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Resolution of Allylic Alcohols via Copper(I) Complexes with a Chiral Diamine

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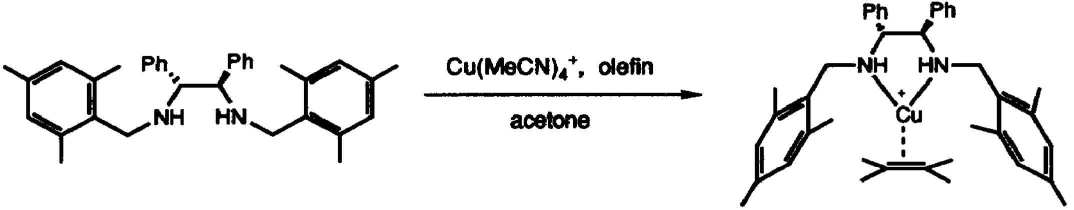
Abstract: By using the Corey diamine 1,2-diphenyl-N,N'-bis[(2,4,6-trimethylphenyl)methyl]-1,2-diaminoethane, Copper(I) olefin complexes are prepared. When the olefin is a racemic allylic alcohol, selective coordination of one enantiomer is observed. Cleavage with aqueous HCl or NaCN allows a two-steps resolution affording excellent enantiomeric excess.

The use of metal complexes with chiral ligands for the resolution of racemic olefins dates back 30 years.[1] The reported methods generally involve platinum compounds,[2] which, besides being expensive, are rather inert to substitution and usually require multistep syntheses. For a practically useful resolution procedure, a cheaper metal and more labile complexes would be desirable, and these requirements are met by trigonal Cu(I) olefin complexes with bidentate nitrogen ligands.[3] In spite of this, no example of chiral recognition involving such species has been reported so far. We were therefore prompted to prepare Cu(I)-olefin complexes with the Corey diamine **1**,[4a] an attractive ligand which from MM2 calculations[4] could be anticipated to create an effective chiral pocket around the metal ion.



1

2

Stable complexes (**2**) were obtained with a large variety of olefins, by simply treating $[Cu(MeCN)_4]BF_4$[5] with an equimolar amount of **1** and an excess of the alkene under nitrogen. They often directly crystallized from the reaction mixture and are moderately stable in air after isolation. At room temperature their ^1H NMR spectra display broad signals, due to exchange phenomena and conformational equilibria,[6] and are seldom suitable for the direct identification of isomeric species. Nevertheless, if a small amount (5-10 μL) of CD_3CN is added to the sample (in $CDCl_3$ or CD_2Cl_2), the olefin is partly displaced in a fast exchange equilibrium, and its NMR signals become sharp and fully assignable. In the case of racemic alkenes, the complex acts as a non paramagnetic chiral shift reagent, allowing a quick determination of the e.e. of the olefin in the sample. The ligands were recovered by cleaving the complexes with aqueous HCl in air or with NaCN. When the olefin recovered was an allylic alcohol, its e.e. was independently determined by ^1H NMR, using the chiral shift reagent (+)-Eu(hfc)$_3$.

While a modest resolution was achieved with the "weakly chiral" alkene 3-methyl-1-pentene (17% e.e.), much better results were obtained with secondary allylic alcohols. In a typical experiment 630 mg (2.0 mmol) of $[Cu(MeCN)_4]BF_4$ and 954 mg (2.0 mmol) of (*S,S*)-**1** ($[\alpha]^{25}_D$ +24.4, *c* = 1.0, $CHCl_3$) were dissolved in 12 mL of deaerated acetone, the solution was cooled to -45 °C and 580 mg (8.0 mmol) of 3-buten-2-ol were added under nitrogen. The mixture was kept at -45 °C for 4 h, and the resulting colorless crystalline product (**2a**) was filtered, washed with diethyl ether and dried (1.33 g, 95% yield, 97% diastereomeric purity). ^1H NMR (CD_2Cl_2: CD_3OD 5:1, -40 °C, 270 MHz): δ 7.7 (br, 1 H), 7.6 (br, 1 H), 7.4 (br, 2 H), 7.2 (br, 2H), 7.05 (br, 2 H), 6.8 (br, 2 H), 6.76 (s, 4 H), 4.2 (br, 2 H, CHPh), 4.04 (dd, 1 H, =CH), 3.6-3.9 (br, 2 H, *H*CH), 3.4 (br, 2 H, HC*H*), 3.14 (d, 1 H, =CH), 2.81 (d, 1 H, =CH), 2.14 (s, 6 H, ArMe), 2.32, 1.92 (br, 6 H each, ArMe), 0.65 (d, 3 H, Me). Anal. Calcd for $C_{38}H_{48}BCuF_4N_2O$: C, 65.28; H, 6.92. Found: C, 65.12; H, 7.03. The diastereomeric purity was found to substantially decrease on raising the temperature, becoming 93% when the experiment was performed at 0 °C. This suggests that the overall stereoselectivity is mainly due to the preferencial coordination of one enantiomer, and in agreement with this hypothesis, no relevant changes in the ^1H NMR spectrum of **2a** were observed after equilibration with an excess of racemic butenol. One recrystallization improved the purity to better than 99%, showing that the above method is much more efficient than the "classical" resolution procedure.[7] In order to recover the free ligands, **2a** (1.19 g, 1.7 mmol, 97% diastereomeric purity) was suspended in 10 mL of 2.5 N aqueous HCl, and 10 mL of diethyl ether were added under stirring. A green colour appeared and faded, while the solid converted to a gelatinous precipitate of diamine hydrochloride. The mixture was stirred for 20 min at room temperature, centrifuged, and the ether layer was collected. After two further extractions with 8 mL of diethyl ether, fractional distillation gave 106 mg of (*R*)-3-buten-2-ol in 93% e.e. ($[\alpha]^{27}_D$ -30.8, neat).

By using essentially the same procedure as for **2a**, the complexes of the following allylic alcohols were obtained in 80-90% yields after a single crystallization (the e.e. of the recovered alcohols are given in parentheses): CH_2=CHCH(OH)Et (91%); CH_2=CHCH(OH)(n-Pr) (84%); CH_2=CHCH(OH)(n-C_5H_{11}) (82%); *E*-MeCH=CHCH(OH)Me (79%); *E*-MeCH=CHCH(OH)Et (82%). These preliminary results clearly show the potentiality of copper complexes with the Corey diamine **1** to induce strong chiral discrimination against other incoming ligands.

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