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Preliminary communication

Transition metal mediated asymmetric synthesis

VII *. 6-Methoxycyclohexadienyliron complexes: access to synthetic equivalents of cyclohexadiene dications

Philip W. Howard, G. Richard Stephenson*,
School of Chemical Sciences, University of East Anglia, Norwich, Norfolk, NR4 7TJ (Great Britain)

and Stephen C. Taylor
ICI Biological Products Business, P.O. Box 1, Billingham, Cleveland, TS23 1LB (Great Britain)

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Abstract

The dimethyl ether of cyclohexa-1,3-diene-5,6-diol, available via microbial oxidation of benzene, was converted into the tricarbonyl-(η^5-6-methoxycyclohexadienyl)-iron(1 +) complex (**1**) by complexation and demethoxylation with TFA. Alkylation and demethoxylation produced a 6-methyl intermediate; the corresponding 6-butyl salt was also obtained. The stereochemistry of complex **1** was determined by conversion into the *endo,exo*-dimethoxy substituted complex **8** by reaction with sodium methoxide.

The stereochemistry of the alkylation reactions of electrophilic transition metal π-complexes is dominated by the controlling effect of the metal centre. We recently described [2] a number of cases in which this influence was used to provide reactivity equivalent to a variety of stereocontrolled cation synthons [3,4] with which alkylation reactions can be performed with complete stereoselectivity. This paper describes preliminary studies aimed at employing the metal to ensure *cis* relative stereochemistry at two adjacent alkylation sites. Despite their proven versatility as intermediates in organic synthesis [4], previous attempts to promote a sequence of alkylation reactions using tricarbonyliron complexes have not found general application because specific substituents [5] or unproven reagent systems [6] have been required to return to η^5-bonding. A simple method for reforming the η^5-cation following an alkylation reaction is needed to stimulate further advances in this area. We now report a convenient method of preparing a 6-alkoxy substituted dienyl salt,

* For part VI see ref. 1.

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which, following alkylation, can be easily converted into a new dienyl complex. This development opens the way for a more general use of double alkylation sequences.

The new microbial oxidation of benzene [7], which makes cyclohexa-1,3-diene-5,6-diol available on a large scale, offered a solution to salt-reformation problem, provided that difficulties expected [8] with the instability of 6-hydroxycyclohexadienyl complexes could be overcome. We report here a successful method for the preparation and double alkylation of the 6-methoxy substituted dienyl complex **1**, which provides a reactivity pattern equivalent to that of the cyclohexa-1,3-diene-5,6-*cis*-dication synthon **2**.

The dimethoxy ether **4** was prepared from the diol **3** in 60–80% yield by reaction with methyl iodide and potassium hydroxide. A small quantity of methoxybenzene produced in the reaction was easily removed at a later stage. Complexation was performed with $Fe_2(CO)_9$ in ether under reflux to produce complex (**5**) in 40% yield, together with a trace of a second material which was not identified. These products were separated by chromatography. Treatment of the major product **5** with TFA, followed by precipitation of the resulting dienyl cation from water in the usual way by addition of ammonium hexafluorophosphate [3] produced a 98% yield of the *endo* methoxy complex **1**. This product was converted into the alkyl derivatives **6**, which were used to form the 6-alkyl salts **7** without further purification. The presence of an OMe substituent in place of the OH group in these alkylation reactions is important for the stability of intermediates of the type **1** and for avoiding complications in alkylations using relatively basic reagents which could deprotonate hydroxy-substituted complexes. The use of organo-cuprate reagents [9] for the formation of **6** amply illustrates this latter point.

Treatment of **6a** with TFA resulted in the removal of the OMe substituent in 70% overall yield from **1**, to form the 6-*exo*-methyl salt **7a** as a single stereoisomer, which was again isolated by precipitation with ammonium hexafluorophosphate. The butyl derivative **7b** was obtained similarly in 44% yield. The *exo* stereochemistry of the alkyl substituted complexes **7** was established by NMR spectroscopy, and arises, as expected [3], through exclusive addition of the nucleophile *trans* to the metal. Comparison of the coupling constants [10] for the *exo*- and *endo*-substituted complexes has provided a useful guide for stereochemical assignments. Distinctive PMR signals for the terminal (1-H and 5-H) hydrogens of the dienyl system, which appear as a triplet for **7** but as a doublet for **1**, gave an initial indication of the *exo*-substitution in **7** and the *endo*-substitution in **1**. These observations provide the basis for simple assignments of stereochemistry in future work. The negligible coupling between 1-H (or 5-H) and the *exo*-6-H position is in accord with data reported [8] for the 6-hydroxyl complex, which was also assigned *endo* stereochemistry for the 6-OH group.

In the case of **1** we confirmed this stereochemical assignment by converting the salt into a new dimethoxy diene complex **8** by reaction with sodium methoxide. Unlike the starting material **5**, which is symmetrical and exhibits a single OMe resonance in the PMR spectrum, **8** contains two distinct OMe groups which were given rise to separate resonances at 3.27 and 3.37 ppm. Since methoxide addition to tricarbonyliron complex has been shown [11] to proceed *trans* to the metal, the formation of the *exo,endo*-dimethoxy isomer **8** established the di-*endo* stereochemistry of the starting material **1**. Complex **8** was demethoxylated in TFA to re-form the *endo* complex **1**, indicating a stereoselective removal of the *exo*-OMe from **8**.

