Asymmetric Catalysis

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Desymmetrization Catalyzed by Transition-Metal Complexes: Enantioselective Formation of Silicon-Stereogenic Silanes**

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asymmetric synthesis · desymmetrization · silicon-stereogenic silanes · transition metals

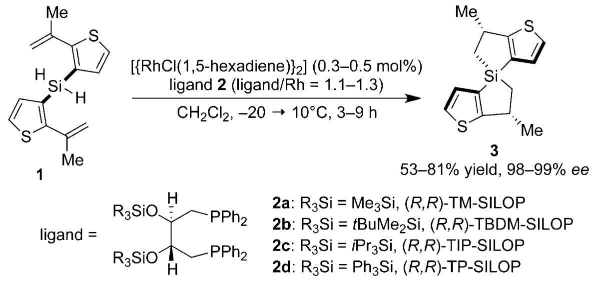
Dedicated to Professor Chun-Gu Xia on the occasion of his 50th birthday

The observation of the stereochemistry of silicon-stereogenic silanes dates back to the pioneering work by Kipping in 1907.[1] However, despite many significant efforts in the past hundred years toward finding new synthetic methodologies to Si-stereogenic silanes, they are still few in number. The enantioselective preparation of these silanes and their functionalized derivatives was not at all a trivial task and remained restricted to optical and kinetic resolution.[1c,d,2] Undoubtedly, the exploration of new and efficient catalytic methods with high enantioselectivity remains one of the principal challenges in asymmetric catalysis.

Fortunately, many research efforts have recently been dedicated to the design and evaluation of chiral metal catalysts that can perform asymmetric transformation of functionalized silanes to Si-stereogenic silanes.[2] A promising solution to this problem lies in the catalytic efficiency of chiral ligands and the selective desymmetrization reaction of dihydrosilanes. Probably the earliest examples of catalytic asymmetric synthesis of Si-stereogenic silanes were independently reported by Corriu and Kumada in 1970s.[3] Corriu and Moreau used a Rh–DIOP (DIOP = 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane) complex to promote the enantioselective dehydrative Si–O coupling of alcohols with hydrosilanes. However, this method resulted in low enantioselectivity.

Although the method described by Corriu and Kumada for the catalytic desymmetrization of dihydrosilanes has been reported almost 40 years ago, limited progress has been made in the preparation of enantiomers of chiral silanes before 1994. The main obstacle when using dihydrosilanes is the high activity of transition metals in the decomposition and nonselective hydrosilylation. A related and important achievement was reported by Takaya and co-workers[4] in 1994; they used rhodium(I) complexes with CyBINAP (CyBINAP = 2,2′-bis(di cyclohexylphosphanyl)-1,1′-binapthyl) as a chiral phosphine ligand to control the enantioselective hydrosilylation of symmetric ketones, and observed excellent enantioselectivity (up to > 99 % *ee*).

A few years later, an alternative and striking methodology was developed by Tamao et al.[5] in 1996, the asymmetric Rh-catalyzed intramolecular hydrosilylation of bis(alkenyl)-dihydrosilane (**1**). The enantioselective intramolecular hydrosilylation of **1** proceeded sequentially to form spirosilane **3** in two steps with a catalytic amount of [{Rh(1,5-hexadiene)Cl_2}$_2$] and chiral phosphine ligands **2**. Relatively high enantio- and chemoselectivities were attained by using diphosphines **2a**–**d**, which bear bulky silicon-based groups, resulting in the desired spirosilane **3** in 98–99 % *ee* and good yields (Scheme 1). This study gives an idea of the potential of designing reactions in which symmetric reactive functionalized moieties in a molecule are used to achieve the highly enantioselective formation of Si-stereogenic silanes.



Scheme 1. Enantioselective intramolecular hydrosilylation of dihydrosilane **1** to spirosilane **3**.

Recently, Katsuki and co-workers[6] described a novel strategy to synthesize derivatives of Si-stereogenic silanes through the selective Si–H insertion reaction of dihydrosilanes catalyzed by chiral iridium(III)–salen complexes (Scheme 2). In this study, they emphasized the desymmetrization of prochiral hydrosilanes through Si–H insertion of *tert*-butyl α-diazopropionate catalyzed by Ir–salen complex **6**. Excellent diastereo- and enantioselectivity was observed, and in each case, only one of the four possible diastereomers was produced (Scheme 2).

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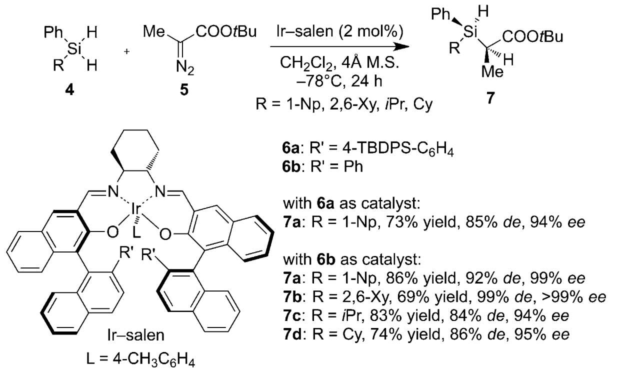
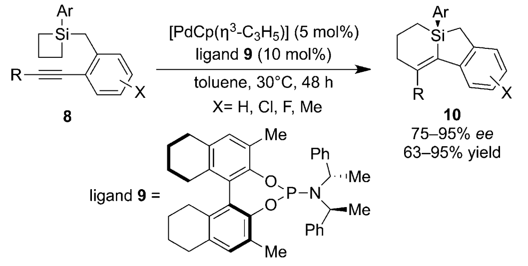


