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Diastereoselective Proton Transfer: A Route to Enantiomerically Pure Half-Sandwich Rhenium Complexes

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The famous separation of the chiral manganese complex [CpMn(CO)(NO)(PPh_3)]PF_6 into its enantiomers by H. Brunner in 1969[1] marks the onset of organometallic stereochemistry.[2] The method used by Brunner—addition of an enantiomerically pure base followed by diastereomer separation—was later employed to separate the analogous rhenium complex.[3] The combination of chiral, enantiomerically pure amine or phosphine ligands with chiral metal complexes may also lead to readily separable diastereoisomers[2] or, if the metal complex is stereochemically labile, to a thermodynamically controlled diastereomer enrichment.[4] Here we communicate a new and potentially very useful method of chirality transfer from a coordinated ligand to the metal, consisting of a kinetically controlled diastereoselective proton transfer.

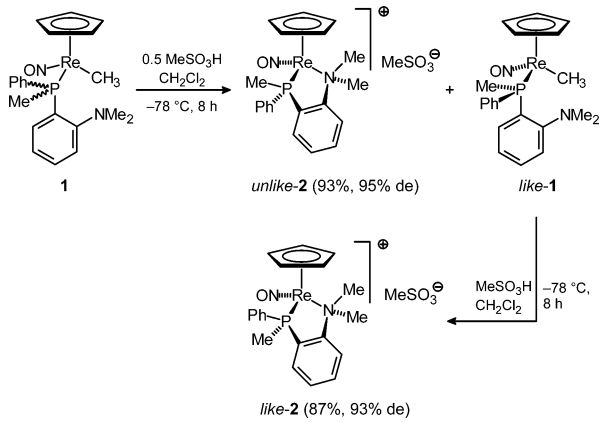
We have recently reported the synthesis of the diastereomeric methyl rhenium complex [CpRe(NO){P(Me)(Ph)(2-C_6H_4OMe)}(CH_3)] and its reaction with acid, which leads to the loss of methane followed by either ring closure or addition of an extraneous ligand.[5] Methyl cleavage from rhenium is considered to involve metal protonation at a site *cis* to CH_3 followed by reductive elimination of methane.[6] The basicity of electron-rich transition metal complexes often exceeds that of typical organic bases, such as amines.[7] The rate of proton transfer to the metal—sometimes called "kinetic basicity"—is, however, smaller by several orders of magnitude.[8] This would imply that a metal complex containing an amine base function on the side arm of one of the ligands would first be protonated at nitrogen followed by intramolecular proton transfer to the metal.[9] For a complex with stereogenic centers at both the metal and the ligand, this should open a route to an efficient, kinetically controlled separation of diastereoisomers.

With the aim to test this hypothesis, the diastereomeric methyl rhenium complex **1** was synthesized (see Supporting Information) and treated at −78 °C with exactly half an equivalent of methanesulfonic acid. This indeed led to the formation of only one diastereoisomer of **2**, while one isomer of **1** was left unreacted (Scheme 1). Both components of the reaction mixture were easily separated by addition of diethyl ether, which induced complete precipitation of the ionic compound. An H,H NOESY spectrum of this material showed strong cross-peaks connecting the cyclopentadienyl protons with the upfield NMe group and the PMe group. This material was thus established as the *unlike* diastereoisomer of **2**. Addition of a slight excess of methanesulfonic acid to the mother liquor and workup as described above produced the *like* diastereoisomer of **2**. This product showed strong cross-peaks connecting the cyclopentadienyl protons with the upfield NMe group and the *ortho* protons of the PPh group.

The stereochemical assignments were corroborated by X-ray structure determinations of both diastereoisomers. Both crystallize monoclinic with $Z = 4$ and both enantiomers present in the unit cell (Figure 1).

In the less readily accessible *like*-**2**, the phenyl group at the phosphorus atom is in an eclipsed position with the cyclopentadienyl ligand, while in *unlike*-**2**, it eclipses with the small NO ligand. While this may not necessarily imply a significant steric strain in the final product *like*-**2**, it hints at an additional kinetic barrier during the proton delivery step (Scheme 2). The protonation of the dimethylamino group is certainly rapid and reversible. Proton transfer from nitrogen to rhenium at a site *cis* to the CH_3 group requires a rotation around the P−Re bond, which is inhibited for the *like* isomer. The last step, methane elimination, is irreversible. Therefore, as long as acid is the limiting reagent, *unlike*-**1** will react preferentially.

Scheme 1. Diastereoselective Acid Cleavage of Methyl Rhenium Complex **1**



To demonstrate the viability of this method for the preparation of enantiomerically pure complexes, (*R*)-P(Me)(Ph)(2-$C_6H_4NMe_2$) was synthesized by an adaptation of the Jugé method[10] and converted to a 1:1 diastereomeric mixture of (R_{Re},S_P)/(S_{Re},S_P)-**1** (note that the stereochemical descriptor at phosphorus changes as the lone pair is formally being replaced by a rhenium atom). Methyl cleavage with 0.5 equiv of $MeSO_3H$ (small quantities of this acid can be handled more accurately than HBF_4) yielded (R_{Re},S_P)-**2** with 93% de and 99% ee as determined by ^{1}H NMR in the presence of the chiral shift reagent, Eu(tfc)$_3$. The residual (S_{Re},S_P)-**1** was similarly converted to a sample of (S_{Re},S_P)-**2** with 94% de and 99% ee (Scheme 3).

