Transition-metal Mediated Asymmetric Synthesis. Part 5.[1] Alternative Methods for the Formation of Tricarbonyl(η^5-cyclohexadienyl)iron(1+) Salts

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The influence of substituents on the preparation of tricarbonyl(η^5-cyclohexadienyl)iron(1+) salts by oxidation using thallium(III) tris(trifluoroacetate) and by hydride abstraction using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone–tetrafluoroboric acid has been examined. Hydride abstraction by thallium oxidation is superior to conventional methods and offers complementary regiocontrol in some cases. An example of hydride abstraction from a blocked tricarbonyl(η^4-cyclohexadiene)iron complex is described.

Complete stereocontrol of alkylations by a wide range of nucleophilic species, combined with the virtue of unusual chemical stability, has stimulated[2] the development in recent years of cationic tricarbonyliron complexes such as **(2)** as attractive and versatile electrophilic intermediates[3] in organic synthesis. Our interest[4] in the use of resolved complexes of this type in enantiomer synthesis has led us to begin studies of two aspects of the formation of these cationic intermediates where the availability of new preparative methods would be of particular value.

The first concerns regiocontrol. Chiral complexes of type **(1b)**—**(1d)** contain a planar chiral element in which binding to the metal atom distinguishes the two enantiofaces of a prochiral ligand. Inevitably unsymmetrical substitution patterns are needed, so care over regiocontrol[5] is essential for an efficient synthetic sequence.

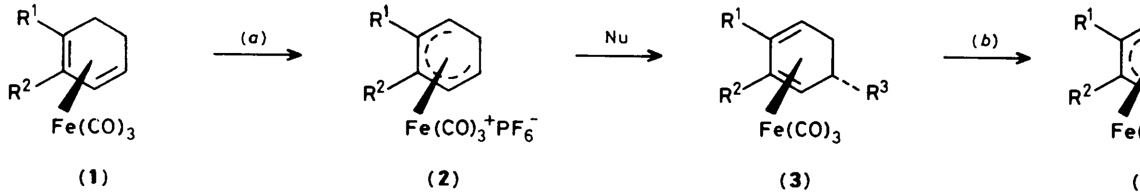
Secondly, general methods are needed that will permit the metal to control a series of alkylation reactions. Although certain nucleophiles will add[6] to neutral intermediates, the ability to reconvert alkylation products such as **(3)** to η^5 cations is highly desirable since the full range[1] of nucleophiles would then be available for use in subsequent alkylation steps. Furthermore, the alkylation/reactivation sequence [such as the example **(2)** to **(3)** to **(4)**] would make available an essentially iterative procedure in which the chiral metal complex can serve[7] to control the stereochemistry at a series of positions within the molecule.

In this paper we describe an examination of some alternatives to the use of triphenylcarbenium reagents[3,8] for the η^4-diene to η^5-dienyl cation interconversions required at steps (*a*) and (*b*) in the Scheme. The procedures normally employed for this purpose suffer from some disadvantages. Triphenylcarbenium tetrafluoroborate and hexafluorophosphate, although very effective reagents in suitable circumstances, frequently show poor regiocontrol and are blocked by substituents *trans* to the metal.[3] Existing alternatives also suffer from limitations since they involve the removal of substituents[9] (it is difficult to promote a series of alkylations in this way), or the mediation of particular side-chain substitution patterns.[10]

Results and Discussion

Regiocontrol of the Formation of Tricarbonyl(η^5-cyclohexadienyl)iron(1+) Salts.—Following the original report[11] of allylic oxidation of the unsubstituted complex **(1a)** by thallium(III) tris(trifluoroacetate), a number of intramolecular examples[10] of the reaction have been performed. Similar reactions are known[12] for other oxidizing agents. We have since described[13] a way to use the thallium(III) oxidation procedure on substrates bearing simple substituents resulting in the direct formation of the disubstituted salt **(2b)**, a specific regioisomer, required for terpene synthesis, which was hard to obtain by conventional methods. Further study has now shown that this reaction is general in application, and complementary in scope to the use of triphenylcarbenium reagents. The degree of regiocontrol observed using oxythallation depends on the experimental procedure that is adopted. The improved results described here have been obtained by variation of our original method[13] by the addition of a source of a tetrafluoroborate counter ion prior to treatment with acid to remove the allylic substituent, in this case presumably O_2CCF_3. This also has the advantage that water-soluble intermediates can be obtained to simplify the reaction work-up.

