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STEREOSELECTIVITY IN THE REACTION OF METHYLMAGNESIUM BROMIDE (CH_3MgBr) AND METHYLLITHIUM (CH_3Li) WITH A TRICARBONYLDIENEIRON DIESTER COMPLEX

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ABSTRACT

Tricarbonyl(η^4-5α,5β-dimethoxycarbonylcyclohexa-1,3-diene)iron (**1**) reacted stereoselectively with CH_3MgBr to furnish in 65% yield a 2:1 epimeric mixture of β-(endo)- and α-(exo)-(1'-hydroxyisopropyl) complexes, **2** and **3**. The reaction of **1** with CH_3Li was complex and showed that the ratio of products from the reaction on the β-(endo) and α-(exo) faces was 13:9. An explanation is advanced for metalalkyl reactions of **1** occurring preferentially on the β-(endo) face, whereas alkaline hydrolysis takes place exclusively on the α-(exo) face.

1. INTRODUCTION

The tricarbonyliron |$Fe(CO)_3$| complexes of cyclohexadienes are useful intermediates in organic synthesis[1] and can function as cationic species of various synthetic equivalents.[2]

The $Fe(CO)_3$ group coordinated to a cyclohexa-1,3-diene ligand, as shown by X-ray studies,[3] occupies a lateral position in the complex. Because of its steric bulk and electronic properties, the $Fe(CO)_3$ group may effectively distinguish the reactivities of the two faces of the diene moiety. In the reduction of a carbonyl group on the diene ligand, for example, bulky hydride transfer reagents approach the complex from the side opposite to the $Fe(CO)_3$ group allowing a stereospecific reaction.[2,4] However, acid catalysed isomeristaion of diene complexes gives products corresponding to protonation on the β-face of the diene ligand.[5,6]

A methoxycarbonyl (CO_2CH_3) group on the diene ligand of a $Fe(CO)_3$ complex is a useful handle for optical resolution,[7] and may serve as a valuable starting point for synthetic manipulation. However, relatively little has been studied on the classical reactivity of such compounds.[6,8] Alkaline hydrolysis of CO_2CH_3 complexes has demonstrated stereo- and regio-selectivity.[8] The diester complex **1**,[8] having CO_2CH_3 groups on the β-(endo) and α-(exo) faces, is an excellent model to study the stereoselective reactions of carboxylic ester groups. We report here the characterization of 3 new compounds (**2** to **4**) from the reaction of **1** with CH_3MgBr and CH_3Li, and that, contrary to expectations on steric reasons, major products arise from reaction with the CO_2CH_3 group of the β-(endo) face.

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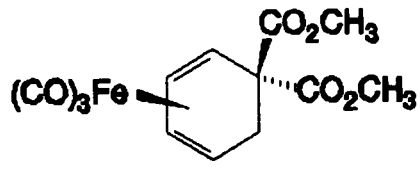
2. RESULTS AND DISCUSSION



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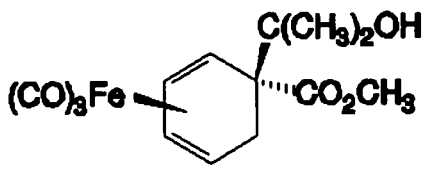

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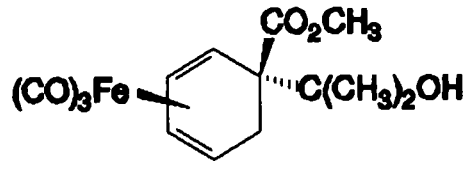

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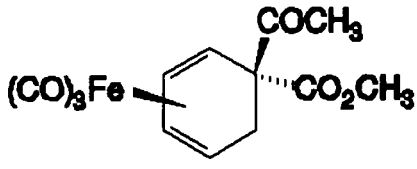