As an independent proof of the stereochemistry, the methyl complex (R_{Re},S_P)/(S_{Re},S_P)-**1** was separated by crystallization from

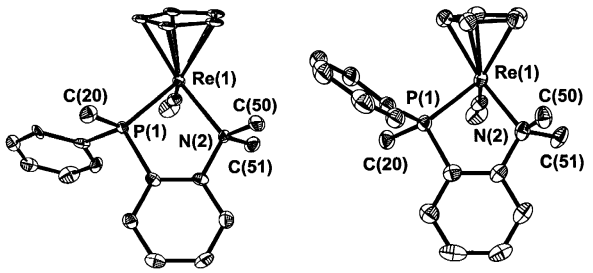
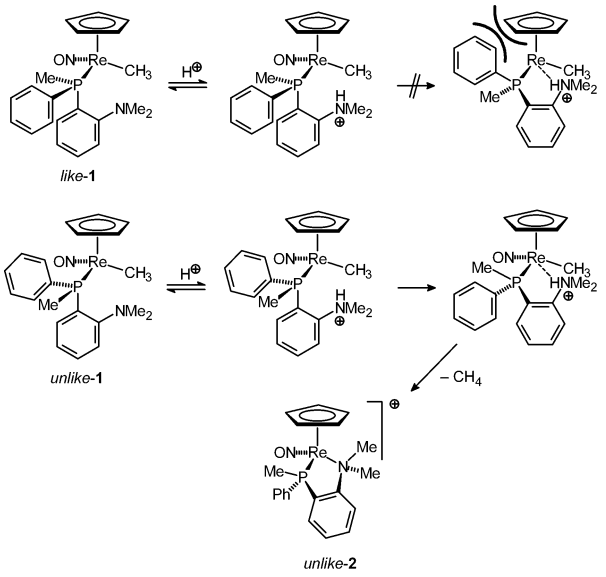


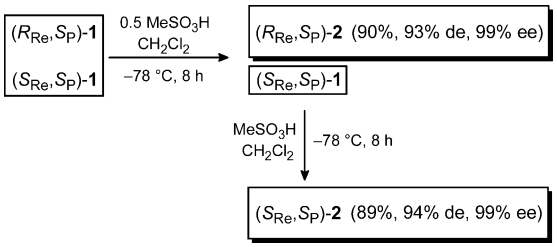
Figure 1. Structures of the cations of *unlike*-**2** (left) and *like*-**2** (right). Hydrogen atoms are omitted for clarity.

10.1021/ja057089z CCC: $33.50

Scheme 2. Origin of the Diastereoselectivity of the Proton Transfer Step (in the formula on the upper right, the NO ligand was omitted for the sake of clarity)



Scheme 3. Synthesis of Enantiomerically Pure (R_{Re},S_P)-**2** and (S_{Re},S_P)-**2**



toluene/pentane into a less soluble fraction of (R_{Re},S_P)-**1** (92% de) and a better soluble one consisting mainly of (S_{Re},S_P)-**1** (62% de). (R_{Re},S_P)-**1** crystallized in the polar space group $P2_1$ with $Z = 2$. The Flack parameter of 0.018(9) indicated that the configuration was indeed (R_{Re},S_P) (Figure 2).

This type of chirality transfer is not limited to this one particular case. For example, an analogue of **1** containing 2-methyl-8-(methylphenylphosphino)quinoline as a ligand was treated with 0.5 equiv of $MeSO_3H$, which resulted in the specific formation of only the *unlike* diastereoisomer of the chelated cation. We conclude that, due to a number of favorable features, this method to synthesize diastereo- and enantiomerically pure metal complexes can be expected to be quite useful: (i) Enantiomerically pure Horner-type phosphines, including those containing functionalized substituents, are now readily accessible by a wide variety of methods;[11] (ii) methane elimination and ring closure as well as ligand exchange proceed with a high degree of stereocontrol;[12] (iii) ring opening is readily controllable by the design of the sidearm, for example, length, donor atom, and substituents;[5] (iv) both diastereoisomers

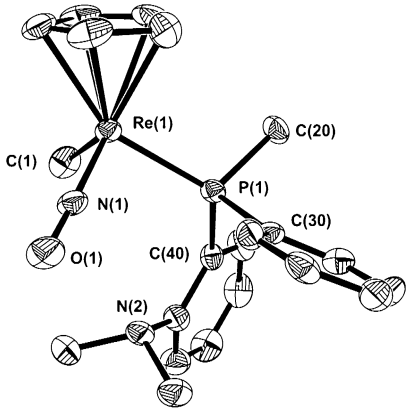


Figure 2. Structure of the methyl complex (R_{Re},S_P)-**1**. Hydrogen atoms are omitted for clarity.

are easily accessible for the study of matched/mismatched pairs; (v) the additional donor function at the phosphine ligand can help to direct an attacking reagent, for example, an organolithium or Grignard compound for highly stereoselective nucleophilic additions.

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Supporting Information Available: Details of the synthesis and characterization of all new compounds as well as crystallographic data for (R_{Re},S_P)-**1** (CCDC-271462), *like*-**2** (CCDC-271463), and *unlike*-**2** (CCDC-271464) (CIF, PDF). Crystallographic data can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223−336−033; or deposit@ccdc.cam.ac.uk). This material is available free of charge via the Internet at http://pubs.acs.org.

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