Oxidation of several 2-methoxy-substituted complexes has revealed a consistent preference for 3-methoxy-substituted products. Product ratios shown in Table 1 indicate good regiocontrol, and in the case of **(1b)**, the salt **(2b)** is formed exclusively. Regiocontrol in this reaction is the reverse of that



(1) **(2)** **(3)** **(4)**

a; $R^1 = R^2 = H$
b; $R^1 = Me$, $R^2 = OMe$
c; $R^1 = H$, $R^2 = OMe$
d; $R^1 = OMe$, $R^2 = Me$

a; $R^1 = R^2 = H$, $R^3 = Nu$
b; $R^1 = OMe$, $R^2 = Me$, $R^3 = H$

Scheme. Nu = nucleophile

Table 1. Formation[a] of tricarbonyl(η^5-cyclohexadienyl)iron(1 +) salts

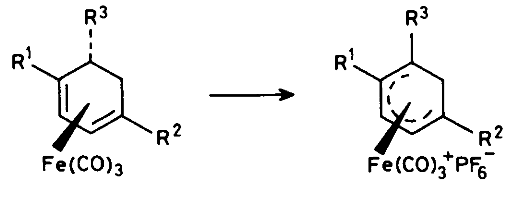
Starting material	Reagent	Products	Ratio	Yield (%)	Ref.
(1a)	$\mathrm{Tl^{III}}$	**(2a)**	—	50	
	ddq–$\mathrm{HBF_4}$	**(2a)**	—	70	
2-OMe Complexes					
(1b)	$\mathrm{Tl^{III}}$	**(2b)**	—	72	
	$\mathrm{CPh_3^+}$	**(6c)**	—	70	
(1c)	$\mathrm{Tl^{III}}$	**(2c)** + **(6a)**	12:1	50	
	ddq–$\mathrm{HBF_4}$	**(6a)**	—	33	
	$\mathrm{CPh_3^+}$	**(2c)** + **(6a)**	1:9	95	3, *b*
(3b)	$\mathrm{Tl^{III}}$	**(2b)** + **(2d)**	22:1	59	
	$\mathrm{CPh_3^+}$	**(2b)** + **(2d)**	1:4	78	13
1-OMe Complexes					
(1d)	$\mathrm{Tl^{III}}$	**(2d)**	—	53	
(5a)	$\mathrm{Tl^{III}}$	**(6a)**	—	58	
	ddq–$\mathrm{HBF_4}$	**(6a)**	—	10	
	$\mathrm{CPh_3^+}$	**(6a)** + **(6d)**	1:4	98	20
(5b)	$\mathrm{Tl^{III}}$	**(6b)**	—	53	
	$\mathrm{CPh_3^+}$	**(6b)** + **(6e)**	9:1	90	20
(5c)	$\mathrm{Tl^{III}}$	**(6c)**	—	10	

[a] Reactions were performed on racemic samples: structures (1)—(6) do not depict absolute configurations. [b] R. E. Ireland, G. G. Brown, R. H. Stanford, jun., and T. C. McKenzie, *J. Org. Chem.*, 1974, **39**, 51.