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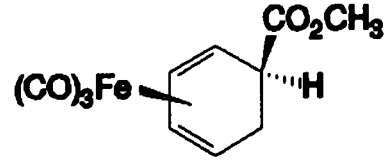

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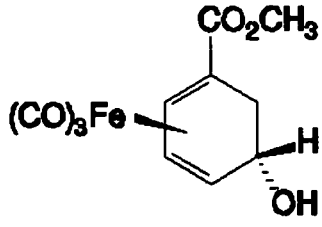

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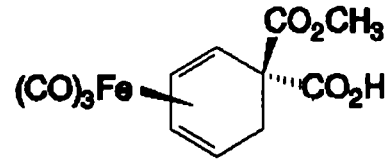

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The diester **1** was prepared by treating dimethyl cyclohexa-2,5-diene-1,1-dicarboxylate with $Fe(CO)_5$ as described previously;[8] the diene precursor was obtained by the reaction of methyl chloroformate with the lithium enolate of methyl cyclohexa-2,5-dienecarboxylate.[9]

The reaction of **1** with CH_3MgBr afforded in 65% yield two major compounds, **2** and **3**, which displayed IR spectra characteristic of alcohols. Their ^1H NMR spectra showed that each alcohol contained a CO_2CH_3 group indicating that the alcohols arose from the reduction of one of the two CO_2CH_3 groups in **1** by CH_3MgBr. Mass spectra and further analysis of the ^1H NMR spectra revealed that the two alcohols were isomeric having a molecular formula of $C_{13}H_{16}O_5Fe$. The isolated yields of **2** and **3** accounted for a ratio of 2:1 (see Table 1).

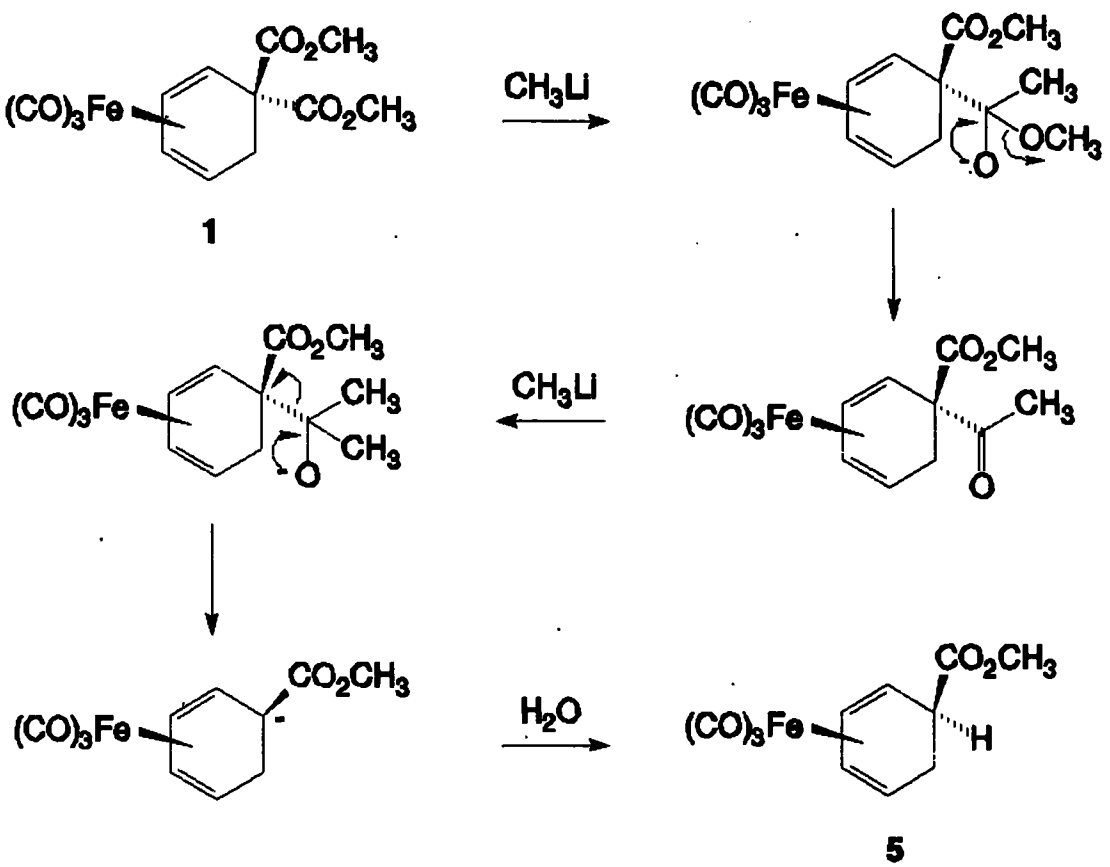
Table 1. Yields of products (**2** to **6**) from reaction of the diester complex **1** with CH_3MgBr and CH_3Li

