

Synthesis of Novel Ferrocene-Derived Chiral Ligands Containing Bisoxazoline

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Abstract: In this paper, the synthesis and loading of ferrocene-based oxazoline chiral ligands were studied. The ferrocene oxazoline ligands with surface chirality and central chirality were synthesized and resolved, and the asymmetric addition of two diastereomers to catalyzed diethylzinc to aromatic aldehydes was investigated.

1. Introduction

Since ferrocene was unexpectedly discovered by Kealy and Pauson in the study of Grignard in 1951, it has attracted the attention and imagination of chemists with its fascinating sandwich structure, and ferrocene has now become metal organic Chemistry, materials science, and especially one of the most important structural parts of the field of catalysis. Due to the availability of ferrocene, unique three-dimensional structure, and fine adjustment of electrons and stereo, ferrocene-based ligands have become one of the most abundant ligand skeletons for asymmetric catalysis. The application of ferrocene-based compounds has not only attracted more and more interest in the academic field, but also in industry. A well-known example of the enormous industrial application of chiral ferrocene ligands is the synthesis of herbicides by the asymmetric catalytic hydrogenation of IR-Xyliphos (5>promethazine precursor OS>NAA application.

In addition to its unique structure, ferrocene has desirable properties such as low cost and high stability to heat, water, oxygen and many reagents. Ferrocene is prone to electrophilic aromatic substitution as an electron-rich aromatic compound, and ferrocene is also easily lithiated and double lithiated (at the 1,1' position), with its benzylic carbon cation. Properties such as stability provide many effective ways to synthesize functionalized or substituted ferrocene compounds. For example, the earliest known ferrocene ligand was reported in 1965 by 1,1'-bis(diphenylphosphino)ferrocene (dppf), which was double lithiated by reaction of ferrocene with n-butyllithium. It is then reacted with diphenylphosphine chloride. Since then dppf and related achiral ferrocenylphosphine compounds have been successfully and widely used in the process of transition metal catalysis.

2. Synthesis of novel ferrocenyl porphyrin chiral ligands

Compounds containing oxazoline ring structures are among the most successful, versatile, and commonly used asymmetric catalyst ligands due to their availability, modular nature, and broad applicability in catalytic conversion of metals. Most of these ligands are synthesized from readily available chiral amino alcohols in several high yields. The resulting chiral carbon atom functioning as an enantioselective control center is adjacent to the coordinating nitrogen atom on the porphyrin ring and therefore also abuts the metal activation site, thereby having a direct effect on the stereochemical results of the reaction. Since Bmnnr first reported the use of oxazoline chiral ligands as asymmetric catalysts in 1986, various ones containing multiple heteroatoms, additional chiral elements and special structural features contain one, two or more tons. Ligands of ligands have been widely used in a variety of asymmetric catalytic reactions with great success. Although asymmetric catalytic technology is currently gaining more and more success in the laboratory, only a handful of chiral catalysts or ligands have been maturely used in industrial production. Most chiral

intermediates or products are still synthesized by the natural chiral product as a starting material or by resolution of the racemate. One of the reasons is that because asymmetric catalysts are relatively expensive, there is currently no effective way to achieve the recycling and recycling of these expensive chiral catalysts in industrial production practices. By loading the catalyst, it is possible to make the recycling and reuse of the catalyst easier and more economical.

Using the cheap and readily available L-tyrosine as the starting material, the methyl group of the carboxyl group is used to protect the amino group with the Boc group, then the phenolic hydroxyl group is loaded with the benzyl bromide, and then reduced by the mild $\text{NaBH}_4/\text{CaCl}_2$ system. The ester group, using a p-toluene mineral acid to remove the Boc protecting group on the amino group, finally produced a key intermediate: phenolic hydroxyl group and the base group loaded; 5-amino alcohol 6. Ferrocenecarboxylic acid was synthesized in large quantities by reacting cheap ferrocene with carbon dioxide under the catalysis of aluminum trichloride. The ferrocenecarboxylic acid is further reacted with oxalyl chloride to form ferrocenecarbonyl chloride, which is directly reacted with amino alcohol 6 to form ferrocenecarboxamide without isolation and purification. The ferrocene oxazoline 10 is then cleaved in a high yield under the action of p-toluenesulfonyl chloride.

The use of sec-butyllithium to lithiation of the ferrocenyl oxazoline 10 oxazoline in the presence of a ring carbon atom, and then reacting with benzophenone to form a central chiral and chiral chiral [G-0] Ferrocenyl morpholine chiral ligand [1].

On the basis of the synthesis of amino alcohol 6 and ferrocenyloxazoline 10, the design of the benzyl group attached to the alcohol 6 phenolic hydroxyl group was replaced by a TBS group to form a ferrocene oxazoline. It is convenient to remove, so that the phenolic hydroxyl group can be exposed as a grafting site loaded on the dendrimer. The ferrocene-protected ferrocene oxazoline 17 was then synthesized in the same manner as in the synthesis of [G-0] ferrocenyl. On the basis of the ferrocene-protected ferrocene-based P-porphyrin 17 on the basis of phenolic hydroxyl group, it is lithiated with sec-butyllithium to react with benzophenone to form TBS-protected ferrocene oxazoline N,0 ligand 18. Then, under the action of TBAF, the TBS protecting group is removed, and the phenolic hydroxyl group is exposed to become a grafting site linked to the polymer. The ferrocenyl porphyrin N,0 ligand 19 having a free phenolic hydroxyl group is further linked to a [G-1], [G-2] or even higher algebraic dendrimer to effect loading. The ferrocene-based oxazoline N,0 ligand 20 supported by different algebraic dendrimers was applied to various asymmetric catalytic reactions, and its catalytic effect was investigated. The convenience of recycling and the effect of recycling were studied.