Table 2. Comparison of results of hydride abstractions from optically active complexes

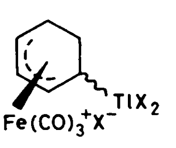
Starting material			Product		
Structure	$\alpha^a/^\circ$ (c/g dm^{-3})	Reagent	Structure	$\alpha^a/^\circ$ (c/g dm^{-3})	Yield (%)
(5a)	+7.7 (0.6)	$\mathrm{Tl^{III}}$	**(6a)**	+5.3 (0.5)	58
		$\mathrm{CPh_3^+}$	**(6a)**[b]	+1.8 (0.3)	6
(5b)	+7.6 (0.8)	$\mathrm{Tl^{III}}$	**(6b)**	+7.8 (0.5)	53
		$\mathrm{CPh_3^+}$	**(6b)**[b]	+7.6 (0.3)	47

[a] λ = 589.3 nm; solvent, MeCN or $\mathrm{CHCl_3}$. [b] After hydrolysis of 1-methoxy isomers.

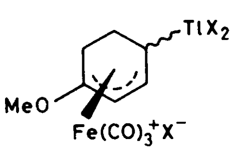


(5) (6)

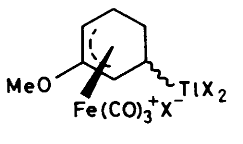
a ; R^1 = OMe, R^2 = R^3 = H
b ; R^1 = OMe, R^2 = Me, R^3 = H
c ; R^1 = OMe, R^2 = H, R^3 = Me
d ; R^1 = R^2 = H, R^3 = OMe
e ; R^1 = Me, R^2 = OMe, R^3 = H



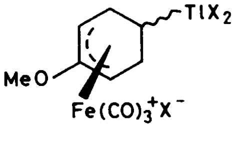
(7)



(8)



(9)



(10)

$X^- = F_3CCO_2^-$

expected from normal hydride abstraction. The salt (**2d**), by far the major product of hydride abstraction[13] from (**3b**), is the minor product from thallium oxidation. The effect of a 1-methyl group in the conversion of (**1b**) to (**2b**) illustrates still more clearly this regiocontrol reversal. Direct hydride abstraction in this case gave only (**6c**).

1-Methoxy substituted complexes have also been examined. In all cases the reaction showed complete regiocontrol. Unlike direct hydride abstraction, which produces both 1- and 2-methoxy-substituted products, the use of thallium(III) oxidation gave exclusively the latter (see Table 1) and hydrolysis of the 1-methoxy isomer was not required. The pronounced regiocontrol in these reactions must reflect powerful selectivity in the interactions of OMe substituents with the developing π-allyl system in reaction intermediates.

The original observation[11] of thallium tris(trifluoroacetate) oxidation of (**1a**) was explained in terms of initial electrophilic attack of $\mathrm{Tl^{III}}$ at the co-ordinated diene to form an allyl intermediate (**7**). On this basis a competition between methoxy-allyl intermediates of the type (**8**) or (**9**) would appear to be important. In cases where substituents can lie on the same plane, it is possible that symmetrical intermediates such as (**10**) could form. Thus it was decided to study the reaction by the use of optically active complexes to test for racemisation, which would be expected if interconversion between (**8**) and (**10**) were to occur. Table 2 compares the results of thallium oxidation and hydride abstraction using samples of (**5a**) and (**5b**) of low optical purity obtained by asymmetric induction.[14] The similar values for the rotatory power of products obtained from (**5b**) by both methods indicates that racemisation does not occur during the thallium oxidation. The low value for (**6a**) obtained by reaction with $\mathrm{CPh_3^+}$ arises from inefficient precipitation of the product.[14]

Hydride Abstraction from Blocked Positions.—It is not normally possible for triphenylcarbenium reagents to remove hydride from cyclohexadiene complexes at positions which are blocked by adjacent substituents that are *trans* to the metal, the large planar structure of the reagent precluding approach to such sites. An interesting exception,[15] the hydride abstraction from a cholesta-2,4-diene complex, employed forcing conditions in which the possibility of a hydride abstraction from an adjacent ring, at a position α to the metal complex, followed by a hydrogen shift, of a type known for other carbenium ion intermediates, might account for the anomaly in this case. Hydride abstraction[14] by $\mathrm{CPh_3^+}$ is possible, however, if a silicon atom replaces carbon in the cyclohexadiene ring or is present as a substituent.[16]

