Communications

Synthesis of Chiral C_2-symmetric Palladium and Rhodium SCS Pincers

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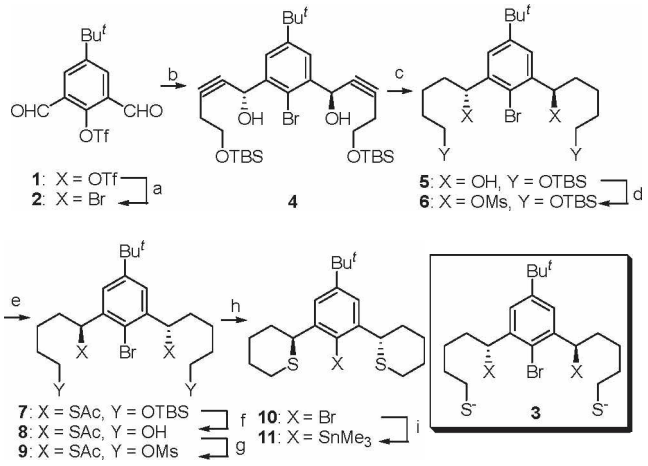
The control of the ligating properties of metal centers of metal catalyst with a well defined ligand system is one of the important goals of organic chemistry. Chiral pincer complexes consist of an enantiopure tridentate skeleton bound to a metal by at least one metal-carbon σ bond.[1] The highly protected environment for the resident metal gives pincer complexes with excellent potential as catalysts in a wide variety of asymmetric organic reactions, even though the degree of asymmetric induction has not been great so far,[1c] which would warrant further endeavor in designing and synthesizing new pincer compounds.

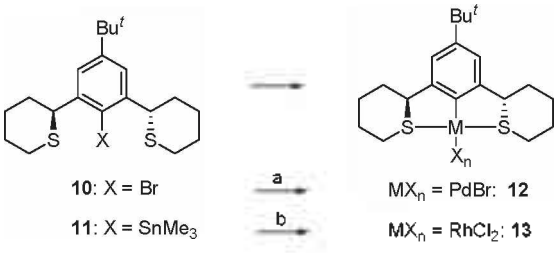
The synthesis of the sulfur-containing C_2-symmetric chiral pincer ligand began with 4-*tert*-butyl-2,6-diformylphenyl triflate **1**, which was prepared from commercially available 4-*tert*-butylphenol in 2 steps.[2] The triflate **1** was reacted with NaBr in the presence of a catalytic amount of CuBr in DMF at 100 °C to give aromatic bromide **2** in 72% yield. The key step of the synthetic strategy is the enantio- and diastereoselective addition of a ω-substituted 4-carbon organometallic to the aromatic dialdehyde **2**. All the efforts to reduce the numbers of steps were fruitless: Chemo- and enantioselectivity was low with the attempted addition of $Zn(CH_2CH_2CH_2CH_2X)_2$ (X= Cl or SPh)[3] to the aldehyde carbonyl groups of **2**, and eventual inward substitution of the mercaptide **3** resulted mostly in E_2 reaction[4] (Scheme 1).



Scheme 1. Reagents and conditions: (a) NaBr, CuBr (cat), 100 °C, 4 h (72%); (b) $TBSOCH_2CH_2C{\equiv}CZnEt$ (4.0 equiv.) [generated from $TBSOCH_2CH_2C{\equiv}CH$ and Et_2Zn], (*R*)-BINOL (1 equiv.), $Ti(O^iPr)_4$ (1 equiv.), rt, 12 h (71% of (*R,R*) alcohol (89% ee) and 23% of *meso*); (c) Pt-Black (cat), H_2, THF, rt, 24 h (92%); (d) MsCl, Et_3N, CH_2Cl_2, -78 °C, 2 h (100%) (e) KSAc (xs.), DMF/THF, rt, 20 h (85%); (f) $AcOH/H_2O$/THF, rt, 24 h (88%); (g) MsCl, Et_3N, CH_2Cl_2, -78 °C, 2 h (100%); (h) K_2CO_3/MeOH, rt, 1 h (95%); (i) (1) *n*-BuLi, THF, -78 °C, 0.5 h; (2) Me_3SnOTf, THF, -78 °C to 0 °C, 2 h (47%).

