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Preliminary communication

Regioselective access to tricarbonyliron complexes: controlled preparation and reactions of trifluoromethyl-substituted complexes

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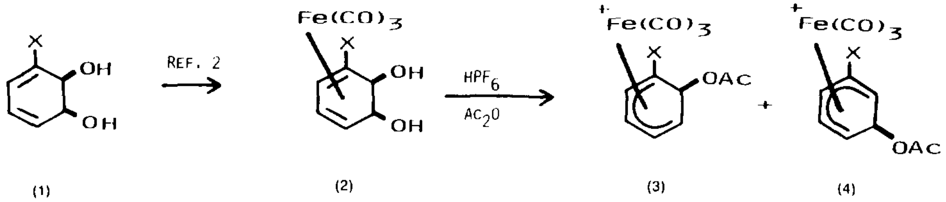
Abstract

Regiocontrol in the formation of 1-substituted 6-acetoxycyclohexadienyl complexes has been studied with both electron-withdrawing and electron-donating regiodirecting groups. Trifluoromethyl-substitution has been found to promote complete regiocontrol both in the formation of the η^5 cation complexes, and in their reactions with nucleophiles.

Optically active cyclohexadiene-5,6-diols are important starting materials for the preparation of tricarbonyl(η^5-cyclohexadiene)iron(0) complexes for use in enantioselective organic synthesis [1,2]. We have recently described [3] the preparation of a selection of diene complexes **2** from a range of diene starting materials of type **1** (Scheme 1) that are available [4] by dioxygenation of arenes by the microorganism *Pseudomonas putida*. In the case of **2a**, the conversion of the neutral diene complex into the cationic cyclohexadienyl complex **3a** has been examined [2]. The process was found to lack regioselectivity, indicating that the methyl substituent was unable to direct the salt formation process by selective stabilisation of the



Scheme 1. **a**: X = Me; **b**: X = OMe; **c**: X = Cl; **d**: X = CF_3.

Table 1

Regioisomer ratios in the formation of 6-acetoxycyclohexadienyl complexes [a]

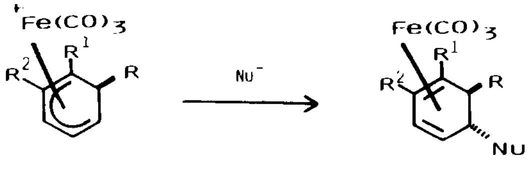
Entry	X	Ratio [b] of **3**:**4**	Yield (%)	Reference
a	Me	1:1	78	2
b	OMe	2:1	51	–
c	Cl	7:2	96	–
d	CF_3	> 99: < 1	86	–

[a] Aqueous HPF_6 was added to a solution of the diol complex in acetic anhydride at −15° C. After 1 h ether was added to precipitate the product. [b] Ratios determined from NMR spectra recorded at 400 MHz.

developing positive charge. To provide synthetic reactions of general utility, more regioselective methods were needed.

Electron-donating and electron-withdrawing substituents would be expected to exert a greater influence on regioselectivity [5*]. In this paper we describe the comparison of a selection of directing groups in a study that has achieved the first preparation of a trifluoromethyl substituted tricarbonyl(η^5-cyclohexadienyl)iron-(1+) complex [6*] and defines the potential of CF_3 control groups in the applications of cyclohexadienyl complexes in organic synthesis [7*]. Inspection of Table 1 indicates that, unlike the methyl substituent in **2a** which provided no regioselectivity (entry **a**), both OMe and Cl substituents promoted preferential formation of **3** (entries **b** and **c**). In order to examine an electron withdrawing substituent that could not interact in a π-fashion with the diene, the trifluoromethyl substituted complex **2d** was required. This complex was obtained in 70% yield by the method used for **2a–c**. Reaction of **2d** with HPF_6 in acetic anhydride in this case proved completely regioselective, affording only **3d** {$[\alpha]_D$ − 2.2° (*c* 1 CH_3CN)} in 86% yield.

When unsymmetrically placed substituents are present in electrophilic π-complexes, information defining regiodirecting effects in reactions with nucleophiles is needed to assist the design of synthetic applications [1,7*]. The preparation of **3d** provided the opportunity to establish the directing effect of CF_3 substituents in the tricarbonyl(η^5-cyclohexadienyl)iron(1+) series (Scheme 2). Reaction of **3d** with



(3d) R = OAc, $R^1 = CF_3$, R^2 = H
(5) R = R^1 = H, $R^2 = CF_3$

(6) R = OAc, $R^1 = CF_3$, R^2 = H, Nu = $CH(CO_2Me)_2$
(7) R = OAc, $R^1 = CF_3$, R^2 = H, Nu = OH
(8) R = OAc, $R^1 = CF_3$, R^2 = Nu = H
(9) R = R^1 = H, $R^2 = CF_3$, Nu = $CH(CO_2Me)_2$
(10) R = R^1 = H, $R^2 = CF_3$, Nu = H

Scheme 2.

