Convenient Access to Homochiral Tricarbonyliron Complexes[1]

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Homochiral 6-methoxy substituted cyclohexadienyltricarbonyliron complexes have been obtained by complexation of the dimethyl ether of 1-methylcyclohexa-1,3-diene-5,6-diol (available *via* microbial oxidation of toluene) and demethoxylation with triphenylcarbenium tetrafluoroborate.

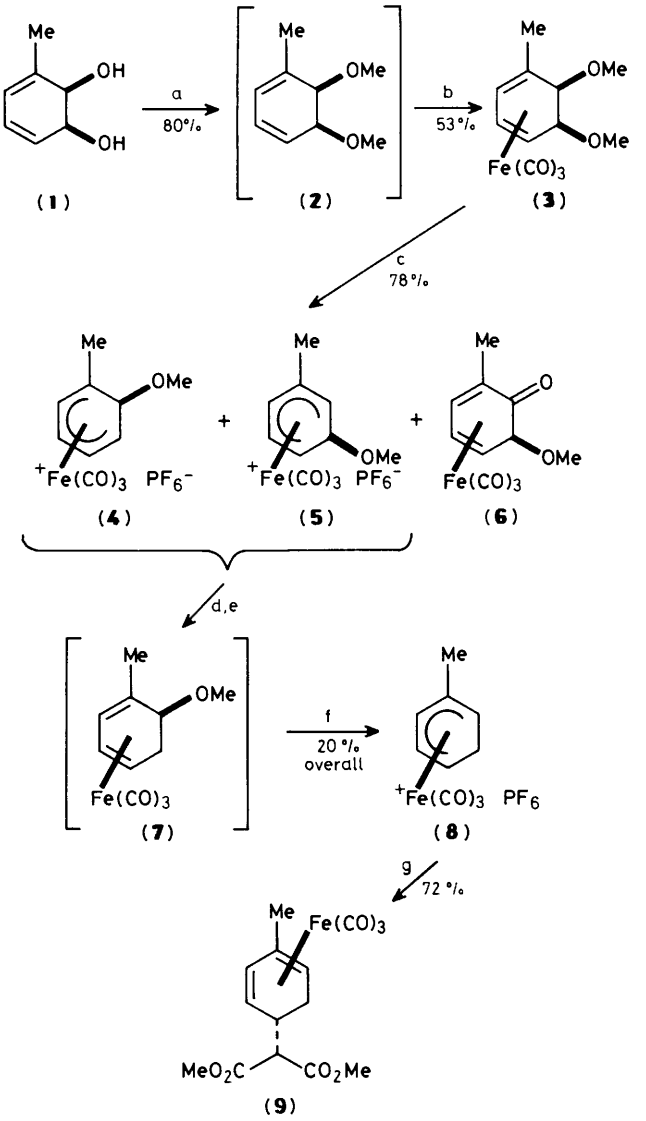
Renewed interest[2,3] in methods for the preparation of homochiral organometallic π-complexes reflects new developments[3,4] employing their fully stereocontrolled alkylation reactions[5] in organic enantiomer synthesis. Work in this laboratory has recently defined[6] strategic advantages available from the use of chiral organoiron and organomanganese complexes as intermediates in asymmetric synthesis. In this paper we describe a new and convenient enantioselective route to simple complexes in the organoiron series, making more generally available in homochiral form complexes of a type already extensively used[7] in synthetic chemistry.

Complexation of natural products offers simple access to homochiral complexes,[8] but previously has been restricted to a narrow range of suitable substrates. Our recent observation[9] that the OMe groups of 5,6-dimethoxycyclohexa-1,3-diene efficiently direct the iron carbonyl moiety to the substituted face of the molecule provides the means to overcome this limitation. Suitable dienes are available[10,11] with a wide range of substitution patterns by the microbial oxidation of arenes by *Pseudamonas putida*. These possibilities have now been demonstrated by the complexation of a diether obtained from a microbial oxidation product[11] of toluene, and the preparation, in this way, of a number of homochiral tricarbonyliron complexes.

The diol, 1-methylcyclohexa-1,3-diene-5,6-diol (**1**)[11] ($[\alpha]_D$ +73.4°, *c* 1, cyclohexane), was converted to the dimethyl ether (**2**), obtained as a mixture with 2- and 3-methylanisoles. In view of its relative instability, the ether (**2**) was complexed without further examination by reaction with $Fe_2(CO)_9$ at 34 °C for 16 h in ether. A tricarbonyliron complex was obtained as a single stereoisomer† ($[\alpha]_D$ +142.9°, *c* 1, cyclohexane) in 42% overall yield from (**1**). This product has been assigned the structure (+)-(**3**) on the basis of the expected[9] stereodirecting effect of the ether substituents and of absolute configuration correlations described below.