	2	**3**	**4**	**5**	**6**
CH_3MgBr	43%	22%	trace	trace	trace
CH_3Li	4%	7%	35%	20%	7%

The assignment of stereochemistry for the isomeric alcohols **2** and **3** was based on the chemical shifts of their CO_2CH_3 groups. The CO_2CH_3 group of **2** appeared at δ 3.63 while that of **3** at δ 3.80. Thus, the alcohol **2** contained an α-(exo)-CO_2CH_3 and **3** had a β-(exo)-CO_2CH_3 because it is known that α-(exo)-CO_2CH_3 groups resonate at fields higher than β-(exo)-CO_2CH_3.[10] The diastereotopic methyl groups of the β-(1'-hydroxyisopropyl) complex **2** resonated at δ 1.19 (3H) and 1.06 (3H), while those of **3** appeared as a singlet at δ 1.06 (6H). Interestingly, in the α-(1'-hydroxyisopropyl) complex **3**, the outer diene proton adjacent to the methylene carbon resonated at a higher field by 0.2 ppm than the corresponding proton of its epimer, **2**.

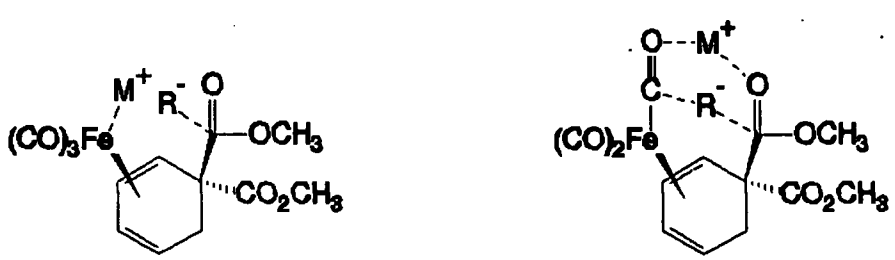
The reaction of **1** with CH_3Li gave in 75% yield six products which were separated by TLC (Table 1). The most mobile band constituted methyl benzoate and the 5β-CO_2Me ester **5**, which were identified by using an authentic sample (^1H NMR).[11] The second most mobile TLC band gave a crystalline yellow compound **4**, which displayed signals characteristic of a $COCH_3$ (δ 2.07, 1710 cm^{-1}) and a CO_2CH_3 (δ 3.62, 1730 cm^{-1}) groups in its ^1H NMR and IR spectra. The molecular formula of **4**, $C_{13}H_{12}O_6Fe$, established that in the reaction with CH_3Li, one of the CO_2CH_3 groups of **1** was converted to $COCH_3$ giving **4**. The absence of a methyl singlet at $\geq$ δ 3.63 indicated the α-CO_2Me steric assignment[10] for **4**; the diester **1** showed its β-CO_2Me at δ 3.73 and α-CO_2Me at δ 3.63.[8] The ^1H NMR spectrum of **4** showed its inner and outer diene protons at usual values (δ 5.38 and 3.26, respectively), and the methylene protons as an ABX at δ 2.34. The least mobile component was identified as the 5α-OH ester **6** from its spectral properties.[6] With CH_3Li, the 1'-hydroxyisopropyl complexes **2** and **3** were isolated only in small amounts (see Table 1).