Consequently, the asymmetric alkynylation[5] of the aldehyde **2** with 3-butynyloxy-*tert*-butyldimethylsilane, which would require a few additional steps, was carried out in two separate stages: (1) treatment of an excess amount of the terminal acetylene with diethylzinc in refluxing toluene; (2) stepwise addition of (*R*)-BINOL, $Ti(O^iPr)_4$, a second solvent (CH_2Cl_2), and finally the aromatic dialdehyde **2**. The first stage probably generated the alkynyl(ethyl)zinc intermediate, which then added to the dicarboxaldehyde **2** in the presence of the catalyst to furnish the chiral propargyl (*R,R*) alcohol **4**, $[\alpha]_D^{23}$ = -2.2 (c 1.0, $CHCl_3$). (71%, 89% ee). In this reaction, the use of an equivalent of BINOL was required for acceptable diastereo- and enantioselectivity, and even though 23% of the corresponding *meso* product was produced, which could be easily separated off from the desired product by column chromatography (TLC (20% EtOAc/*n*-Hexane) R_f 0.44 (*R,R*) *vs.* 0.27 (*meso*)). The chiral propargylic alcohol **4** was hydrogenated (H_2, Pt black) to give the saturated alcohol **5**, without affecting the C^{sp^2}-Br linkage, in 92% yield, which was converted into the corresponding mesylate **6** by mesylation with MsCl and Et_3N (100% yield) (Scheme 1).

Subsequent treatment of the mesylate **6** with potassium thioacetate at rt for 20 h in a mixture of DMF and THF provided 85 % yield of the chiral bisthioacetate **7**. Deprotection of the silyl ether **7** with AcOH in aqueous THF at rt for 24 h (88% yield) followed by methanesulfonylation of the resulting primary chiral diol **8** by treatment with MsCl in the presence of Et_3N in CH_2Cl_2 at -78 °C for 2 h provided the mesylate **9** in quantitative yield. Finally, the outward substitution, rather than the inward substitution mentioned above, of the dimesylate **9** by the sulfide anion generated with K_2CO_3 in MeOH (rt, 1 h) provided cleanly the corresponding C_2-symmetric chiral pincer ligand, bis(tetrahydrothiapyran) **10** in 95% yield through intramolecular cyclization. For additional preparation of metallic pincers, the bromide **10** was treated with *n*-BuLi (1 equiv.) in THF at -78 °C for 0.5 h and the resulting lithio derivative was treated with trimethyltin



Scheme 2. Reagents and conditions: (a) $Pd_2(dba)_3{\cdot}CHCl_3$ (0.5 equiv.), Benzene, rt, 48 h (72%); (b) $[Rh(COE)_2Cl]_2$ (0.5 equiv.), THF/CCl_4, rt, 16 h (60%).

triflate (Me_3SnOTf)[6] to afford organotin compound **11** in 47% yield (Scheme 1).[7]

Finally, with the precursors of pincers, **10** and **11**, in hand, we tried to synthesize the corresponding C_2-symmetric SCS pincers of various metals (Scheme 2). The organopalladium(II) complex **12** was prepared directly from the reaction of $Pd_2(dba)_3{\cdot}CHCl_3$ complex with the bromide **10**. Thus, the chiral pincer ligand **10** was treated with $Pd_2(dba)_3{\cdot}CHCl_3$ in benzene at room temperature for 48 h, after which the mixture was filtered off and the solvent was concentrated *in vacuo*. The resulting residue was purified by column chromatography to give **12**[8] in 72% yield. For some unknown reasons, the chiral pincer ligands, **10** and **11**, resisted any conversion into the corresponding Ni pincers. Thus, the reactions of the chiral bromide ligand **10** with $Ni(COD)_2$ and of the chiral tin ligand **11** with a number of Ni(II) compounds did not proceed even though there existed a number of precedents on related reactions.[9]

On the other hand, the organorhodium(III) catalyst **13** could be prepared as yellow solid directly in 60% yield by the reaction of the organotin complex **11** with chlorobis(cyclooctene)rhodium(I) dimer in THF/CCl_4 for 16 h at room temperature after recrystallization from CH_2Cl_2/pentane.[10] Once again, the corresponding Ir pincer could not be obtained.

The evaluation of the chiral pincers, **12** and **13** as a catalyst (5 mol%) was carried out in the reaction of benzaldehyde with allyltrimethyltin in the presence of silver hexafluoroantimonate as an activator.[11] Unfortunately, only racemic products were obtained under numerous reaction conditions.

