

Preliminary communication

**REVERSAL OF REGIOCONTROL IN THE ALKYLATION
 OF AN ARENE π -COMPLEX**

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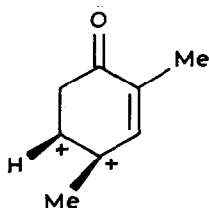
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Summary

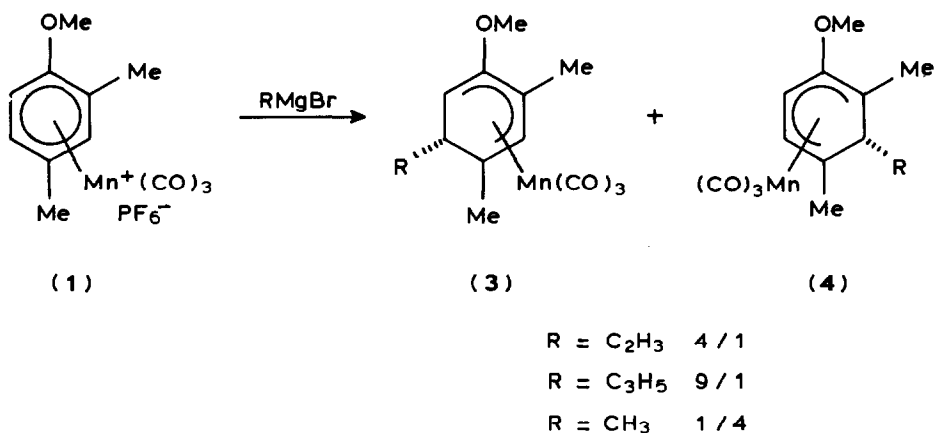
Tricarbonyl(η^6 -1-methoxy-2,4-dimethylbenzene)manganese(1+) hexafluorophosphate(1-) was preferentially alkylated by vinyl Grignard reagents at C(5). When methylmagnesium bromide was used, however, reaction occurred predominantly at C(3), the more hindered of the two sites *meta* to the methoxy substituent.

Organometallic π -complexes have an increasingly important role as electrophiles in organic synthesis. To assist in synthesis design, the reactivity of such complexes can be described in terms of their equivalence to cation synthons. Our interest in the use of chiral complexes [1] as intermediates in enantiomer synthesis led us to seek an equivalent of the dication synthon **2**, and, in view of the powerful *meta*-directing



(2)

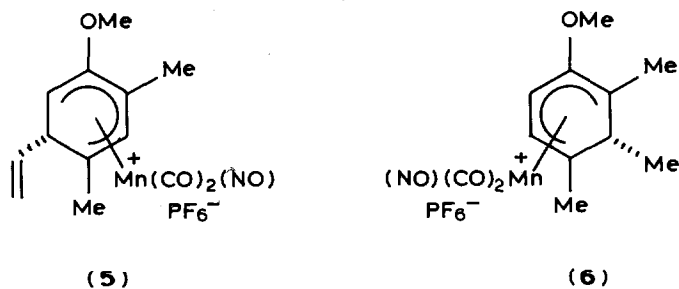
influence [2] of OMe substituents on arene complexes, we have examined equivalents based on chiral organomanganese complexes. In such compounds, there is an inevitable requirement for unsymmetrical substitution patterns; consequently, a clear understanding of the factors that determine regiocontrol of the alkylation of unsymmetrically substituted ligands is important for the rational development of new applications of their chemistry. In this paper we report our initial investigations of this topic which revealed an unusual reversal of the expected pattern of regiocontrol, resulting in predominant alkylation at the most hindered position on the aromatic ring, an observation with important implications for synthesis design.



SCHEME 1

To prepare the cationic complex **1**, we employed the method used by Pauson and Segal [3] for complexation of anisole. Reaction of **1** with vinylmagnesium bromide, using the normal procedures for Grignard additions [2], gave a 4/1 mixture of the neutral dienyl complexes **3** and **4**. The identity of the major product was apparent from the separation of the two methyl resonances which appeared at δ 2.40 and 1.56 ppm. These complexes proved relatively unstable but the major product (**3**, $\text{R} = \text{CH}=\text{CH}_2$) was separated by chromatography and immediately converted by nitrosonium hexafluorophosphate [4] to the dicarbonylnitrosyl salt **5**, which was isolated in 50% overall yield from **1**. The structure of **5** was apparent from its NMR spectrum which included resonances of the dienyl protons at δ 5.76 and 4.30 ppm and the signals of the two methyl resonances, now shifted to lower field by the charge on the complex. Reaction of **1** with the Grignard reagent derived from (*E,Z*)-1-bromopropene occurred in a similar fashion, but with greater selectivity for alkylation at C(5). A 9/1 mixture of **3** and **4** was obtained in 75% yield.

Most unexpectedly, the reverse regioselectivity was observed when the alkylation was performed with methylmagnesium bromide. A 1/4 mixture of **3** ($\text{R} = \text{Me}$) and **4** ($\text{R} = \text{Me}$) was produced. Again the neutral tricarbonylmanganese complexes proved unstable and were converted directly into a mixture of cationic nitrosyl complexes, obtained in 39% overall yield from **1**. The NMR signals from the major product included low field resonances at 6.64 (d) and 5.46 (d) ppm, that are typical for the adjacent protons at H(3) and H(4) of the 6-methyl complex **6**. The resonances of the dienyl protons of the minor product appeared at similar positions to those observed in **5**. Unlike **5**, both methyl groups in **6** occur at the termini of the dienyl system.



The structure of **6** was supported by examination of the methyl resonances of the major isomer, which occurred together at high field, at 1.94 and 1.8 ppm; the signals due to the minor isomer included the expected low field singlet at 2.63 ppm. From this it was clear that the minor product obtained from reaction with methylmagnesium bromide corresponded to the major product obtained when a vinyl Grignard reagent was used. The neutral complex **4**, ($R = \text{Me}$) was separated from **3** and converted to 1-methoxy-2,3,4-trimethylbenzene by oxidation [3] with ceric ammonium nitrate, so confirming the unexpected regiochemistry of this alkylation.

The reversal of regiocontrol indicates the high degree of sensitivity in alkylation reactions of this type to the nature of the nucleophilic species employed, and the need for further detailed experimental and theoretical studies to probe the properties that underlie the control of reactions of this type, to put their synthetic exploitation on a firmer footing. For the development of the chemistry of **1** as an equivalent of the dication synthon **2**, vinyl Grignard reagents are suitable for use in the initial alkylation reaction. Regiocontrol in the second alkylation is currently under investigation. In this case, the OMe group should now direct nucleophiles to C(4), in the manner previously determined [5] for the related tricarbonyliron complex *. Initial experiments, however, suggest that the alkylation reactions of the $\text{Mn}(\text{CO})_2\text{NO}$ complexes are more difficult than in the iron series.

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References

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* Attention has recently been drawn to the similarity between $\text{Mn}(\text{CO})_2\text{NO}^+$ and $\text{Fe}(\text{CO})_3^+$ moieties which have been found, in kinetic studies of the alkylation reactions of their dieny complexes, to confer a similar degree of activity on the ligand (ref. 6).