Studies on the Regioselective Preparation of Tricarbonyl(cyclohexadienyl)iron(1+) Salts

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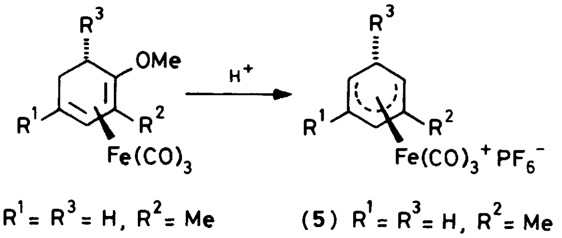
The mixture of tricarbonyliron complexes produced from 1-methoxy-2,4-dimethylcyclohexa-1,4-diene was converted by CF_3CO_2H into a single product, tricarbonyl(1—5-η-2,4-dimethylcyclohexadienyl)iron hexafluorophosphate, without prior separation by chromatography. The corresponding 2-methoxy-3,5-dimethylcyclohexadienyl salt was the only complex obtained by hydride abstraction from the same mixture.

The value of tricarbonyliron complexes as intermediates in organic synthesis has been demonstrated in recent work[1] which has established η⁵-cyclohexadienyl salts as synthetic equivalents to cyclohexenone cations, and in natural product syntheses[2] developing this concept. More widespread application of the method is limited by a lack of simple ways to prepare substituted tricarbonylcyclohexadienyliron salts in pure form. In this paper we describe the effect of steric blocking by adjacent substituents to control the regiochemistry of the acid-catalysed route[3] (Scheme 1) to such intermediates from OMe-substituted precursors, and the application of this method to provide a convenient, highly selective, preparation of the 2,4-dimethyl-substituted salt from a mixture of complexes without the need for prior chromatographic separation.



(1) $R^1 = R^3 = H$, $R^2 = Me$
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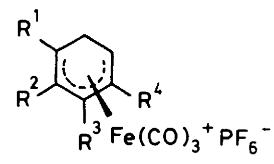
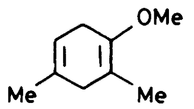
(3) $R^1 = R^3 = Me$, $R^2 = H$
(4) $R^1 = R^2 = Me$, $R^3 = H$

(5) $R^1 = R^3 = H$, $R^2 = Me$
(6) $R^1 = R^2 = Me$, $R^3 = H$
(7) $R^1 = R^3 = Me$, $R^2 = H$

Scheme 1.



(8) $R^1 = R^2 = R^4 = H$, $R^3 = Me$
(9) $R^1 = R^3 = Me$, $R^2 = R^4 = H$
(10) $R^1 = R^3 = Me$, $R^2 = H$, $R^4 = OMe$



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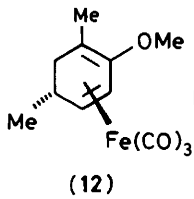

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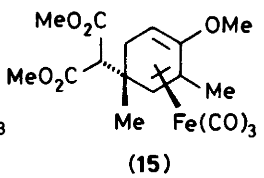

(15)

