Sterically hindered tricarbonyl(cyclohexadiene)iron complexes: preparation, isomer formation and isomerization reactions

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Abstract

The reaction of $Fe(CO)_5$ with 1-alkoxy-4-alkyl-cyclohexa-1,3-dienes, in which the alkyl substituent is a sterically demanding group such as isopropyl or tert-butyl, has been studied. An unprecedented rearrangement of the 1,3-diene was found to take place during the reaction to give a mixture of $Fe(CO)_3$-complex isomers. Tricarbonyl[(1,4-η)-2-isopropyl-5-tert-butyl-cyclohexa-1,3-diene]iron was the predominant product after p-toluenesulfonic acid-catalyzed isomerization of a mixture of isomers. This is in contrast to tricarbonyl[(1,4-η)-1-isopropoxy-4-ethyl- or methyl-cyclohexa-1,3-diene]iron which is a more stable form. Thus, the stability of the isomer of the $Fe(CO)_3$ complexes is also controlled by the bulkiness of the C-4 alkyl substituents.

Introduction

Organoiron complexes have received considerable attention in recent years, particularly in attempts to establish their role in the synthesis of natural products. In general, 1,4-cyclohexadiene derivatives are converted into the corresponding tricarbonyl(cyclohexa-1,3-diene)iron complexes where it invariably undergoes rearrangement, so that, for example, 1-methoxycyclohexa-1,4-diene, when treated with $Fe(CO)_5$, gives a mixture of tricarbonyl[(1,4-η)-1-methoxycyclohexa-1,3-diene]iron and tricarbonyl[(1,4-η)-2-methoxycyclohexa-1,3-diene]iron [1]. At present, the problem of formation of mixture of isomers of the $Fe(CO)_3$ complexes can be avoided by preconjugation of the 1,4-cyclohexadiene into the 1,3-cyclohexadiene derivatives which give mainly tricarbonyl[(1,4-η)-1-methoxycyclohexa-1,3-diene]iron without rearrangement [2]. We felt the need to investigate whether preconjugation into the 1,3-cyclohexadiene always led to the formation of the predominant $Fe(CO)_3$-(cyclohexa-1,3-diene) without rearrangement as reported previously in several cases

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[3]. In this work we have studied the influence of a sterically more demanding alkyl group, such as isopropyl and tert-butyl group at the C-4 position of cyclohexadiene derivatives, on the isomer formation of $Fe(CO)_3$ complexes. The synthesis of tricarbonyl[(1,4-η)-1-isopropoxy-4-tert-butyl-cyclohexa-1,3-diene]iron described here is novel.

Results and discussion

Preparation and isomer formation of Fe(CO)₃complexes

The Birch reduction of 1-alkoxy-4-alkylbenzene derivatives gave the unconjugated dienes, which were then treated with a catalytic amount of p-toluenesulfonic acid to give the equilibrium mixture of 1-alkoxy-4-alkyl-cyclohexa-1,4-diene and 1,3-diene derivatives. This equilibrium mixture of diene was refluxed with $Fe(CO)_5$ in di-n-butyl ether to give the corresponding 1,3-diene-$Fe(CO)_3$ complexes. Pearson has reported that 1-methoxy-4-methylcyclohexa-1,3-diene (**2a**) [4], and 1-isopropoxy-4-ethylcyclohexa-1,3-diene (**2b**) [3] upon reaction with $Fe(CO)_5$ gave nearly exclusively tricarbonyl[(1,4-η)-1-methoxy-4-methylcyclohexa-1,3-diene]iron (**3a**) and tricarbonyl[(1,4-η)-1-isopropoxy-4-ethylcyclohexa-1,3-diene]iron (**3b**) respectively, without rearrangement of the 1,3-diene (Scheme 1).

Reaction of an equilibrium mixture of 1-isopropoxy-4-isopropylcyclohexa-1,4-diene (**1c**) and 1,3-diene (**2c**) (1 : 4 mixture) with $Fe(CO)_5$ was found to give a mixture of tricarbonyl[(1,4-η)-1-isopropoxy-4-isopropylcyclohexa-1,3-diene]iron (**3c**) and tricarbonyl-[(1,4-η)-2-isopropoxy-5-isopropylcyclohexa-1,3-diene]iron (**4c**) in a 1.3 : 1 ratio, indicating that rearrangement of the 1,3-diene had taken place. Increasing the
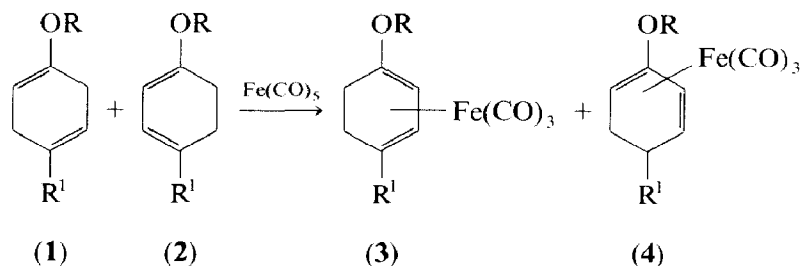
a: R = Me, R¹ = Me
b: R = ¹Pr, R¹ = Et
c: R = ¹Pr, R¹ = ¹Pr
d: R = ¹Pr, R¹ = ¹Bu