The β-(endo) approach of CH_3Li would lead to the formation of the products **2** (4%) and **4** (35%) whereas the α-(exo) approach would provide **3** (7%) and **5** (20%). The 5β-CO_2Me complex **5** arose from the loss of the α-CO_2Me group from **1**. This may occur through a retro-aldol type cleavage as shown in Scheme 1. The complex **5** is formed from the resulting carbanion which has already been noted in the alkaline hydrolysis of **5**.[8] The mechanism for the formation of the 5α-OH ester **6** from **1** is not clear.



Scheme I. A possible mechanism for the formation of **5** from the reaction of the diester complex **1** with CH_3Li

In a previous study we have shown that the hydrolysis of **1** under alkaline conditions gave in 84% yield the monocarboxylic acid **7**,[8] the expected product on the basis of steric factors. However, both CH_3MgBr and CH_3Li reacted preferentially with the CO_2Me group of the β-(endo)-face of **1**. This implicates an initial coordination between the metalalkyl reagent and the $Fe(CO)_3$ group, as shown in **A** and/or **B**.



M^+R^- = metalalkyl reagent

A **B**

3. EXPERIMENTAL

Infrared (IR) spectra were recorded on a Perkin-Elmer 257 instrument, using polystyrene as a calibrant. ^{1}H NMR spectra were measured for solutions with tetramethylsilane as the internal standard on JEOL Minimar 100 and Varian HA100 spectrometers. The mass spectra were recorded on an AE1 MS902 double-focussing mass spectrometer, using heptacosafluorotributylamine as the reference for determination of high resolution data. Melting points (m.p.) were determined on a Reichert hot stage apparatus and are uncorrected. Thin layer chromatography (TLC) was performed on plates (20 cm × 20 cm × 1 mm) coated with Merck Kieselgel KGF_{254}. Light petroleum refers to the fraction that boils between 60°C and 80°C. Microanlyses were performed by the Australian National University Analytical Services Unit.

Reaction of tricarbonyl(η^4-5α,5β-dimethoxycarbonylcyclohexa-1,3-diene)iron (1) with CH_3MgBr

The diester **1** (500 mg, 1.49 mmol) in CH_2Cl_2 (15 ml) was cooled to -78°C, CH_3MgBr (1.0 M in ether, 4.5 ml) added, and the reaction mixture magnetically stirred for 2 h. The reaction mixture was added to water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried ($MgSO_4$) and concentrated in vacuo to obtain a viscous yellow oil (497 mg) which indicated the presence of at least 5 components by TLC analysis (Rf = 0.70, 0.52, 0.43, 0.29, and 0.08; eluant, a 1:1 mixture of light petroleum and diethyl ether). The products corresponding to Rf = 0.70, 0.52, and 0.08 were of very low concentration (TLC) and, therefore, were not isolated; however, these compounds were subseqeuntly characterised by isolating them in sufficient yield from the reaction of **1** with CH_3Li (see below).

The third band (Rf = 0.43) gave a yellow solid (215 mg, 43%) which was identified as tricarbonyl(η^4-5β-(1'-hydroxyisopropyl)-5α-methoxycarbonylcyclohexa-1,3-diene)iron(**2**), m.p. 69-71°C (from light petroleum), ν_{max} ($CHCl_3$) 3560-3420 (br, OH), 2050, 1980, 1715, 1690 cm^{-1}; δ ($CDCl_3$) 5.29 (2H, m, 2- and 3-H), 3.63 (3H, s, CO_2CH_3), 3.36 (1H, m, 1-H), 3.20 (1H, dd, $J_{3,4}$ = 7 Hz, $J_{2,4}$ = 1.5 Hz, 4-H), 2.53 (1H, dd, $J_{6\alpha,6\beta}$ = 16 Hz, $J_{3,4}$ = 3.5 Hz, 6-H), 2.02 (1H, dd, $J_{6\alpha,1}$ = 3.0 Hz, 6α-H), 1.19 (3H, s, CH_3), 1.06 (3H, s, CH_3); (M-CO calculated for $C_{13}H_{16}O_5Fe$ 308.0347; found 308.0348).