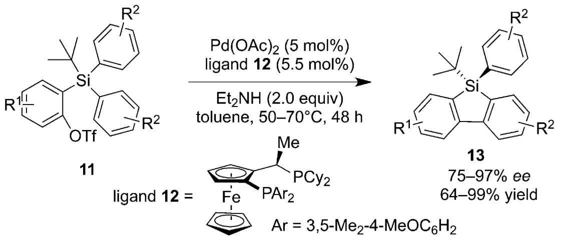
Scheme 2. Selective Si–H insertion reaction of dihydrosilanes. Cy = cyclohexyl, Np = naphthyl, Xy = xylyl.

Perhaps the most exciting, elaborate, and ambitious studies on enantioselective synthesis of Si-stereogenic silanes were recently conducted by Shintani, Hayashi, and co-workers.[7–10] In 2011, this group described the development and use of a chiral palladium catalyst for the enantioselective desymmetrization of silacyclobutanes to Si-stereogenic silacycles.[7] This intramolecular desymmetrization reaction proceeds through the oxidative addition of a carbon–silicon bond of the silacyclobutane to palladium(0), the intramolecular insertion of the alkyne, and the subsequent reductive elimination along with the regeneration of palladium(0) to give silacycles that possess a tetraorganosilicon stereocenter. Among the phosphines that were tested as ligands for the palladium complex, phosphine **9** was highly effective in the enantioselective desymmetrization of silacyclobutanes. Most of the desired products with a Si-stereogenic center were obtained in good yields and excellent enantioselectivities (up to 95% *ee*; Scheme 3). Very recently, the same group also described the intermolecular palladium-catalyzed ring-opening desymmetrization of various 1-alkyl-1-arylsilacyclobutanes with alkyne using the same palladium catalyst system ([PdCp(η^3-C_3H_5)] and ligand **9**), giving Si-stereogenic 1-sila-2-cyclohexanes in uniformly high yields and excellent enantioselectivities (up to 94% *ee*).[8]



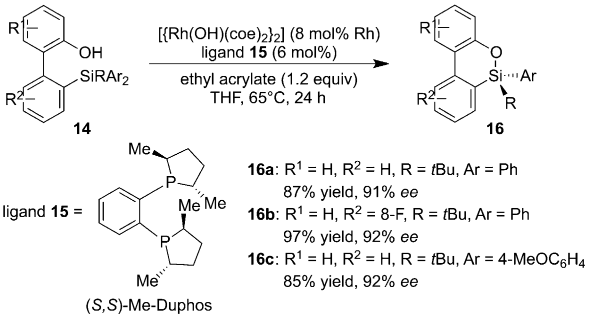
Scheme 3. Enantioselective desymmetrizaton of silacyclobutanes. Cp = cyclopentadienyl.

Recognizing the potential of desymmetrization-induced selective synthesis of chiral silanes, the same group[9] made a significant breakthrough in the synthesis of Si-stereogenic silanes through enantioselective C–H bond functionalization of 2-(arylsilyl)aryl triflates. The use of Josiphos-type ligand (R,S_p)-**12** resulted in good yields and excellent enantioselectivities in the Pd-catalyzed intramolecular C–H bond arylation reaction of prochiral aryl triflates that contain a *tert*-butyldiphenylsilyl (TBDPS) group. Regarding the substitution pattern at the prochiral aryl triflates, a wide variety of functional groups were tolerated on the aromatic ring (Scheme 4). An important finding from this study was that an unsymmetric cross-coupling procedure may be used to synthesize Si-stereogenic diarylsiloles with high enantioselectivity.



Scheme 4. Enantioselective C–H bond functionalization of prochiral aryl triflates. Tf = trifluoromethanesulfonyl.

The latest contribution addressing the rhodium-catalyzed asymmetric synthesis of Si-stereogenic silanes was also reported by Hayashi and Shintani.[10] They used hydroxy-functionalized tetraorganosilanes, in which the silicon atoms bear two identical aryl groups, as the transmetalating reagents in rhodium-catalyzed transmetalation-based silylations (Scheme 5). With [{Rh(OH)(coe)$_2$}$_2$] and ligand **15** ((S,S)-Me-Duphos), they observed the effective formation of various substituted dibenzooxasilines **16** containing an Si-stereogenic moiety with high enantioselectivities (71–92% *ee*). This contribution is very important for the preparation of Si-stereogenic backbones through catalytic desymmetrization and asymmetric transmetalation.



Scheme 5. Transmetalation-based silylation. coe = cyclooctene.

Overall, the protocol that was developed by several groups for the desymmetrization catalyzed by transition-metal complexes for the synthesis of Si-stereogenic silanes shows the potential of asymmetric catalysis in organosilicon research. Within the last year, four ground-breaking, highly successful examples of silylation based on catalytic enantioselective desymmerization were reported. There is no doubt that important gaps still need to be filled through asymmetric catalysis. The story of synthesis and application of Si-stereogenic functionalized silanes through unprecedented reactions will continue with the rise of new asymmetric methodologies in organic synthesis.

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