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Resolution of Planar Chiral Cationic (η^6-Arene)tricarbonylmanganese Complexes

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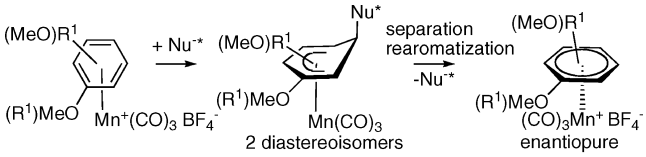
Planar chiral transition-metal π complexes of ortho- and meta-disubstituted arenes, such as (η^6-arene)tricarbonylchromium complexes, have been widely applied as stoichiometric auxiliaries and suitable starting materials for asymmetric preparation of biologically active substances as well as ligands for asymmetric catalysis.[1] In contrast, very little is known about the planar chirality of the isoelectronic cationic (η^6-arene)tricarbonylmanganese complexes, in spite of their potential usefulness.[2] Indeed, there have been no reports of their resolution, and to date the synthesis of only two nonracemic planar chiral cationic η^6-arene−Mn complexes starting from (*p*-cresol)$Mn(CO)_3^+$ has been described.[3] In this context, the discovery of a general methodology for preparing enantiomerically pure planar chiral cationic η^6-arene−Mn complexes may be deemed as an exciting challenge. We describe herein the first strategy for the resolution of ortho- and meta-disubstituted planar chiral racemic η^6-arene−Mn complexes using D-(+)-camphor enolate as the chiral auxiliary.[4] A potential application is illustrated by the enantioselective synthesis of 4-substituted cyclohexenones.

Our approach relies on the following observation. Stabilized carbanions add easily to the arene ring of η^6-arene−Mn complexes, giving the corresponding η^5 derivatives.[2] These neutral η^5-cyclohexadienyl−Mn complexes give back the starting material, but this requires harsh conditions such as a mixture of CF_3CO_2H and HPF_6 used to provide the counteranion.[5] To take advantage of this drawback, we tried to find an appropriate chiral stabilized carbanion that could be used in such an addition/elimination ($\eta^6-\eta^5$)/($\eta^5-\eta^6$) "round trip" sequence (Scheme 1).

Scheme 1. Resolution of (η^6-Arene)$Mn(CO)_3^+$ Complexes Using a Chiral Nucleophile "Round Trip"



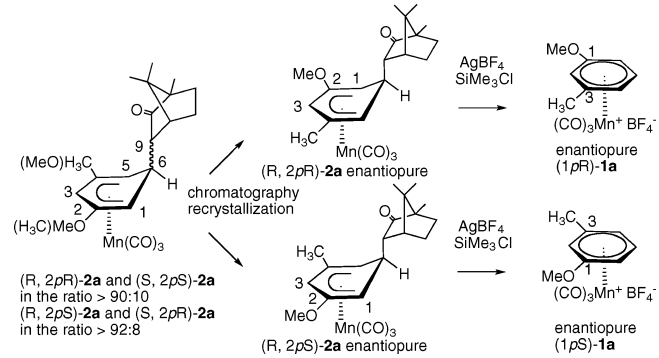
(*rac*)-**1a** R^1=Me (*rac*)-**1b** R^1=Cl (*rac*)-**1c** R^1=Br

2a R^1=Me **2b** R^1=Cl **2c** R^1=Br

(*ent*)-**1a** R^1=Me (*ent*)-**1b** R^1=Cl (*ent*)-**1c** R^1=Br

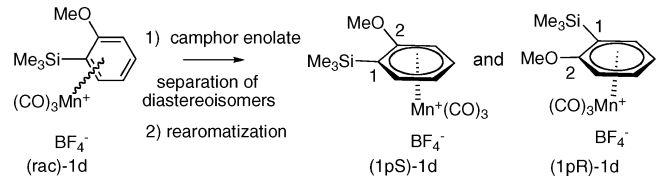
Camphor enolate, obtained by treatment of D-(+)-camphor with *n*-BuLi in THF at −78 °C, appeared to be the best chiral enolate for efficient separation of the diastereoisomers by TLC plates. Thus, we settled on the following protocol: a solution of D-(+)-camphor enolate was added to complex **1a**, giving a mixture of four diastereoisomers because of the planar chirality of the Mn system and the new C9 stereogenic center formed on the camphyl group once linked to the Mn complex. The axial hydrogen H9 was epimerized, giving the more thermodynamically stable complex upon transfer of a saturated solution of K_2CO_3 in MeOH to the crude mixture. On TLC plates, two spots were clearly distinguished, and purification by chromatography afforded two diastereoisomers in 44 and 48% yield with >80 and 84% de, respectively, as measured by ^{1}H NMR spectroscopy. After recrystallization, the complexes (*R*, 2*pR*)-**2a** and (*R*, 2*pS*)-**2a**[6] were isolated, each with >98% de (Scheme 2).

Scheme 2. Separation of the Diastereoisomers **2a** and Rearomatization



Complexes (*R*,2*pR*)-**2a** and (*R*,2*pS*)-**2a** were stirred in CH_2Cl_2 at room temperature in the presence of $AgBF_4$/$SiMe_3Cl$. Under these conditions, the presence of a silicium derivative favors enolate trapping by formation of a silyl enol ether, while the BF_4^- anion plays the role of the counteranion, stabilizing the cationic species after the chiral auxiliary elimination. Thus, complexes (1*pR*)-**1a** and (1*pS*)-**1a** were successfully isolated in 94 and 96% yield, respectively, each with >98% ee (Scheme 2). We succeeded in extending the present methodology to achieve the resolution of *m*-chloro compound (*rac*)-**1b**, *m*-bromo compound (*rac*)-**1c**, and *o*-trimethylsilylanisole complexes (*rac*)-**1d**, and we obtained the corresponding complexes (1*pR*)-**1b** and (1*pS*)-**1b**, (1*pR*)-**1c** and (1*pS*)-**1c** (Scheme 1), and (1*pR*)-**1d** and (1*pS*)-**1d** (Scheme 3) in yields ranging from 91 to 99%, each with >98% ee, after rearomatization of the parent enantiopure η^5 complexes.

