol) of trimethylsilylcyanide, 4 mg (0.125 mmol) of ZnI_2, and the solution was stirred overnight. Removal of the solvent yielded a solid residue that was purified by column chromatography on a (1×25 cm^2) column of neutral alumina using hexane/dichloromethane (75:25) as eluant. Further purification was achieved by recrystallization from hexane/dichloromethane (90:10) to produce 1.91 g (6.09 mmol, 61%) of the desired product.

3.6. Reaction of 2-naphthaldehyde with LDA and TMSCN

Into a cooled (0°C) 100-ml 2-neck round-bottomed flask equipped with a magnetic stirring bar and gas-tight septa was placed 1.56 g (10 mmol) of 2-naphthaldehyde and 12.5 mmol of LDA solution in 50 ml THF. After the carbonyl absorption band had disappeared, 1.4 ml (10.38 mmol) of trimethylsilylcyanide was added, and the solution stirred overnight. The crude material was pre-purified by filtration through 5 cm of alumina (hexane/dichloromethane, 50:50). After removal of solvent, the residue was purified by column chromatography on neutral alumina using hexane/dichloromethane (10:90, 50 ml; 50:50, 100 ml). Recrystallization from hexane/dichloromethane (10:90) yielded 0.30 g

(1.13 mmol, 11.3%) of white solid [2-Np(H)C(N-$^{i}Pr_2$)CN and the mother liquor contained a yellow oil [2-NpCH$_2$OTMS] (0.25 g, 1.08 mmol, 10.9%).

3.7. Calculation of H-bonding $\Delta\nu$ and K_f values

The shift in O–H stretching frequencies and formation constants were determined using carbon tetrachloride solutions (0.01 M in phenol, 0.1 M in silylether, in a 1-mm pathlength NaCl cell.

3.8. Attempts to synthesize [FcCH(N{^{i}Pr}$_2$)OSiR$_3$]

Into a 100-ml side-arm round-bottomed flask equipped with a magnetic stirring bar and a gas-tight septa a THF solution of LDA was prepared by adding n-butyllithium (3.1 ml, 5 mmol) and diisopropylamine (0.70 ml, 5 mmol) in 5 ml of the solvent at −78°C, stirring for 15 min. Ferrocenecarboxaldehyde (1.07 g, 5 mmol) was dissolved in 3 ml of THF and added to the LDA solution. The disappearance of the carbonyl band was monitored by IR spectra (ν(CO) band 1685 cm^{-1}) and after complete disappearance of the band, trimethylchlorosilane (0.7 ml, 5 mmol) was added and the solution allowed to reach room temperature. Upon removal of the solvent *in vacuo*, only starting material, FcCHO, was recovered.

Repeats of the above procedure quenching with MeI, PhMe$_2$SiCl, ^{t}Bu(Me$_2$)SiCl over a reaction temperature range from 0° to −40°C, and involving reverse addition, all resulted in the recovery of FcCHO.

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