Demethoxylation of 1-substituted tricarbonyl(cyclohexadiene)iron complexes of type (**1**)—(**4**) generally proceeds to give products which are consistent with the minimum rearrangement prior to loss of OMe. In early work, however, Birch and Haas[3] described the unexpected formation of the complexes (**5**) and (**8**) from (**1**) and (**2**) by treatment with H_2SO_4. We have examined the recent modification[4] of this method, which employs trifluoroacetic acid, with similar complexes derived from 2,4-dimethylanisole, and demonstrated the synthetic convenience of this effect. Birch reduction[5] of 2,4-dimethylanisole gave the required 1,4-diene (**11**). Reinvestigation of the complexation of this diene led in our hands to the isolation of three isomeric compounds (**3**), (**4**), and (**12**) that could be separated by chromatography. Treatment of the 1-methoxy-complex (**3**) with CF_3CO_2H at −15 °C gave the 2,4-dimethyl salt (**6**) as the major product, together with a small amount (*ca.* 3%) of a second compound which appeared, from its ¹H n.m.r. spectrum, to be the isomeric salt (**7**). This minor product is anticipated from direct protonation of (**3**) at C^1. Since the formation of the alternative salt (**6**) as the major product implied the predominant rearrangement of the complex (**3**) to form (**4**) before loss of OMe from an allylic position, all three compounds obtained from the complexation should give the same result on treatment with CF_3CO_2H. This was found to be the case. The product (**6**), obtained from the unseparated mixture of complexes, contained only a trace (< 1%) of the isomer (**7**). Recrystallisation from acetonitrile gave convenient access to the pure salt (**6**). Regiocontrol of the demethoxylation process was superior at low temperature. When the reaction was performed with CF_3CO_2H at room temperature a 95:5 mixture of products was produced. Treatment of the 2-methoxy-complex (**12**) with H_2SO_4 has been shown[6] to give a mixture of the salts (**6**) and (**9**). We have found that reaction of complex (**12**) with CF_3CO_2H at −15 °C gave a *ca.* 99:1 mixture of the isomers (**6**) and (**7**).

Complexes (**2**) and (**3**) both have α-methyl substituents (substituents on the face of the ligand opposite to the metal[1]) adjacent to the OMe group. It appears that under these circumstances direct protonation at C^1 and loss of OMe to form α-methyl-substituted salts is not a favourable process. This may be due to the production of intermediates of the type (**13**) (Scheme 2) that have two adjacent α substituents. In contrast, the alternative protonation at C^4 would produce the intermediate (**14**) in which the α-substituents are not at adjacent positions on the ring, and so would commence the series of

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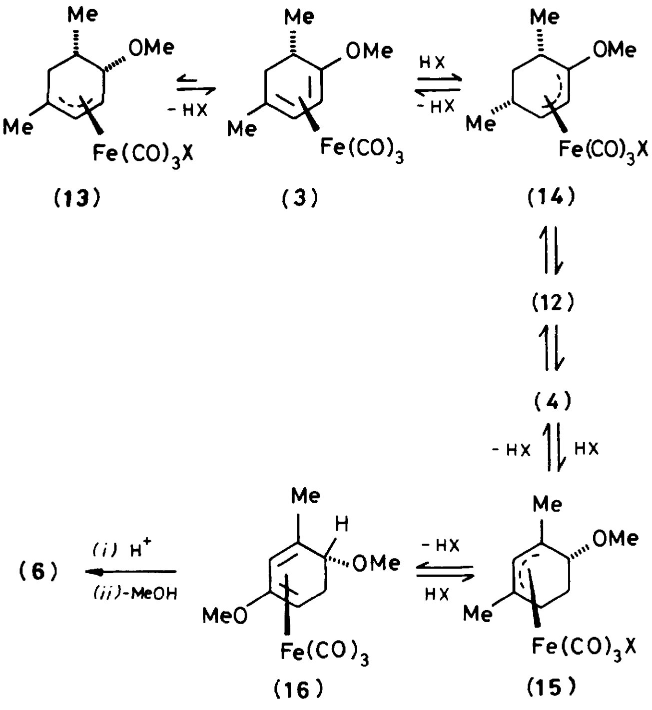

Scheme 2.

rearrangements shown in Scheme 2, that interconvert the complexes (**3**), (**12**), and (**4**). Complex (**4**) can be protonated at C^1 to form the product (**6**) by loss of OMe *via* the allyl intermediate (**15**) and the diene complex (**16**), by reactions that do not involve the production of intermediates bearing adjacent α substituents. The last steps of this mechanism [the formation of salt (**6**) from intermediate (**14**)] are supported by the observation that the 1-methoxy-substituted complex (**4**) forms only the salt (**6**) on treatment with CF_3CO_2H.

α-Methyl groups are known[7] to block hydride abstraction. This reaction should thus also provide a route to a single product without prior chromatography, since only the complex (**4**) should undergo hydride abstraction. Treatment of the mixture of isomers obtained from the diene (**11**), with triphenylcarbenium tetrafluoroborate and then with water, gave the salt (**10**), together with traces of other compounds. The unreacted starting material, complexes (**3**) and (**12**), was recovered from the hydride-abstraction reaction and treated directly with CF_3CO_2H without purification to give the second salt (**6**).