The use of alternatives to triphenylcarbenium reagents offers two possible advantages. If smaller in size, they may be able to approach a hindered position on the cyclohexadiene ring. Alternatively, effective reagents for hydride abstraction might be discovered that have sufficiently different redox potentials to promote reaction by an electron-transfer pathway.[17] Before this study no alternative reagents for direct hydride abstraction from tricarbonyliron complexes were available. A report by

Green *et al.*[18] showing that ddq–HBF_4 (ddq = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone) can be used to effect hydride abstraction from dicarbonyl(η^3-cyclohexenyl)(η^5-indenyl)-manganese(0) complexes has led us to examine the use of the reagent with tricarbonyliron complexes in the hope that the smaller size of the reagent might reduce the effect of steric blocking. Initial results with the unsubstituted complex (**1a**) were encouraging and the hydride abstraction product (**2a**) was obtained in 70% yield showing this reagent system to be the first viable alternative to triphenylcarbenium reagents for this purpose. The results given in Table 1 indicate that regioselectivity is analogous to normal hydride abstraction, although the yields of products with methoxy substitution were low. Unfortunately, when this method was tried with hindered complexes, unsatisfactory results were obtained.

A second approach to hydride abstraction in such cases is to employ a reagent that does not react directly at the hindered position. The thallium oxidation method offers interesting possibilities from this point of view, since initial reaction is expected[11] at the co-ordinated π system. Because of the powerful directing influences of 1-methoxy substituents discussed above, it was decided to examine the reaction of the 6-methyl-substituted complex (**5c**) in which the methyl group should be forced to a terminus of the dienyl system if a 2-methoxy-substituted product is to be formed. This proved to be the case and the product, (**6c**), identical to material obtained by hydride abstraction from (**1b**) using CPh_3^+, was obtained together with a small amount of the isomer (**2d**). Since (**6c**) was formed in low yield, (**2d**) present in the product most probably arose through the far more efficient reaction of remaining traces of the diene complex (**1d**) from which the substrate (**5c**) had been separated[13] by chromatography. Formation of (**6c**) from (**5c**) indicates that it is possible to form η^5 cations from blocked substrates in this way.

Experimental

All reactions were performed under a nitrogen atmosphere. Product ratios were obtained from proton n.m.r. spectra recorded on Varian Associates HA100, Bruker WP80 SV, or JEOL FX60 spectrometers. I.r. spectra were recorded using a Perkin-Elmer 257 instrument and α values were measured with a Perkin-Elmer 241 polarimeter using chloroform (for neutral complexes) and acetonitrile (for salts) as the solvent. Complexes were prepared by standard literature methods,[2,3,13] except where otherwise indicated, and known products were identified by comparison of n.m.r. spectra with those of authentic samples obtained by conventional hydride abstraction using triphenylcarbenium tetrafluoroborate in dichloromethane.