	1,3-Diene ratio (1):(2)	Fe(CO)₃-1,3-diene ratio (3):(4)	Ratio after isomerization (3):(4)
a	1:3	95: 5	95: 5
b	1:5	90:10	92: 8
c	1:4	13:10	10:10
d	1:4	10:26	6:94

Scheme 1

steric demand of the C-4 alkyl substituent was found to further favor the 1,3-diene rearrangement during complex formation. Thus, 1-isopropoxy-4-tert-butylcyclohexa-1,3-diene (**2d**) reacted with Fe(CO)$_5$ to give tricarbonyl[(1,4-η)-2-isopropoxy-5-tert-butylcyclohexa-1,3-diene]iron (**4d**) as the major product together with tricarbonyl(1,4-η-1-isopropoxy-4-tert-butylcyclohexa-1,3-diene)iron (**3d**) in a 2.6 : 1 ratio. The stereochemistry of **4c** and **4d** is consistant with the system bearing the less hindered *exo*-alkyl and this can be readily confirmed by the *endo*-H(5) peaks at δ 2.00 to 1.70 in their ^{1}H NMR spectra.

The ratio of isomers of the Fe(CO)$_3$ complexes described was readily determined from the ^{1}H NMR spectra by way of the integrated intensities of the doublets attributable to H(3) and H(2) for **3c,d** and the doublet of doublets attributable to H(3) or the multiplet from H(5) for **4c,d**. The isomers of the complexes were readily separated by column chromatography and thus assignments could be made with absolute certainty.

The rearrangement products **4c** and **4d** could also have arisen from the deconjugation of the 1,3-diene to the 1,4-diene by Fe(CO)$_5$ under the experimental conditions, before complex formation. In order to prove that this is not the case, an equilibrium mixture of the 1,4-diene and 1,3-diene (1 : 4 ratio) was treated with a catalytic amount of Fe(CO)$_5$, and was found not to influence the initial ratio of the dienes. The rearrangement of 1,3-diene must have occurred during the complex formation, which is dependent on the steric influence of the C-4 alkyl substituents.

Isomerization of tricarbonyl(cyclohexa-1,3-diene)iron

Several methods for the isomerization of Fe(CO)$_3$ complexes have been reported [4]. In our studied, we chose to use a catalytic amount of *p*-toluenesulfonic acid to effect isomerization under mild conditions. The previously synthesized 4-methyl- and 4-ethylcyclohexa-1,3-diene Fe(CO)$_3$ complexes **3a** and **3b** did not isomerize under these conditions. Isomerization of an isomeric mixture of the isopropyl counterpart, **3c** and **4c** (1 : 1.3 ratio) under the same conditions resulted in little change in the initial ratio. Thus, a balance between electronic stability of the 1,3-diene and steric demand at the C-4 substitution must be attained in this complex during its preparation. In contrast, isomerization of an isomeric mixture of its tert-butyl counterpart, **3d** and **4d** (1 : 2.6 ratio), gave **4d** nearly exclusively. Thus, we have observed that the stability of the Fe(CO)$_3$-complexes is dependent on the steric demand at the C-4 substituent in the 1,3-diene. The tert-butyl group in **3d** can interact sterically with the Fe(CO)$_3$ group, which may make the isomer **3d** less stable, whereas in **4d** the tert-butyl group can point away from the Fe(CO)$_3$ group. This may account for the fact that 1,3-diene rearrangement takes place with sterically more demanding alkyl substituents at C-4 rather than by direct complexation with Fe(CO)$_5$ during preparation.

Conclusion

The results reported here confirm that sterically demanding C-4 alkyl substituents in **2** have a strong directing effect on Fe(CO)$_3$-complex formation. We suggest that the generality concerning the reaction of conjugated diene **2** with Fe(CO)$_5$ to give mainly Fe(CO)$_3$ complex **3** should be made with caution; indeed, sterically demanding C-4 alkyl substituents in **2** promote rearrangement of the diene during complex formation to give **4**.

Experimental

IR spectra were recorded with a Perkin–Elmer 1320, mass spectra with JOEL JMS-D100, and ^{1}H NMR with Varian 390 or VXR 300 (300 MHz) spectrometers. Melting point are uncorrected. All preparative and chromatographic operations with iron complexes were conducted under nitrogen. n-Butyl ether was passed through a column of alumina oxide to remove impurities.