Efficient conversion to cationic dienyl complexes required the regiochemical differentiation of the two OMe groups. Because of its far greater bulk, the triphenylcarbenium reagent proved more regioselective than trifluoroacetic acid (TFA),[9] preferentially removing the less hindered OMe group to produce a 5 : 1 mixture† of (**4**) and (**5**) (78%). A small and variable amount (5—10%) of the dienone complex (**6**)† was also produced by competing hydride abstraction. A sample of the 1-methyl cation (+)-(**4**) {46% recovery, *ca.* 97% purity (n.m.r.), $[\alpha]_D$ +37.8°, *c* 1, acetonitrile} was obtained from this mixture by deprotonation with triethylamine, chromatographic purification of the neutral triene intermediate, and reprecipitation by protonation with TFA.[12]

Conversion of (**4**) to the simple 2-methyl substituted dienyl complex (**8**), which is also available in racemic form and had previously been shown[13] to be suitable for use in optical purity determination using our n.m.r. method, was performed to measure the enantiomeric excess of complexes obtained from (**2**). Reduction of the mixture of dienyl complexes (**4**) and (**5**) using sodium borohydride produced a mixture of regioisomeric neutral diene complexes. These were separated by chromatography to provide a sample of the 1-methyl-6-methoxydiene complex (**7**), which was converted immediately to the required dienyl salt to confirm its identity. Treatment of (**7**) with TFA produced the (+)-isomer of (**8**) {$[\alpha]_D$ +25.1°, *c* 1, acetonitrile, 20% overall yield from the mixture of (**4**) and (**5**)} which was alkylated to form the corresponding malonate adduct (−)-(**9**) ($[\alpha]_D$ −2.4°, *c* 1, cyclohexane) as described[13] for the racemic sample. The 400 MHz n.m.r. spectrum of (−)-(**9**) was recorded in the presence of the chiral shift reagent tris-[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]-



Scheme 1. *Reagents*: a, MeI, KOH; b, $Fe_2(CO)_9$; c, (i) $Ph_3C^+BF_4^-$; (ii) NH_4PF_6; d, $NaBH_4$; e, chromatography; f, (i) TFA, (ii) NH_4PF_6; g, $NaCH(CO_2Me)_2$, tetrahydrofuran (THF).

† New compounds isolated gave satisfactory elemental analyses.

europium(III). Only signals due to a single enantiomer of (**9**) were observed, together with minor signals, presumably arising from residual traces of another regioisomer introduced in the reduction step. Addition of racemic (**9**) to the n.m.r. experiment demonstrated that the minor signals observed did not originate from (+)-(**9**), since the second pair of signals from the ester groups of this material were recorded at different chemical shifts.

The absolute configuration of (**1**)[14] and (**8**)[15] are both known. The preparation of (+)-(**8**) from the 6-*endo* substituted salt (+)-(**4**) confirmed the attachment of the tricarbonyliron group to the diastereoface of the unsymmetrically substituted diene shown in Scheme 1. While the preparation of a 6-*endo*-methoxy substituted dienyl cation has been unambiguously demonstrated,[9] the initial formation of 5,6-di-*endo*-dimethoxy substituted η^4-complexes has previously been assigned only by inference from this result, and remained uncertain because *endo–exo* isomerisation of alkoxy substitution is possible[16] in acidic conditions. The conversion of (+)-(**1**) into (+)-(**4**) has now ruled out the possibility that kinetically controlled,‡ acid catalysed epimerisation of OMe substitution might occur in the conditions used for the formation of 6-methoxy substituted complexes.

These experiments have demonstrated the formation of one series of enantiomers of homochiral tricarbonyliron complexes from a readily accessible biologically derived starting material of a type available with a wide variety of substitution patterns, and have determined unequivocally for the first time that the dimethoxy ether substitution of the substrates draws the tricarbonyliron group exclusively to the substituted face of the diene during complexation with $Fe_2(CO)_9$.

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‡ We have shown that the *endo*-OMe substituent is exclusively removed from a diene complex bearing both *exo*- and *endo*-OMe substituents, ref. 9. Epimerisation of a di-*exo*-complex to an *exo*, *endo*-complex could thus be followed by selective removal of the remaining *exo*-OMe group to produce a 6-*endo* substituted cation.

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