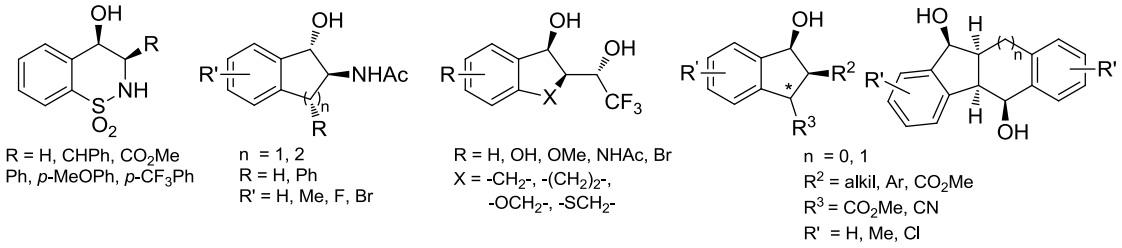
Abstract

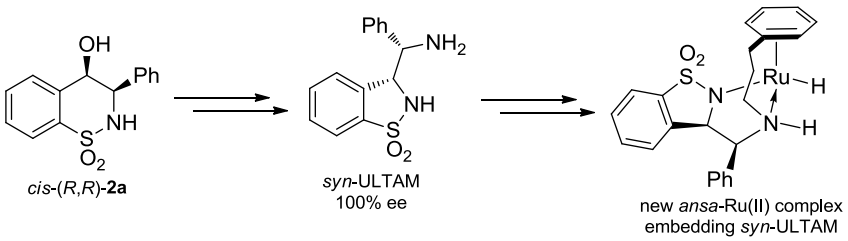
Synthesis of diversified categories of chiral secondary alcohols possessing multiple contiguous stereogenic carbon atoms, useful as chiral building blocks of complex molecules, is described. These were accessed via dynamic kinetic resolution-asymmetric transfer hydrogenation (DKR-ATH) of the corresponding racemic α- and/or β-substituted ketones possessing stereolabile carbon atoms, using our laboratory developed chiral Ru(II) catalysts.

This way, new benzo-fused cyclic alcohols having two to four contiguous stereogenic carbons (>60 compounds) were successfully prepared in excellent diastereo- and enantiomeric purity (d.r.>99, >99% ee):



Thus, subjecting α-(*N*-sulfonilimino) or α-(*N*-sulfonilamino) aryl ketones to Ru(II)-catalyzed ATH in a HCO_2H/Et_3N mixture, these underwent DKR leading to *cis*-3-substituted 4-hydroxybenzo-δ-sultams possessing two vicinal stereogenic carbons. By opposition, DKR-ATH of 2-acetamido-indanones and tetralones afforded the unexpected *trans*-configured 1-hydroxy-2-acetamides via hydrogen bond-driven diastereoselectivity. Moreover, α-CF_3C(O)-substituted benzo-fused cyclic ketones underwent unprecedented two consecutive DKR during their reduction leading to γ-hydroxy-α-CF_3-carbinols possessing three contiguous stereogenic carbons. DKR-ATH of α,β-disubstituted indanones to 2,3-disubstituted indanols was either highly *cis*,*cis*- or *cis*,*trans*-diastereoselective as a result of 1,2-*cis* directivity of the Ru(II) catalyst in the reduction step, while configuration at C3 was thermodynamically controlled. Such synthetic methodology allowed us to prepare as well conformationally rigid chiral 1,4-diols with indenoindene scaffold possessing four contiguous chiral centers which is found in naturally occurring resveratrole dimers such as Pallidol.

Furthermore, stereopure alcohol *cis*-(*R*,*R*)-**2a** was transformed in a stereocontroled manner to chiral ''*syn*-ULTAM'' ligand, which has been prepared previously by our group via chiral HPLC separation of its racemic mixture. This was embedded in a new *ansa*-Ru(II) catalyst design wherein the η^6-arene moiety is intra-covalently tethered to the ligand amine terminal, and was successfully applied to the DKR-ATH of the above presented 2-acetamido-indanones.



Keyword: asymmetric catalysis, dynamic kinetic resolution, ruthenium, transfer hydrogenation