

Monomethoxylation of (Dichlorobenzene)(η^5 -cyclopentadienyl)iron Hexafluorophosphate Salts¹

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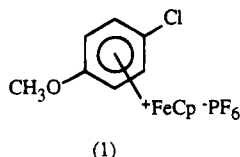
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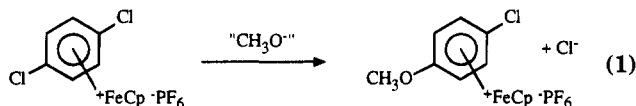
Summary: A general method for the monomethoxylation of the (*ortho*-, (*meta*-, and (*para*-dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphate salts is described. The method is shown to be specific to methoxylation.

Introduction

During the course of an investigation into an iron-mediated synthesis of methyljoubertamine, it was necessary to obtain large quantities of (4-chloroanisole)(η^5 -cyclopentadienyl)iron hexafluorophosphate (**1**). As



the standard method of (arene)(η^5 -cyclopentadienyl)iron salt synthesis (reaction of the arene, ferrocene, aluminum chloride, and aluminum powder)³ is not satisfactory for systems with heteroatoms, it was necessary to manufacture **1** from an accessible precursor. The method chosen was to monomethoxylate (*p*-dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphate (eq 1). This type of substitution reaction involving a chlo-



roarene coordinated to cyclopentadienyliron moiety is well-documented.⁴ The monoalkoxylation of (dichlorobenzene)(η^5 -cyclopentadienyl)iron salts has been reported,⁵ but the best procedure for monomethoxylation involved the action of diazomethane on chlorophenoxide complexes formed from the corresponding (dichlorobenzene)(η^5 -cyclopentadienyl)iron salt and hydroxide ion.

The main problem with attempts at monoalkoxylation is the tendency toward dialkoxylation. Sodium meth-

**Table 1. Monomethoxylation of
(Dichlorobenzene)(η^5 -cyclopentadienyl)iron Salts**

arene	reactn time/h	yield/% ^a
<i>p</i> -dichlorobenzene	48	85
<i>m</i> -dichlorobenzene	24	82
<i>o</i> -dichlorobenzene	48	81

^a Yields are of isolated product.

oxide in methanol solvent at high dilution has been reported to monomethoxylate dichlorobenzene complexes,⁵ but in our hands, this led to significant dimethoxylation. It seemed likely that the second alkoxylation took place more slowly than the first, as the electron-donating effect of the oxygen should increase the electron density on the arene and thus lessen its electrophilicity. Therefore, if the alkoxylation were carried out under milder conditions than those previously reported, we felt it may be possible to stop the reaction after a single methoxylation.

Results and Discussion

In practice, dissolving (*p*-dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphate in an excess of methanol, in the presence of sodium carbonate, led to excellent yields of monomethoxylated material after 48 h at ambient temperature. Longer reaction times led to increasing amounts of dimethoxylated material.

The monomethoxylation of (*ortho*- and (*meta*-dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphates was investigated. The *ortho* isomer behaved in a manner similar to the *para* isomer, generating excellent yields of the monomethoxylated material after 48 h. However, the *meta* isomer led to significant amounts of dimethoxylated material after the same time span. In this case, reducing the reaction time to 24 h led to excellent yields of the monomethoxylated product. The reactions are summarized in Table 1.

A possible explanation for the increased propensity of the *meta* isomer to lead to dimethoxylated product can be seen in the electron donation of the alkoxy group. The introduction of an alkoxy group to an arene results in increased electron density at the *ortho* and *para* positions; as a result, these positions will be less subject to nucleophilic attack than the *meta* position. This means that a halide at the *meta* position will be more easily replaced by a nucleophile than one at an *ortho* or *para* position. Mezey has recently demonstrated that,

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in agreement with a Boltzmann probability-based prediction, methoxy substituents direct incoming nucleophiles preferentially to the meta position.⁶ Furthermore Pauson has demonstrated that electron-donating groups do, in fact, direct incoming nucleophiles to the meta position in the analogous (arene)tricarbonylmanganese salts.⁷ This is in accordance with the theory of Davies, Green, and Mingos that nucleophiles will attack the carbon of a coordinated polyene which has the lowest electron density.⁸