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* Reference number with asterisk indicates a note in the list of references.

dimethyl sodiomalonate was examined first. A single regioisomer **6** was obtained but in a disappointing yield of 26%. Since electron-withdrawing substituents such as esters and ketones at C-1, typically direct nucleophiles to the far end of the dienyl system [5*,8], selective formation of **6** was not unexpected, but examples proceeding in better yield were needed to properly define the directing effect of the C-1 substituent in **3d**. Both hydroxide and borohydride nucleophiles were examined; again selective reaction at the far terminus of the dienyl system was observed, affording **7** and **8** in 72 and 52% yields, respectively. The preparation of **8** offered a means of access to the cation **5** which would permit the study of the directing effect of the CF_3 group at the 2-position. Reaction of **8** with HPF_6 in acetic anhydride afforded the cation **5** $\{[\alpha]_D +28°$ $(c\ 0.3\ CH_3CN)\}$ in 96% yield. In this case, reaction with the malonate enolate proved more efficient, and again proceeded at C-5 affording only the regioisomer **9** in 55% yield. With the cation **5**, however, reaction with sodium borohydride was not regiocontrolled, producing a 6:5 mixture (NMR) of C-5 and C-1 adducts. The major product (**10**) was isolated for characterisation by separation from the C-1 adduct by chromatography.

CD spectroscopy is normally useful in the correlation of absolute configurations of tricarbonyl(η^4-cyclohexadiene)iron(0) complexes, and has been employed to prove that **2a–c**, which all have negative values for $\Delta\epsilon$ in the highest wavelength band, have the same configuration of the planar chirality of the metal complex [3]. However, in the case of **2d**, the CD curve took a different form with a clear *maximum* at 320 nm [9*]. Thus while the absolute configurations of **2a–c** and of the products of types **3** and **4** are known [3] to correspond to the structures drawn in Scheme 1, the absolute configurations in the trifluoromethyl-substituted series cannot yet be assigned with certainty. Examination of the chiroptical properties of a wider selection of these complexes is now in progress. The differences between **2d** and **2a–c** are, however, consistent with our earlier observation [3] that changes in substitution pattern can cause crucial changes in the form of CD curves.

Trifluoromethyl-substituted cyclohexadienyl complexes are important as chiral building blocks for use in the asymmetric synthesis of CF_3 analogues of methyl-group containing target molecules. Our studies have demonstrated that the CF_3 group can provide efficient regiocontrol both in the formation of the cationic complexes, and in their reactions with nucleophiles. This study has provided the first examples of the regiodirecting influence of CF_3 control groups in electrophilic π-complexes, providing essential information to allow these complexes to be employed as intermediates in organic synthesis. With CF_3 substituents at either C-1 and C-2, the examples studied here undergo C–C bond formation by reaction with nucleophiles at the far terminus of the π-system.

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References and notes

1 G.R. Stephenson, R.P. Alexander, C. Morley and P.W. Howard, Philos. Trans. R. Soc. London, Ser. A, 326 (1988) 545.

2 P.W. Howard, G.R. Stephenson, and S.C. Taylor, J. Organomet. Chem., 370 (1989) 97.

3 G.R. Stephenson, P.W. Howard and S.C. Taylor, J. Chem. Soc., Chem. Commun., (1991) 127.

4 For examples of dioxygenations, see: D.T. Gibson, J.R. Koch, C.L. Schuld and R.E. Kallio, Biochemistry, 7 (1968) 3795; D.T. Gibson, M. Hensley, H. Yoshioka and T.J. Mabry, Biochemistry, 9 (1970) 1626; H. Ziffler, R. Kabuto, D.T. Gibson, V.M. Kobal and M. Jerina, Tetrahedron, 33 (1977) 2491; S.C. Taylor and S. Brown, Performance Chemicals, (1986) 18; T. Hudlicky, H. Luna, J.D. Price and F. Rulin, Tetrahedron Lett., 30 (1989) 4053; R. Agarwal, D.R. Boyd, R.A.S. McMordi, G.A. O'Kane, P. Portter, N.D. Sharma, H. Dalton and D.J. Gray, J. Chem. Soc., Chem. Commun., (1990) 1711.

5 Electron-withdrawing and donating groups effect regioselectivity of hydride abstraction reactions: A.J. Birch and L.F. Kelly, J. Organomet. Chem., 285 (1984) 267.

6 New products have been characterised by IR, NMR, MS, and by microanalysis or high resolution MS: in the case of the mixture of **3c**/**4c** poor analytical data (Found: C, 28.2; H, 1.6, $C_{11}H_8ClF_6FeO_5P$ calc. C, 28.9; H, 1.8%) was ascribed to the presence of traces of a hydrolysis product derived from **3c**. The cations **3c**/**4c** were identified by comparison of their 400 MHz NMR spectra with spectra of other members of the series, and, in view of the lack of regiocontrol, were not further investigated.

7 On-going work in Norwich seeks to define new regiodirecting effects in tricarbonyliron complexes. For recent examples, see: D.A. Owen, G.R. Stephenson, H. Finch and S. Swanson, Tetrahedron Lett., 30 (1989) 2607; G.R. Stephenson, P.W. Howard, D.A. Owen and A.J. Whitehead, J. Chem. Soc., Chem. Commun., (1991) 641.

8 A.J. Birch and D.J. Williamson, J. Chem. Soc., Perkin Trans. 1, (1973) 1892; B.M.R. Bandara, A.J. Birch and L.F. Kelly, J. Org. Chem., 49 (1984) 2496; P.W. Howard, G.R. Stephenson and S.C. Taylor, J. Chem. Soc., Chem. Commun., (1990) 1182.

9 The form of the CD curve was qualitatively similar to those observed with ester or ketone electron withdrawing substituents at the terminus of the diene, except that the highest wavelength band in **2d** occurred at lower wavenumbers: F. Djedaini, D. Grée, J. Martelli, R. Grée, L. Leroy, J. Bolard and L. Toupet, Tetrahedron Lett., 30 (1989) 3781; see also ref. 3.