In summary, a highly diastereoselective synthesis of sulfur containing C_2-symmetric chiral pincer ligands, **10** and **11**, has been achieved. Additionally, we have succeeded in a syntheses of new sulfur containing C_2-symmetric chiral pincer compounds such as organopalladium(II) **12** and organorhodium(III) **13**.

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4. This intermediate was prepared by several reactionsfrom the addition products of $Zn(CH_2CH_2CH_2CH_2Cl)_2$ or $EtZn(C{\equiv}CCH_2CH_2Cl)$ to the dialdehyde **4**.
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7. **(*S,S*)-2,6-Bis(tetrahydrothiopyran-2-yl)-1-bromo-4-*tert*-butylbenzene (12).** $[\alpha]_D$ = -57.8 (c 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, $C(CH_3)_3$, 9H), 1.68-1.91 (m, CH_2, 6H), 1.95-2.10 (m, CH_2, 4H), 2.10-2.20 (m, CH_2, 2H), 2.65-2.75 (m, CH_2, 2H), 2.89-2.97 (m, CH_2, 2H), 4.40 (dd, J = 2.4, 9.0 Hz, CH, 2H), 7.39 (s, PhH, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ26.93, 27.33, 31.14, 31.37, 34.93, 35.22, 47.54, 122.2, 124.9, 141.7, 150.8; Anal. Calcd for $C_{20}H_{29}BrS_2$: C, 58.10; H, 7.07; S, 15.51. Found: C, 58.14; H, 6.71; S, 15.40. MS (EI, 70 eV) m/z: 414 (M^+), 333, 277, 101, 87, 57.
(*S,S*)-2,6-Bis(tetrahydrothiopyran-2-yl)-1-trimethylstannyl-4-*tert*-butylbenzene (13). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.47 (s, $Sn(CH_3)_3$, 9H), 1.31 (s, $C(CH_3)_3$, 9H), 1.40-1.50 (m, CH_2, 2H), 1.60-1.75 (m, CH_2, 2H), 1.90-2.15 (m, CH_2, 8H), 2.64 (d, J = 13.5 Hz, CH_2, 2H), 2.83 (td, J = 2.4, 13.2 Hz, CH_2, 2H), 3.86 (dd, J = 2.1, 11 Hz, CH, 2H),7.37 (s, PhH, 2H); Anal. Calcd for $C_{23}H_{38}S_2Sn$: C, 55.54; H, 7.70; S, 12.89. Found: C, 55.42; H, 7.73; S, 12.25.
8. **Organopalladium(II) complex (14).** ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (s, $C(CH_3)_3$, 9H), 1.35-1.55 (m, CH_2, 2H), 1.90-2.20 (m, CH_2, 8H), 2.30-2.40 (m, CH_2, 2H), 2.91 (td, J = 3.0, 13 Hz, CH_2, 2H), 3.51 (d, J = 14.1 Hz, CH_2, 2H), 4.25 (dd, J = 4.2, 11.1 Hz, CH, 1H), 7.00 (s, PhH, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 24.17, 24.47, 31.58, 32.22, 34.75, 40.53, 56.34, 60.56, 118.64, 148.84, 151.72, 154.43 Anal. Calcd for $C_{20}H_{29}BrPdS_2$: C, 46.20; H, 5.62; S, 12.34 Found: C, 46.24; H, 5.59; S, 12.31.
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10. **Organorhodium(III) complex (15).** ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.33 (s, $C(CH_3)_3$, 9H), 1.56-1.64 (m, CH_2, 2H), 1.73 (d, J = 13.5 Hz, 2H), 1.92-2.08 (m, CH_2, 4H), 2.23 (t, J = 14.5 Hz, CH_2, 2H), 2.68 (d, J = 15.5 Hz, CH_2, 2H), 2.79 (t, J = 12 Hz, CH_2, 2H), 2.97 (d, J = 17 Hz, CH_2, 2H), 4.98 (s, CH, 2H), 6.83 (s, PhH, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 20.29, 26.06, 28.36, 31.74, 31.91, 34.46, 50.57, 121.85, 145.74, 146.09 Anal. Calcd for $C_{20}H_{29}Cl_2RhS_2$: C, 47.34; H, 5.76; S, 12.64 Found: C, 47.28; H, 5.72; S, 12.60.
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