Thus the salts (**6**) and (**10**) can be prepared conveniently from the diene (**11**) by utilising highly selective reactions that employ steric effects of α-methyl substituents to provide control over potentially competing reaction paths. The selective preparation of single compounds from mixtures of precursor complexes, without the need for chromatographic separations, is attractive for large-scale preparations of tricarbonyl(cyclohexadienyl)iron(1 +) salts required as key intermediates in synthesis.

Experimental

Di-n-butyl ether was filtered through alumina before use. All reactions were performed under a nitrogen atmosphere. The product ratios were obtained from proton n.m.r. spectra recorded on a Bruker WP 80 SY spectrometer, and ^{13}C n.m.r. spectra were recorded using a Bruker WM 250 spectrometer.

Preparation of Complexes.—Lithium wire (15 g, 2.1 mol) was added in pieces to a solution of 2,4-dimethylanisole (68 g, 0.5 mol) in a mixture of liquid ammonia (2 l), 2-methylpropan-2-ol (270 cm^3), and tetrahydrofuran (150 cm^3). After 2 h the blue colour was quenched by addition of ammonium chloride and the reaction mixture was allowed to evaporate overnight. After addition of ice and water, the mixture was extracted while still cold with four portions (250 cm^3) of light petroleum (b.p. 40—60 °C). The extracts were washed with iced water and brine, dried over K_2CO_3, and evaporated to give the crude product, 1-methoxy-2,4-dimethylcyclohexa-1,4-diene[5] (**11**) (62 g, 90%), which was used for the next step without purification.

