Facile synthesis of amino-functionalised ferrocenes and vanadocenes

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We report a general and high yielding route to the synthesis of late and early metallocenes; reported is an amino-functionalised vanadocene which is an unusual example of a 1,1-substituted vanadocene outside of a group 14 substituted derivative.

The importance of metallocenes has been documented recently with potential applications in several areas of chemistry.[1,2] There has been a considerable amount of research done with functionalised ferrocenes, and besides potential therapeutic activity,[3] other useful functions with these types of molecules have been their ability to recognise neutral molecules,[4] as well as cations and anions.[5] Multidentate functionalised ferrocenes have also been prepared where there are more than two donor heteroatoms.[6] These, like many bis-functionalised ferrocenes, start with ferrocene as the starting material and quite often there are many steps to arrive at the end product. For example, there has been a report of one primary alkylaminoferrocene synthesised in small amounts, but this takes four steps starting from ferrocene.[7] Whilst it is relatively facile to make the mono-functionalised aminoferrocene, it is somewhat more difficult to make the bis-functionalised analogues. The main problem about preparing bis-1,1-aminoferrocenes is the poor yield of the substitution of the second ring.

Conversely, research into vanadocene chemistry has been remarkably low. This is unfortunate given the potential anti-tumour properties of such complexes,[8] but one of the main problems is the highly sensitive nature of these compounds.[2] With both of these criteria in mind, this paper presents a general, convenient and efficient method of synthesising bis-functionalised ferrocenes and vanadocenes from the parent substituted cyclopentadienyl analogue and the appropriate metal halide. We have deliberately chosen a late and an early metal derivative to show the general nature of the methodology.

A high yielding route to synthesise and isolate the pure amino-functionalised sodium cyclopentadienide salt routinely on a scale of 15–20 g has been developed.[9] Using this method, we can methodically and easily vary the length of the spacer group between the cyclopentadienyl group and the amino group; the substituents attached to the nitrogen atom can also be modified. This paper describes the high yielding route to different bis-1,1-amino-ferrocenes and -vanadocenes which have different spacer groups and end groups. Yields have been typically 65–80%.

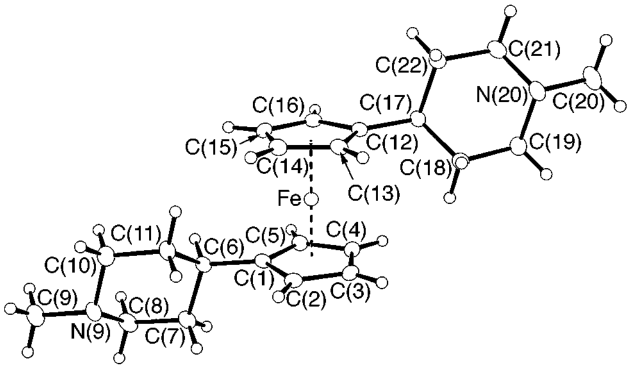
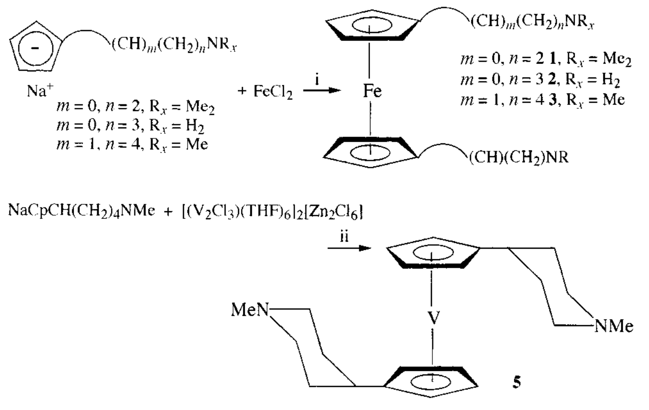


Fig. 1 X-Ray structure of ferrocene **3**.

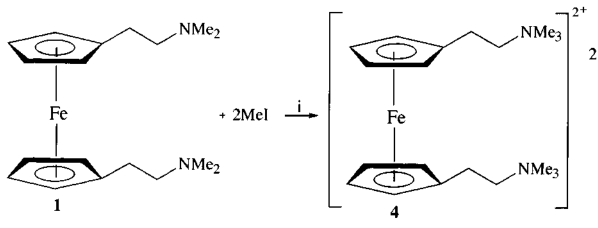
Reaction of 2 equivalents of $NaCp(CH_2)_2NMe_2$ with $FeCl_2$ yields $Fe[Cp(CH_2)_2NMe_2]_2$ **1** in 76% yield as an analytically pure yellow–orange oil (Scheme 1).† Using this versatile and facile method, we can produce primary alkylaminoferrocenes as well. As already mentioned, these compounds are notoriously difficult to synthesise by other means[7] and to our knowledge $Fe[Cp(CH_2)_3NH_2]_2$ **2** is only the second example of this type. It is synthesised by readily available starting materials such as $FeCl_2$ and 2 equivalents of $NaCp(CH_2)_3NH_2$ and has the advantage that it is high yielding and is one step. Decreasing the flexible nature of the substituted arm has a profound effect on the ferrocene in that we can isolate an orange solid $Fe[CpCH(CH_2)_4NMe]_2$ **3** as opposed to the oils obtained for **1** and **2**.‡ The molecular structure§ of **3** can be seen in Fig. 1 and the steric encumbrance of the piperidyl groups is evident as they lie *trans* to each other.