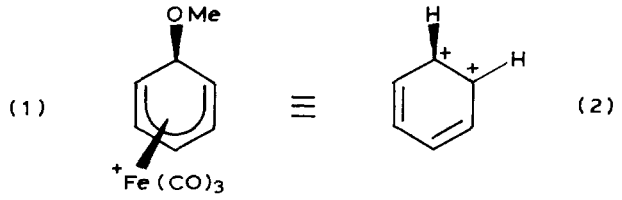
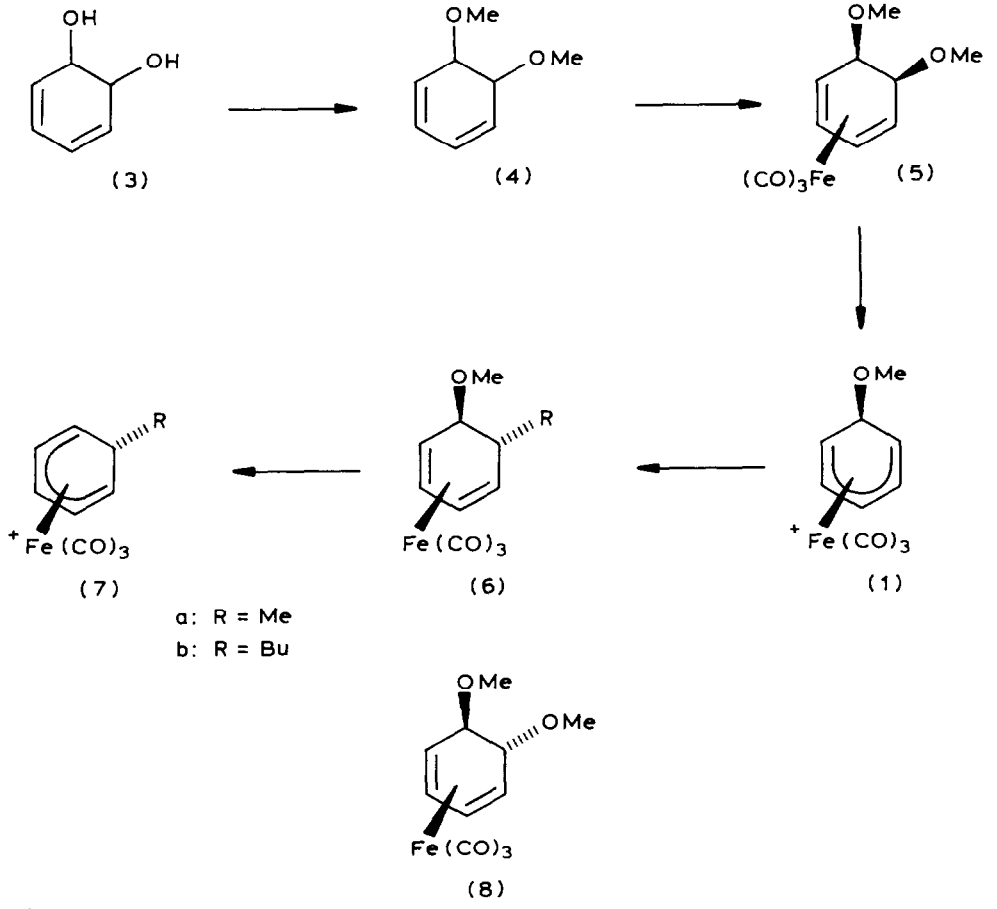


Fig. 1.

Di-*endo* stereochemistry for **5** would be consistent with the relative stereochemistry assigned to **1**. Here, also, NMR coupling constants provided valuable information. The methylene hydrogens of the 5,6-dimethoxy complex **5** gave a broad singlet ($J_{1,6} < 1$ Hz) even at 400 MHz, an observation which supports the di-*endo* formulation for **5**. This would require the preferential complexation of the face of the diene **4** that is *cis* to the two OMe groups, which is not unreasonable. Control of



Scheme 1.

stereochemistry of complexation by pre-coordination of iron carbonyls by substituents bearing lone pairs has been described for other systems [8,12].

The results of the preliminary experiments reported in this paper have established the essential features of chemistry of 6-alkoxydienyl cations and provides the basis for their development as *cis*-dication equivalents. The scope and efficiency of the double alkylation reaction, the variety of nucleophiles for which this approach can be used, and methods [13 *] for the removal of the metal from the organic products, are currently under investigation to confirm the synthetic equivalence proposed in Fig. 1. This work will make available in a stereocontrolled manner a class of *cis*-5,6-disubstituted cyclohexa-1,3-dienes which are not readily accessible by conventional methods, and should stimulate new uses of disubstituted 1,3-diene intermediates in organic synthesis.

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