The fourth band (Rf = 0.29) afforded a yellow oil (110 mg, 22%) which was identified astricarbonyl(η^4-5α-(1'-hydroxyisopropyl)-5β-methoxycarbonylcyclohexa-1,3-diene)iron(**3**), ν_{max} ($CHCl_3$) 3550-3400 (br, OH), 2050, 1980, 1720 cm^{-1}; δ ($CDCl_3$) 5.40 (2H, m, 2- and 3-H), 3.80 (3H, s, CO_2CH_3), 3.28 (1H, dd, $J_{3,4}$ = 7 Hz, $J_{2,4}$ = 1.5 Hz, 4-H), 3.16 (1H, m, 1-H), 2.88 (1H, hump, OH), 2.54 (1H, dd, $J_{6\alpha,6\beta}$ = 16 Hz, $J_{6\beta,1}$ = 4 Hz, 6β-H), 1.93 (1H, dd, $J_{6\alpha,1}$ = 2.0 Hz, 6α-H), 1.06 (6H, s, 2 × CH_3); *m/z* 308 (M-CO), 280 (M-2CO), 252 (M-3CO).

Reaction of 1 with CH_3Li

In a similar procedure as above, the diester **1** (1.0 g, 2.98 mmol) was treated with CH_3Li (1.4 M in ether, 6.4 ml) in CH_2Cl_2 (30 ml) at -78°C for 2 h, and the reaction mixture worked up to give a viscous yellow oil (842 mg) comprising of 6 compounds (TLC, Rf = 0.70, 0.52, 0.43, 0.29, 0.08). The mixture was separated by preparative TLC (ca 200 mg on each plate), using a 1:1 mixture of diethyl ether and light petroleum.

The spectral properties (^{1}H NMR, MS) of the fraction (172 mg) corresponding to Rf = 0.70, were consistent with a mixture of tricarbonyl(η^4-5β-methoxycarbonylcyclohexa-1,3-diene)iron **5**[11] (20% yield, calculated from ^{1}H NMR) and methyl benzoate (2% yield).

The band at Rf = 0.52 gave a yellow solid (332 mg, 35%) which displayed spectral properties consistent with tricarbonyl(η^4-5β-acetyl-5α-methoxycarbonylcyclohexa-1,3-diene)iron **4**, m.p. 90-92°C (first transition), 115-117°C (complete melting); ν_{max} ($CHCl_3$) 2040, 1975, 1730, 1710 cm^{-1}; δ ($CDCl_3$) 5.38 (2H, m, 2- and 3-H), 3.62 (3H, s, CO_2CH_3), 3.26 (2H, m, 1- and 4-H), 2.34 (2H, m, 6-H), 2.07 (3H, s, $COCH_3$); (Found: C, 48.8; H, 3.8%. $C_{13}H_{12}O_6Fe$ requires C, 48.8; H, 3.8%).

The band at Rf = 0.43 gave **2** (43 mg, 4%) and that at Rf = 0.29 furnished **3** (74 mg, 7%). The least mobile band (Rf = 0.08) gave a yellow oil (65 mg, 7%), which was identified as tricarbonyl(η^4-5α-hydroxy-1-methoxycarbonylcyclohexa-1,3-diene)iron **6**,[6] by IR, ^{1}H NMR, and mass spectroscopic analysis.

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