Preparation of 1,3-cyclohexadiene derivatives

4-Alkylphenols were converted to their isopropyl ethers by reaction with sodium in absolute ethanol and 2-bromopropane. The Birch reduction was performed in liquid ammonia containing tetrahydrofuran and ethanol, by use of lithium metal. The usual workup afforded crude 1-alkyl-4-isopropoxycyclohexa-2.5-dienes, which were heated to 80°C with p-toluenesulfonic acid to effect partial conjugation.

^{1}H NMR spectroscopy was used to determine the proportions of conjugation. The resonances around δ 5.23 and 4.55 attributed to the olefinic protons of the 1,4-diene decreased with conjugation, while two new resonances appeared–around δ 5.51 and 4.80 (doublets)—attributable to the olefinic protons of the conjugated dienes: 1-isopropoxy-4-isopropylcyclohexa-1,3-diene (4:1 ratio with 1,4-diene); 1-isopropoxy-tert-butyl-cyclohexa-1,3-diene (4:1 with 1,4-diene).

Preparation of (1,3-diene)-Fe(CO)$_3$ complexes

A crude mixture of 1,3-diene and 1,4-diene was treated with pentacarbonyliron (2.5 equiv.) in di-n-butyl ether at 140°C under nitrogen for at least 48 h. The mixture was cooled, filtered through Celite, and the solvent was removed first at aspirator pressure, and then under high vacuum. ^{1}H NMR was first performed on the mixtures of Fe(CO)$_3$ complexes obtained and then a small amount was chromatographed to afford the pure individual complex for characterization.

Tricarbonyl[(1,4-η)-1-isopropoxy-4-isopropylcyclohexa-1,3-diene]iron (3c) and tri-carbonyl[(1,4-η)-2-isopropoxy-5-isopropylcyclohexa-1,3-diene]iron (4c)

Complex (3c): $\nu_{max.}$(CHCl$_3$) 2035 and 1965 cm^{-1}; δ (CDCl$_3$) 5.10 (1H, d, J 4.5 Hz, 3-H), 4.90 (1H, d, J 4.5 Hz, 2-H), 4.09 (1H, hept.), 2.30–1.43 (4H, m, 2 × CH$_2$), 1.83 (1H, hept), 1.22 (12H, 4 × d each); m/e 320, 292, 264 and 236.

Complex (4c): $\nu_{max.}$(CHCl$_3$) 2036, 1970 cm^{-1}; δ(CDCl$_3$) 5.10 (1H, dd, J 2.7 and 6.3 Hz, 3-H), 4.26 (1H, hept.), 3.25 (1H, m, 5-H), 2.63 (1H, dd, J 2.7 and 6.3 Hz, 2H), 1.85 (2H, m, CH$_2$), 1.32 (6H, q), 1.26 (1H, hept.) and 0.83 (6H, q); m/e 320, 292, 264, 236. (Found: C, 56.13; H, 5.52. C$_{15}$H$_{19}$O$_4$Fe calcd.: C, 56.22; H, 5.90%). The total yield from 65 g of diene was 38%.

Tricarbonyl[(1,4-η)-1-isopropoxy-4-tert-butylcyclohexa-1,3-diene]iron (3d) and tri-carbonyl[(1,4-η)-2-isopropoxy-5-tert-butylcyclohexa-1,3-diene]iron (4d)

Complex (3d): m.p. 39°C, $\nu_{max.}$(CHCl$_3$) 2040 and 1980 cm^{-1}; δ(CDCl)$_3$ 5.12 (2H, d, each, J 6.0 Hz, 2-H and 3-H), 4.00 (1H, hept.), 2.30–1.40 (4H, m, CH$_2$ × 2), 1.26 (6H, q, isopropyl), 1.08 (9H, s, ^{t}butyl); m/e 334, 306, 278, 250. (Found: C, 57.50; H, 6.60. C$_{16}$H$_{22}$O$_4$Fe calcd.: C, 57.40; H, 6.50%).

Complex (4d): m.p. -10°C; $\nu_{max.}$(CHCl$_3$) 2040, 1985 cm^{-1}; δ(CDCl$_3$) 5.10 (1H, dd, J 3 and 6 Hz, 3-H), 4.22 (1H, hept.), 3.22 (1H, m, 5-H), 2.62 (1H, d, J 3

and 6 Hz, 2-H), 1.90–1.40 (3H, m), 1.36 and 1.26 (3H each, d each, isopropyl), 0.79 (9H, s, 'butyl); *m/e* 334, 306, 278, 250. The total yield from 40 g of diene was 35%.

Isomerization reaction

A solution of isomeric mixture of the complexes and a catalytic amount of *p*-toluenesulfonic acid was left to stand at room temperature under nitrogen for 48 h. The solution was washed with aqueous sodium hydrogen carbonate and water, and dried over anhydrous magnesium sulfate. Removal of the solvent gave the product(s) in at least 90% yield. The ratio of the isomer was again determined by ^{1}H NMR.

Acknowledgement

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