General Procedure for the Formation of Tricarbonyl(η^5-*cyclohexadienyl*)*iron*(1+) *Salts using Thallium Tris*(*trifluoroacetate*).—The tricarbonyl(η^4-cyclohexadiene)iron(0) complex (1 mmol) was ground in small portions with thallium(III) tris(trifluoroacetate) (1 mmol) using a pestle and mortar in a glove bag. A vigorous reaction occurred. After thorough mixing, solid ammonium tetrafluoroborate (1.1 mmol) was added and grinding continued to form a thick paste. Concentrated sulphuric acid (6—8 drops) was added and after thorough mixing the slurry was dissolved in distilled water to form a yellow aqueous solution that was separated from a small quantity of insoluble material and washed with small portions of diethyl ether until the washings were colourless. A saturated aqueous solution of ammonium hexafluorophosphate was added and the precipitated hexafluorophosphate salt was isolated by filtration, washed with diethyl ether, and dried under vacuum. The following compounds were obtained in this way (yields in parentheses): tricarbonyl(η^5-cyclohexadienyl)-iron(1+) hexafluorophosphate, (**2a**) (50%), tricarbonyl(η^5-3-methoxy-2-methylcyclohexadienyl)iron(1+) hexafluorophosphate, (**2b**)[13] (72%), tricarbonyl(η^5-3-methoxycyclohexadienyl)-iron(1+) hexafluorophosphate, (**2c**)[19] (50%) (>90% one regioisomer), tricarbonyl(η^5-2-methoxy-3-methylcyclohexadienyl)-iron(1+) hexafluorophosphate, (**2d**)[13] (53%), tricarbonyl(η^5-2-methoxycyclohexadienyl)iron(1+)hexafluorophosphate, (**6a**)[20] (58%), tricarbonyl(η^5-2-methoxy-5-methylcyclohexadienyl)-iron(1+) hexafluorophosphate, (**6b**)[20] (53%), and tricarbonyl(η^5-2-methoxy-1-methylcyclohexadienyl)iron(1+) hexafluorophosphate, (**6c**) (10%) (which was identified by comparison with a sample obtained by hydride abstraction).

Reaction of Tricarbonyl(η^4-2-*methoxy*-1-*methylcyclohexa*-1,3-*diene*)*iron*(0) *with Triphenylcarbenium Hexafluorophosphate*.—Triphenylcarbenium hexafluorophosphate (0.427 g, 1.1 mmol) was dissolved in a minimum volume of dry dichloromethane, shaken with anhydrous potassium carbonate, and filtered into a flask containing tricarbonyl(η^4-2-methoxy-1-methylcyclohexa-1,3-diene)iron(0), (**1b**) (0.264 g, 1 mmol), in dichloromethane (5 cm^3). The reaction mixture was stirred at room temperature overnight. Addition of diethyl ether produced a precipitate that was collected by filtration, washed with diethyl ether, and recrystallised from acetonitrile by slow addition of diethyl ether to afford (**6c**) (0.286 g, 70%) as a fine yellow powder (Found: C, 32.45; H, 2.55. $C_{11}H_{11}F_6FeO_4P$ requires C, 32.40; H, 2.70%); $\nu_{max.}$(CO) at 2 107 and 2 056 cm^{-1} (CH_3CN); δ_H(CD_3CN) 6.91 (1 H, d, *J* 6, H^3), 5.81 (1 H, t, *J* 6, H^4), 4.26 (1 H, t, *J* 6, H^5), 4.06 (3 H, s, OMe), 2.98 (1 H, ddd, *J* 15, 6, 1, $H^{6\beta}$), 2.25 (1 H, d, *J* 15, $H^{6\alpha}$), and 1.65 (3 H, d, *J* 1 Hz, Me).

General Procedure for the Formation of Tricarbonyl(η^5-*cyclohexadienyl*)*iron*(1+) *Salts using ddq and Tetrafluoroboric Acid*.—Tetrafluoroboric acid (diethyl ether adduct) (1 mmol) was added dropwise to a stirred suspension of ddq (1 mmol) in dry dichloromethane (6 cm^3) at −78 °C. After 3 min a solution of the tricarbonyl(η^4-cyclohexa-1,3-diene)iron(0) complex (1 mmol) was added in dichloromethane (2 cm^3) and the reaction mixture stirred for a further 30 min at −78 °C. The mixture was poured into diethyl ether (50 cm^3) and the precipitated tetrafluoroborate salt was collected by filtration, washed with diethyl ether, and dissolved in water (20 cm^3). Saturated aqueous ammonium hexafluorophosphate was added and the resulting hexafluorophosphate salt was isolated by filtration and dried under vacuum. The following complexes were obtained in this way: (**2a**) (70%) (Found: C, 29.65; H, 1.75. $C_9H_7F_6FeO_3P$ requires C, 29.70; H, 1.95%), (**6a**)[20] (33%).

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