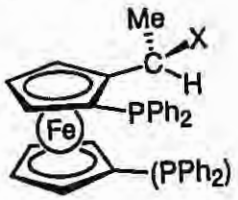
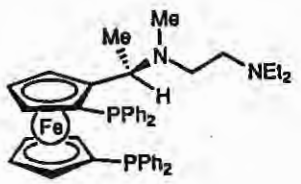
Ferrocenylphosphines as Ligands in Asymmetric Catalysis

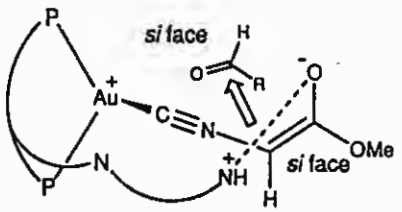
Ramin Khayatpoor Literature Seminar October 31, 1996

Chiral ferrocenylphosphines have been applied as ligands in a number of asymmetric catalytic reactions.[1] These ligands can co-ordinate to a metal center in the mono-dentate or bi-dentate mode via their phosphine substituents. In cases where the ligand contains both P and N atoms, metal coordination can occur through these atoms. These ligands contain ferrocene planar chirality, which will never undergo racemization. Also depending on the substituents on the side chain, they may posses a chiral center.



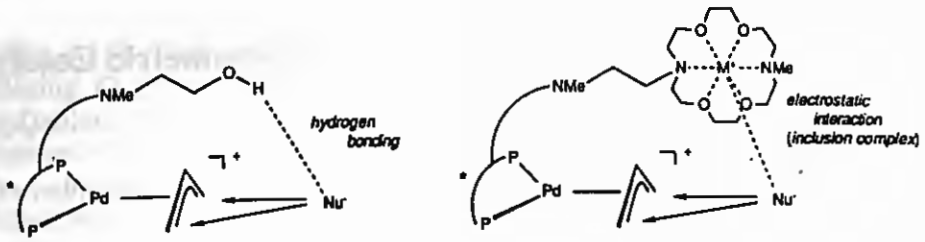
Direct involvement of the functional groups on the side chain has been investigated in gold(I) catalyzed asymmetric aldol reactions. In these reactions, typically 1 mol % of the chiral catalyst is used to catalyze the reaction of an aldehyde with an isocyanoacetate ester to selectively yield *trans*- oxazolines in high enantiomeric excess.[2] The successful ligands in this catalysis contain a terminal amino group on the pendant side chain,[2,3] an example of which is shown below. Also a hypothetical transition state, offered by Ito and Hayashi from the initial report of this type of catalysis, is shown.





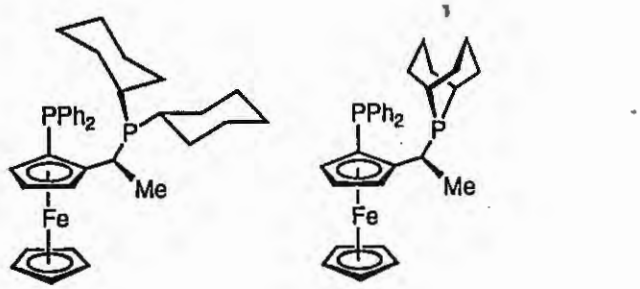
The structure of the terminal amine has a strong influence on stereoselectivity. Interestingly, asymmetric aldol reactions of isocyanoacetates with fluoroaryl aldehydes yield oxazoline products with opposite geometry and absolute configurations.[4] Hence the initially proposed transition state model has been re-interpreted. Togni and Pastor have offered a different transition state model, which avoids the highly unusual, four co-ordinate gold cation center.[5] The crystal structure of a gold(I) complex of a chiral aminoferrocenylphosphine is available.[6] The solution conformation and behavior of such complexes have been investigated by NMR.[7]

Secondary interactions of the ligand side chain with the reacting substrate have also been proposed in asymmetric palladium catalyzed allylic substitution reactions, as well as in Ni or Pd catalyzed Grignard cross-coupling reactions. These proposed interactions have been reviewed in the literature.[8] Ferrocenylphosphine ligands bearing hydroxy functionality,[9] as well as ligands modified on the side chain by crown ethers,[10] are effective in palladium-catalyzed asymmetric allylation of diketones. The attack of a soft nucleophile is thought to occur on the palladium-bound allylic unit from the opposite side of the allyl-palladium fragment. The ligand is proposed to interact via the functional group on the side chain, to direct the incoming nucleophile preferentially to one side of the allylic unit. Interestingly, the resulting product has opposite configurations, when asymmetric malonates are used as nucleophile, in the hydroxy- and crown ether-containing ferrocenylphosphine ligands.



In the Ni or Pd catalyzed asymmetric Grignard cross-coupling reactions,[11] amine functionality on the side chain of ferrocenylphosphine ligand is also critical in enantioselectivity. These cross-coupling reactions have found use in asymmetric synthesis of binaphthyls,[12] which are otherwise notoriously difficult to achieve due to the bulky nature of the reactants. The absolute configuration of the stereogenic carbon on the side chain, which links the amino group to the ferrocenyl moiety, does not greatly affect enantioselectivity and the absolute configuration of the product; whereas, the planar chirality of the ligand defines, in this case, the configuration of the product. This is in contrast to ligands used in asymmetric aldol reaction, where the absolute conformation of the side chain at the stereogenic carbon is critically important. For the gold catalyzed aldol reaction, the preferred time averaged conformation of the ligands have been determined, and speculatively carried over to the catalytically active intermediate.[13]

One method of synthesis of chiral ferrocenylphosphines is by directed lithiation of ferrocenylamines,[14] a method pioneered by Ugi[15] et al. A more recent method allows introduction of two different phosphine groups on the ferrocenyl unit.[16] The resulting JOSIPHOS ligand (shown on the left) and similar ferrocenylphosphine ligands, are successful in asymmetric hydrogenation of a variety of substrates. This new synthetic method has allowed the design of ligands, for the purpose of investigation of steric effects of the ligand,[17] and electronic configuration[18] of the ligand, in their effectiveness in asymmetric, catalytic reactions.



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