Since this procedure had proved to be a general method for the monomethoxylation of (dichlorobenzene)(η^5 -cyclopentadienyl)iron salts, an effort was made to determine if the same procedure would work with other alcohols. Use of the same protocol, with the substitution of ethanol or 2-propanol for methanol, was investigated. Neither of these systems generated alkoxyated product, instead returning unreacted dichlorobenzene salts, even after extended reaction times (up to 1 week). Since the iron salts were only sparingly soluble in these alcohols (unlike methanol, in which they are very soluble), it was thought that perhaps the use of a cosolvent would allow the reaction to proceed. Use of acetone-alcohol mixtures in which the iron salt was completely dissolved, however, gave only unreacted dichlorobenzene salts. Apparently, only methanol has sufficient nucleophilicity to react under these conditions.

In summary, a mild method for the monomethoxylation of (dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphates has been described. Although the process appears to be limited to methoxylation, it works well for all three isomeric dichlorobenzene complexes and eliminates the problem of dimethoxylation found in other methods.

Experimental Section

General Methods. All reactions were performed under an atmosphere of dry argon. Chemicals were obtained from commercial sources and used as received. The (dichloroben-

zene)(η^5 -cyclopentadienyl)iron hexafluorophosphates were made by the standard method.³ Analyses were performed by Texas Analytical Laboratories, Inc., Stafford, TX.

Methoxylation Reactions. General Procedure. A 50-mL round-bottom flask was charged with a magnetic stirring bar, 150 mg (0.36 mmol) of the desired (dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphate, 38 mg (0.36 mmol) of sodium carbonate, and 10 mL of anhydrous methanol. The system was placed under a balloon pressure of argon and wrapped in foil, and the solution was allowed to stir for the indicated amount of time at ambient temperature. After the reaction period, 59 mg (0.36 mmol) of ammonium hexafluorophosphate was added and the solution allowed to stir for 15 min. The solvent was removed in vacuo, and the yellow residue was partitioned between methylene chloride and water. The organic layer was dried (MgSO_4) and filtered, and the solvent was removed in vacuo. The resultant yellow semisolid was recrystallized from acetone-diethyl ether to give the product as a yellow solid.

(*p*-Chloroanisole)(η^5 -cyclopentadienyl)iron Hexafluorophosphate. A reaction time of 48 h utilizing (*p*-dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphate yielded 125 mg (85%) of product, mp 162–165 °C. ¹H NMR [60 MHz, (CD_3)₂CO]: δ 6.7 (d, $J = 7$ Hz, 2H, Ar H), 6.4 (d, $J = 7$ Hz, 2H, Ar H), 5.3 (s, 5H, Cp H), 4.0 (s, 3H, -OCH₃). IR (CH_2Cl_2): 3050, 1520, 1430, 1400 cm^{-1} . Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{ClF}_6\text{FeOP}$: C, 35.28; H, 2.96. Found: C, 35.24; H, 2.98.

(*o*-Chloroanisole)(η^5 -cyclopentadienyl)iron Hexafluorophosphate. A reaction time of 48 h utilizing (*o*-dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphate yielded 119 mg (81%) of product, mp 120–121 °C. ¹H NMR [60 MHz, (CD_3)₂CO]: δ 6.3–7.0 (m, 4H, Ar H), 5.3 (s, 5H, Cp H), 4.3 (s, 3H, -OCH₃). IR (CH_2Cl_2): 3020, 1440, 1410 cm^{-1} . Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{ClF}_6\text{FeOP}$: C, 35.28; H, 2.96. Found: C, 35.44; H, 3.00.

(*m*-Chloroanisole)(η^5 -cyclopentadienyl)iron Hexafluorophosphate. A reaction time of 24 h utilizing (*m*-dichlorobenzene)(η^5 -cyclopentadienyl)iron hexafluorophosphate yielded 121 mg (82%) of product, mp 158–162 °C. ¹H NMR [60 MHz, (CD_3)₂CO]: δ 6.0–6.5 (m, 4H, Ar H), 5.1 (s, 5H, Cp H), 4.1 (s, 3H, -OCH₃). IR (CH_2Cl_2): 3050, 1530, 1425 cm^{-1} . Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{ClF}_6\text{FeOP}$: C, 35.28; H, 2.96. Found: C, 35.30; H, 2.95.

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