Scheme 3. Resolution of *o*-Trimethylsilylanisole Complex (*rac*)-**1d**



The assignment of the absolute configuration of the planar chiral η^5-cyclohexadienyl moiety was possible through X-ray analysis of suitable crystals of the diastereoisomer (*R*,2*pR*)-**2a** (Figure 1). On this basis, the configuration of the corresponding cationic η^6-arene−Mn complex (1*pR*)-**1a** was deduced and then unambiguously

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confirmed by X-ray analysis (Figure 1). Thus, the planar chirality was preserved during the rearomatization process.

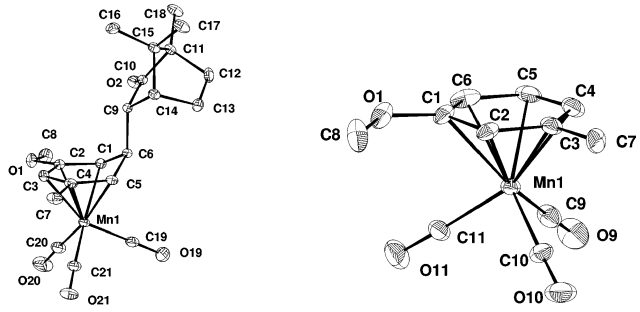
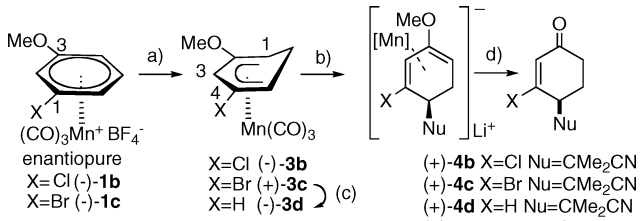


Figure 1. ORTEP views of complexes (*R*,2*pR*)-**2a** and (1*pR*)-**1a**.

We next investigated the potential of these enantiopure η^6 complexes in the enantioselective synthesis of substituted cyclohexenones **4**[7] using a strategy of manganese-mediated double nucleophilic addition (Scheme 4).[2d,8] Regioselective meta addition of $LiAlH_4$ to the enantiopure *m*-chloro- and *m*-bromoanisole complexes (−)-**1b** and (−)-**1c** yielded complexes (+)-**3b** and (+)-**3c**, respectively. Dearomatization[9] by addition of a second nucleophile, $LiC(CH_3)_2CN$, to the C5 carbons of complexes (+)-**3b** and (+)-**3c**, followed by $FeCl_3$ oxidative demetalation of the anionic η^4-Mn intermediate and acidic hydrolysis, generated the corresponding enantiopure 3-chloro- and 3-bromo-substituted 2-cyclohexen-1-ones (+)-**4b** and (+)-**4c** in 76% yield. They could be easily transformed by nucleophilic substitution of the halogeno groups into a wide panel of chiral organic compounds. Treatment of (+)-**3c** with 1 equiv of BuLi followed by hydrolysis gave the enantiopure (η^5-2-methoxycyclohexadienyl)$Mn(CO)_3$ complex (−)-**3d**, a key organometallic chiral synthon that cannot be obtained through resolution of the (η^6-anisole)$Mn(CO)_3$ parent complex because this monosubstituted complex has no planar chirality. By the same procedure, the enantiopure 2-cyclohexen-1-one (+)-**4d** was generated in 75% yield, as was the enone (+)-**4e** in 80% yield by addition of $LiCHPh_2$ as the second nucleophile (Scheme 4).

Scheme 4. Preparation of Enantiopure 2-Cyclohexen-1-ones



In conclusion, our preliminary results describe the first resolution of cationic ortho- and meta-disubstituted (η^6-arene)$Mn(CO)_3$ complexes through D-(+)-camphor enolate addition, isomerization of the C9 stereogenic center, separation of the corresponding η^5-cyclohexadienyl diastereoisomers, and then elimination of the chiral auxiliary by a quantitative method of rearomatization with total conservation of stereochemical information. This general methodology corresponds to an addition/elimination ($\eta^6-\eta^5$)/($\eta^5-\eta^6$) "round trip" sequence using a cheap, commercialy available chiral nucleophile. As it is compatible with the presence of a halide or an alkoxy group, a huge field of applications involving functionalizations by Pd cross-coupling reactions[2b] as well as by lithiation/electrophilic quench[2f,g,6] can be envisaged. This finding opens novel perspectives for the development of (arene)tricarbonylmanganese complexes in organometallic and organic enantioselective syntheses, as illustrated in the present work by dearomatization of enantiopure meta-disubstituted (arene)$Mn(CO)_3^+$ complexes into enantiopure 4-substituted and 3,4-disubstituted cyclohexenones.

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Supporting Information Available: Crystallographic data for compounds (*R*, 2*pR*)-**2a** and (1*pR*)-**1a** (CIF) and full experimental procedures with analytical data. This material is available free of charge via the Internet at http://pubs.acs.org.

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