The 1,4-diene (**11**) (62 g) was heated with pentacarbonyliron (45 cm^3) in di-n-butyl ether (300 cm^3) at 140—150 °C for 16 h. The reaction mixture was cooled, filtered through alumina, and evaporated under reduced pressure (oil pump) to leave the crude product (30 g) as a dark oil. Pentacarbonyliron (20 cm^3) was added to the yellow distillate and the process was repeated three times until further product ceased to be formed. The crude complexes (92 g) were distilled [57—63 °C, 10^{-3} mmHg (0.133 Pa)]; to provide a mixture of methoxydimethylcyclohexa-1,3-diene complexes (85 g, 62% from 2,4-dimethylanisole) (Found: C, 51.85; H, 5.15. $C_{12}H_{14}FeO_4$ requires C, 51.85; H, 5.05%). A portion (2 g) of this mixture was separated by chromatography on silica (400 g) by elution with toluene–hexane (1:10 v/v). The following products were obtained in order of elution. *Tricarbonyl*(η-2-*methoxy*-1,5α-*dimethylcyclohexa*-1,3-*diene*)-iron(0) (**12**) (0.73 g, 44% of mixture); $\nu_{max.}$(CO) 2 041, 1 971, and 1 967 cm^{-1} (cyclohexane); $\delta_H(CDCl_3)$ 0.89 (3 H, d, *J* 6.5, C^5Me), 1.59 (3 H, d, *J* < 1, C^1Me), 1.1—1.4 and 1.9—2.3 (3 H, m, m, H^5 and H^6), 2.55 (1 H, dd, *J* 6.5, 4, H^4), 3.70 (3 H, s, OMe), and 4.90 (1 H, d, *J* 6.5 Hz, H^3); $\delta_C(CDCl_3)$ 20.7 [q, *J*(CH) 127, C^5Me], 25.5 [q, *J*(CH) 126, C^1Me], 33.1 [d, *J*(CH) 132, C^5], 40.7 [t, *J*(CH) 129, C^6], 54.2 [q, *J*(CH) 145, OMe], 57.3 [d, *J*(CH) 155, C^4], 62.5 [dd, *J*(CH) 171, *J*(CCH) 7 Hz, C^3], 68.2 (s, C^1), 138.1 (s, C^2), and 212.0 (s, M–CO); *m*/*z* 278 (M^+, 6), 250 (18), 222 (4), 220 (13), 192 (100), 178 (12), 176 (7), and 162 (13%). *Tricarbonyl*(η-1-*methoxy*-2,4-*dimethylcyclohexa*-1,3-*diene*)*iron*(0) (**4**) (0.66 g, 40% of mixture); $\nu_{max.}$(CO) 2 035, 1 967, and 1 962 cm^{-1} (cyclohexane); $\delta_H(CDCl_3)$ 1.52 (3 H, s, C^4Me), 1.6—1.9 (4 H, m, H^5, H^6), 2.08 (3 H, s, C^2Me), 3.49 (3 H, s, OMe), and 4.89 (1 H, s, H^3); $\delta_C(CDCl_3)$ 15.8 [q, *J*(CH) 129, C^4Me], 25.6 [q, *J*(CH) 126, C^2Me], 25.7 [t, *J*(CH) 130] and 30.3 [t, *J*(CH) 129] (C^5 and C^6), 57.0 [q, *J*(CH) 143, OMe], 70.1 (s, C^4), 83.5 [d, *J*(CH) 164 Hz, C^3], 92.4 (s, C^2), 114.5 (s, C^1), and 213.1 (s, M–CO); *m*/*z* 278 (M^+, 3) 250 (17), 222 (2), 220 (17), 192 (100), 178 (5), 176 (4), and 162 (9%). *Tricarbonyl*(η-1-*methoxy*-4,6α-*dimethylcyclohexa*-1,3-*diene*)*iron*(0) (**3**) (0.27 g, 16% of mixture); $\nu_{max.}$(CO) 2 038, 1 971, and 1 964 cm^{-1} (cyclohexane); δ_H $(CDCl_3)$ 0.98 (3 H, d, *J* 6.5, C^6Me), 1.48 (3 H, s, C^4Me), 1.1—1.4 and 2.0—2.4 (3 H, m, m, H^5 and H^6), 3.41 (3 H, s, OMe), 4.92 (1 H, d, *J* 4.5, H^3), and 5.11 (1 H, dd, *J* 4.5, 1, H^2); $\delta_C(CDCl_3)$ 21.5 [q, *J*(CH) 127, C^6Me], 25.7 [q, *J*(CH) 126, C^4Me], 33.2 [d, *J*(CH) 132, C^6], 40.1 [t, *J*(CH) 127, C^5], 56.4 [q, *J*(CH) 143, OMe], 71.6 (s, C^4), 74.9 [d, *J*(CH) 171] and 80.9 [d, *J*(CH) 171 Hz] (C^2 and C^3), 120.0 (s, C^1), and 213.3 (s, M–CO); *m*/*z* 278 (M^+, 2), 250 (24), 222 (3), 220 (20), 192 (100), 178 (14), 176 (7), and 162 (10%).

Treatment of Complexes with Trifluoroacetic Acid.—Cold CF_3CO_2H (20 cm^3) was added to a chilled sample of the complex and the flask was sealed and cooled at *ca.* −15 °C overnight. The red solution gradually became lighter in colour. The reaction mixture was poured into a solution of ammonium hexafluorophosphate (1 equivalent) in water (50 cm^3). The yellow precipitate was collected, washed with ether, and dried over potassium hydroxide.

Tricarbonyl(1—5-η-2,4-*dimethylcyclohexadienyl*)*iron*(1 +)