3. Ferrocene-based development of chiral ligands

Brunner et al. first reported a chiral ligand 39 containing an oxazoline ring in 1986, and used this ligand in an asymmetric catalytic reaction to obtain a good catalytic effect. The oxazoline ligands have the following advantages: (1) the starting material is a chiral amino alcohol, which is cheap and easy to obtain; (2) the preparation is simple and the yield is high; (3) the chiral center is next to the coordination atom, Can be applied to a variety of catalytic reaction types. Therefore, porphyrin ligands have attracted widespread attention. The ferrocene oxazoline type ligands are mainly divided into two types: one is the synthesis of 1,2-disubstituted chiral ligands by ortho-position substitution of oxazolines, and the other is ferrocene and two ferrocene rings. Both are substituted with an oxazoline ring and have a C₂ symmetric 1, r-disubstituted double porphyrin ligand.

In 1997, the ligands reported by the Sammakia group were the first type of monoferroline ligands of the ferrocene skeleton that achieved the desired effect in asymmetric catalytic reactions. A value of 83% was obtained in the asymmetric cross-coupling reaction, and 92% was obtained in the asymmetric cyclization catalytic reaction. The monooxazoline ligands, which were independently completed by Ikeda, Zhang Wanbin, Hou Xuelong, and Dai Lixin, achieved good catalytic results in the asymmetric allyl substitution reaction catalyzed by metal palladium, among which the value is up to 99% [2]. Ligand reported by Hou Xuelong and Dai Lixin's group also showed good catalytic activity and effect in the asymmetric allyl substitution reaction catalyzed by

metal palladium. The ferrocene skeletons of the Uemura group, achieved a value of up to 96% in the asymmetric reduction of simple ketones. The Bolm team developed the ferrocene skeletons of single porphyrin ligands, which have a value of up to 95% in the selective addition reaction of diethylzinc to aldehydes.

For the disubstituted bisoxazoline ligands, in 19%, Ikeda and Zhang Wanbin first introduced C2 symmetric chiral oxazoline rings on ferrocene, ie ligands, in the basis of this, ligands were synthesized by ortho-lithiation. The ligands have a maximum value of 99% in the allyl substitution reaction catalyzed by metal palladium, ligand 593- 511 showed a good catalytic effect in catalyzing the selective addition reaction of diethyl zinc to aldehyde [3].

Compounds containing oxazoline ring structures are among the most successful, versatile, and commonly used asymmetric catalyst ligands due to their availability, modular nature, and broad applicability in catalytic conversion of metals. Most of these ligands are synthesized from readily available chiral amino alcohols in several high yields. The resulting chiral carbon atom functioning as an enantioselective control center is adjacent to the coordinating nitrogen atom on the oxazoline ring and therefore also abuts the metal activation site, thereby having a direct effect on the stereochemical results of the reaction. Since Brunner first reported the use of a wow oxa chiral ligand as an asymmetric catalyst in 1986, contains one, two or more of a variety of heteroatoms, additional chiral elements and special structural features. Ligands of oxazoline rings have been widely used in a variety of asymmetric catalytic reactions with great success.

In 1993, Pfaltz, Helmchen and Williams independently developed a highly efficient non-Ci symmetrically symmetric asymmetric allyl thiolation ligand ligand phosphine- porphyrin (PHOX) ligand, which has been used in asymmetric synthesis reactions. It has achieved great success. For certain specific reactions, asymmetric monooxazoline ligands containing two heteroatoms coordinated are generally considered to have better enantioselectivity than Ci symmetric ligands. The alkylation of guanidinopropyl group catalyzed by a transition metal is a good example gas single-tonoline N, P ligand successfully applied, stimulated the monooxazoline with other heteroatoms In vivo, a series of monooxazoline ligands such as NN, NP, NS, N-O have been developed [4]. When studying chiral ligands with C2 symmetric structure applied to asymmetric catalytic reactions, the reactants are positive. In the same chiral environment, the anti-two-sided attack may reduce the number of transition states in the catalytic reaction, so usually good catalytic results can be obtained. Ligands of C2 symmetric structure have thus become a class of ligands in the field of asymmetric catalysis research, and are also considered to be potential ligands for practical industrial applications. In 1986, Pfaltz reported a chiral semi-porphyrin ligand 7 with a C2 symmetry structure. The complex of this ligand with copper was used as a chiral catalyst to achieve greater than 95% of the asymmetric cyclopropanation of styrene. The value is f52l. Although the chiral semi-porphyrin ligand 18 has a good asymmetric catalytic effect, its synthesis is complicated, and only one of the ligands has a good asymmetric catalytic effect. Therefore, the bisoxazoline chiral ligand 19, which is structurally similar and convenient to synthesize, has attracted more attention.

4. Conclusion

Based on laboratory conditions, a practical analytical method for the enantioselective and diastereoselective selectivity of asymmetric cyclopropanation of styrene and diazoacetic acid ethyl acetate was established: using gas chromatography column SE A 30 is used to detect the progress of the reaction and determine the diastereoselectivity of the reaction, and the enantioselectivity of the trans is determined by epimerization of the cyclopropanation product. The preferred configuration of the product is by gas chromatography corresponding to the literature. Analytical data were correlated; the enantioselectivity of the cis isomer product was determined by laboratory-made acoustic cyclodextrin chiral capillary gas chromatography column by converting the product to the corresponding A.

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