Complex **1** reacts with equivalents of MeI to afford the ferrocene salt $Fe[Cp(CH_2)_2NMe_3]_2{}^{2+}2[I]^-$ **4** (Scheme 2) which was recrystallised from methanol. **4** crystallises as a yellow microcrystalline analytically pure material which was characterised by ^1H and ^{13}C spectroscopy and again occurs in high yield, 75%. It is methanol and water soluble and air stable. Alternative entry into this class of compound has been achieved by a three step synthesis from ferrocene to yield ferrocene-1,1′-diylbis(methyltrimethylammonium iodide).[10]

The functionalised sodium cyclopentadienide salts can also be used to prepare early metal metallocenes. The only heteroatom ring substituted vanadocenes that we are aware of are $(C_5H_4EMe_3)_2V$ (E = Si, Ge, Sn).[11] Thus, outside of the group 14 ring substituted vanadocenes, we report here an unusual fully characterised example of a 1,1-substituted



Scheme 1 Reagents and conditions: i, THF, 65–76%; ii, THF, 72%.



Scheme 2 Reagents and conditions: i, Et_2O, 75%.

vanadocene. This has been synthesised using the starting material $[(THF)_3V(\mu\text{-}Cl)_3V(THF)_3]_2[Zn_2Cl_6]$[12] and $NaCpCH(CH_2)_4NMe$ to yield compound **5** in 72% yield. This highly air and water sensitive paramagnetic material is deep purple in colour and difficult to characterise. The X-ray crystal structure§ has been determined and is isomorphous with **3**. We are currently carrying out oxidation reactions of this and other analogues of amino-substituted vanadocenes.[13] It is important to note that, for both the vanadocene and ferrocene analogues highlighted in this paper, we have had no need to use chromatographic techniques and they have been synthesised as analytically pure compounds.

We have also embarked on a strategy of synthesising ligands where there would be more chance of the nitrogen moiety interacting with a metal centre. Therefore we synthesised the ligand **6**. During the course of this work the preparation of the ligand **6** and the thallium salt and the reactivity with group IV transition metals have been reported.[14] We have used our methodology to isolate the sodium salt **7** from the reaction of **6** with NaH giving the new compound **7** which is air and water sensitive. This has been characterised by ^1H and ^{13}C NMR. Like previously reported compounds[9] this compound undergoes exchange with the deuterated solvent (CD_3CN) where the protons from the ring exchange with the deuterons of the solvent.

$$\underset{\mathbf{6}}{C_5H_5CH_2C_6H_4N} + NaH \xrightarrow{THF} \underset{\mathbf{7}}{NaCpCH_2C_6H_4N}$$

In summary, we feel that the generality of our procedures will allow the isolation and tailoring of many types of amino-substituted metallocenes in high yields starting from the sodium salts of the substituted cyclopentadiene and a transition metal halide salt. We have proved this by the isolation of amino-functionalised ferrocenes; especially significant is the isolation of the primary alkylaminoferrocenes. We have also found an effective route into amino-functionalised vanadocenes, which have been synthesised and fully characterised for the first time.

Notes and references

† All compounds were characterised by CHN analyses, ^1H, ^{13}C NMR and FAB mass spectrometry.

‡ A typical procedure is as follows: to a solution of $FeCl_2$ (1 g, 0.0078 mol) in THF (30 ml) was added two equivalents of $NaCpCH(CH_2)_4NMe$ (2.9 g, 0.0176 mol). An orange colour was observed. After several hours the THF was removed under vacuum, and the residues extracted twice with toluene (20 ml) and then dried under vacuum. The product was recrystallised from toluene. Yield = 1.9 g, 67%.

§ Crystal data for **3**: $C_{22}H_{32}FeN_2$, 380.35, triclinic, space group $P\bar{1}$, a = 7.1259(5), b = 10.7296(10), c = 13.4298(11) Å, α = 103.584(8), β = 96.905(7), γ = 101.691(8)°, V = 962.08(13) Å^3, Z = 2, D_c = 1.313 Mg m^{-3}. 3780 unique reflections collected (Stoe STADI4 diffractometer, Mo-Kα, 150 K) of which 3678 were observed [$F^2 > 2.0\sigma F^2$]. Solved by direct methods (SHELXS-97) and refined by full-matrix least squares (SHELXL-97) on F^2 of all unique data to R_1 = 0.0248 (observed data), wR = 0.0695 (all data), S = 1.093. For **5**: $C_{22}H_{32}VN_2$, 375.44, triclinic, space group $P\bar{1}$, a = 7.6238(2), b = 10.4591(3), c = 13.8715(2) Å, α = 102.695(2), β = 98.438(2), γ = 101.3270(12)°, V = 1036.97(4) Å^3, Z = 2, D_c = 1.202 Mg m^{-3}. 12278 reflections collected (Nonius KappaCCD diffractometer, Mo-Kα, 190 K) of which 4434 were unique and 3629 were observed [$F^2 > 2.0\sigma F^2$]. Structure solution and refinement as above, R_1 = 0.0339 (observed data), wR = 0.0996 (all data), S = 1.095. CCDC 182/1099. See http://www.rsc.org/suppdata/cc/1999/77/, for crystallographic files in .cif format.

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