hexafluorophosphate (**6**). The mixture of complexes (2 g) obtained from the diene (**11**) was treated with CF_3CO_2H to give the salt (**6**) (2.02 g, 72%, >99% pure) and a barely detectable trace of a second salt. Crystallisation from acetonitrile at − 15 °C afforded the pure product as a microcrystalline yellow *powder* (Found: C, 33.45; H, 3.10. $C_{11}H_{11}F_6FeO_3P$ requires C, 33.7; H, 2.85%); $\nu_{max.}$(CO) 2 109 and 2 026 cm^{-1} (CH_3CN); δ_H(CD_3CN) 1.95 (1 H, d, *J* 15, β-H^6), 2.14 (6 H, s, Me), 2.99 (1 H, dt, *J* 15, 6.5, α-H^6), 4.09 (2 H, dt, *J* 6, 1.5, H^1 and H^5), and 6.95 (1 H, t, *J* 1.5, H^3); δ_C(CD_3CN) 21.1 [q, *J*(CH) 131, Me], 27.7 [t, *J*(CH) 139, C^6], 64.5 [d, *J*(CH) 171, C^1 and C^5], 91.5 [d, *J*(CH) 185 Hz, C^3], 120.1 (s, C^2 and C^4), and 203.6 (s, M–CO). The filtrate was partially evaporated and crystallised a second time, filtered, and finally evaporated to provide a sample that was enriched in the minor product which was identified by its proton n.m.r. spectrum as *tricarbonyl*(1—5-η-2,6α-*dimethylcyclohexadienyl*)-*iron*(1+) *hexafluorophosphate* (**7**): δ_H(CD_3CN) 0.62 (3 H, d, *J* 7.5 C^{6}Me), 1.74 (1 H, d, *J* 7.5, H^6), 2.13 (3 H, s, C^{2}Me), 4.3—4.7 (2 H, m, H^1 and H^5), 5.80 (1 H, d, *J* 7, H^4), and 6.92 (1 H, d, *J* 7 Hz, H^3). When the reaction of the diene complexes with CF_3CO_2H was performed at room temperature the salts (**6**) and (**7**) were formed in the ratio (^{1}H n.m.r.) of *ca.* 95:5. Complex (**6**) was obtained in pure form by treatment of (**4**) with CF_3CO_2H. A *ca.* 99:1 mixture of the salts (**6**) and (**7**) was produced by treatment of (**12**) with CF_3CO_2H. A *ca.* 97:3 mixture of the same products was obtained from complex (**3**).

Tricarbonyl(1—5-η-2-*methoxy*-3,5-*dimethylcyclohexadienyl*)-*iron*(1+) *Hexafluorophosphate* (**10**).—The mixture of complexes (4 g, 14 mmol) obtained from the diene (**11**) was stirred with triphenylcarbenium tetrafluoroborate (3.2 g, 9.6 mmol) in CH_2Cl_2 (50 cm^3) overnight. Ether (200 cm^3) was added and a gummy yellow precipitate was collected and heated in water (20 cm^3) for 15 min on a steam-bath. After extraction with ether (2 × 10 cm^3) the aqueous phase was poured into a solution of ammonium hexafluorophosphate (1.5 g, 9.1 mmol) in water (2 cm^3). The *product* (1.9 g, 31%) was purified by precipitation from acetonitrile by slow mixing with ether (Found: C, 34.1; H, 2.95. $C_{12}H_{13}F_6FeO_4P$ requires C, 34.2; H, 3.10%); $\nu_{max.}$(CO) 2 103 and 2 052 cm^{-1} (CH_3CN); δ_H(CD_3CN) 1.73 (3 H, d, *J* < 1, C^{5}Me), 2.27 (1 H, dm, *J* 15, β-H^6), 2.63 (3 H, s, C^{3}Me), 2.96 (1 H, ddd, *J* 15, 6.5, 1, α-H^6), 3.69 (3 H, s, OMe), 3.94 (1 H, dd, *J* 6.5, 1.5 Hz, H^1), and 5.77 (1 H, s, H^4); δ_C(CD_3CN) 15.4 [q, *J*(CH) 131, C^{5}Me), 23.4 [q, *J*(CH) 130, C^{3}Me], 34.1 [t, *J*(CH) 137, C^6], 41.7 [d, *J*(CH) 171, C^1], 58.3 [q, *J*(CH) 148, OMe], 99.9 [d, *J*(CH) 172 Hz, C^4], and 203.2 (s, M–CO) (C^2, C^3, and C^5 were not detected). The filtrate from the hydride-abstraction reaction was evaporated and the crude residue was treated with CF_3CO_2H as described above. Complex (**6**) (2.24 g, 40%) was obtained.

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