Chiral sulfur-containing ligands for asymmetric catalysis

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1. Introduction

The preparation of chiral compounds is an important and challenging area of contemporary synthetic organic chemistry.[1] In particular, the preparation of new chiral ligands for application in asymmetric catalysis has been and continues to be an important area of synthetic organic research.[2] New classes of ligands that might offer new opportunities for applications or provide insight into fundamental chemical processes are always of interest. One relatively rare class of ligands is that in which stereogenicity resides not at carbon atoms, but at heteroatomic sites such as sulfur atoms. Practical asymmetric catalysis using transition-metal complexes was inspired by the work of Kagan[3] and Knowles.[4] Their important results, based on the use of chiral phosphines as ligands for asymmetric hydrogenation, have induced a tremendous amount of work, dealing with the synthesis and use of new chiral phosphine-containing complexes as catalysts. Numerous catalytic asymmetric reactions have been discovered over the last 30 years, often with spectacular results in terms of efficiency and selectivity, allowing access to biologically important molecules. Nevertheless, the contribution of asymmetric catalysis in the overall production of chiral chemicals is much lower than originally expected, which is surprising given the huge amount of work devoted to this subject. Factors such as the price of the catalyst precursor and the difficulties

Abbreviations: Ac, acetyl; acac, acetylacetone; Ad, adamantyl; Ar, aryl; BINAP, 2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl; BINOL, 1,1′-binaphthalene-2,2′-diol; BITIANP, 2,2′-bis(diphenylphosphino)-3,3′-bi(benzo-[*b*]thiophene); BITIOP, 4,4′-bis(diphenylphosphino)-3,3′-bithiophene; Bn, benzyl; Boc, *tert*-butoxycarbonyl; Bu, butyl; BSA, *N,O*-bis(trimethylsilyl)acetamide; Bz, benzoyl; *c*, *cyclo*; cod, cyclooctadiene; Cp, cyclopentadienyl; Dec, decyl; dba, (*E,E*)-dibenzylideneacetone; de, diastereomeric excess; EDA, ethyl diazoacetate; ee, enantiomeric excess; Et, ethyl; Fm, fluorenylmethyl; Fur, furyl; Hept, heptyl; Hex, hexyl; L, ligand; M, metal; Me, methyl; Mes, mesyl; Naph, naphthyl; NBD, norbornadiene; Pent, pentyl; Ph, phenyl; Piv, pivaloyl; Pr, propyl; py, pyridine; siam, bis(sulfinyl)imidoamidine; SES, 2-(trimethylsilyl)ethanesulfonyl; suc, succinimide; TADDOL, α,α,α′,α′-tetraphenyl-2,2-dimethyl-1,3-dioxolane-4,5-dimethanol; Tf, trifluoromethanesulfonyl; TMBTP, 4,4′-bis(diphenylphosphino)-2,2′,5,5′-tetramethyl-3,3′-bithiophene; TMS, trimethylsilyl; Tol, toluene; Tr, triphenylmethyl (trityl); Ts, 4-toluenesulfonyl (tosyl); TsDPEN, *N*-tosyl-1,2-diphenylethylenediamine; TsOH, *p*-toluenesulfonic acid; VERDI, verbenone dimers.

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encountered in the separation and recycling of the catalyst are responsible for this lack of practical application. Only a few processes have, however, permitted high turnovers. Apart from these economic considerations, it is almost impossible to recycle, for example, phosphine-containing catalysts, due to their low stability towards oxidation. Indeed, the chemical and economic characteristics of these catalysts were partly responsible for problems encountered in the development of catalytic asymmetric processes in general. The field of asymmetric catalysis is witnessing an ever-growing interest, and several highly efficient catalytic methods are nowadays known in the literature. Despite the positive results, knowledge in this field is still limited, and much work will be needed to make this methodology a comprehensive and well-established technique. The nature of the ancillary ligands used for a given metal-catalysed process is central, with chiral P- and N-based ligands occupying an incontestable leading position. Despite the vast knowledge on sulfur-metal interactions in coordination chemistry,[5] the use of chiral S-based ligands in catalysis appears, however, to be still rather underdeveloped.

Over the last three decades, more than 40 different classes of chiral sulfur compounds have been described in the literature, and a large number of useful procedures for the synthesis of enantiomerically pure sulfur compounds have been developed.[6] Transition-metal complexes with chiral sulfur ligands are powerful catalysts in a considerable number of reactions, although, they have been generally less investigated than complexes with other donor atoms. The goal of the present review is to cover the recent advances in the use of chiral sulfur-containing ligands in asymmetric catalysis, focusing on those, which have been published since the beginning of 1999. In fact, a preceding review has reported the chemistry of transition-metal complexes containing, more generally, both achiral and chiral sulfur ligands, covering the literature up to the end of 1998.[7] The present review is divided into seven sections corresponding to the different types of reactions based on the use of complexes containing chiral sulfur ligands, such as allylic substitution, hydrogenation, hydrogen transfer, conjugated additions, addition of organometallic reagents to aldehydes, Diels–Alder reactions and miscellaneous reactions.

The coordination chemistry of sulfur ligands has shown a unique variety of structures with most of the transition metals in different oxidation states.[8,5] The use of chiral sulfur ligands in reactions catalysed by transition metals is still relatively unexplored, however, compared with other ligands.[9] It is important to note that the synthesis and applications of chiral thioether ligands were reported by Masdeu-Bulto et al. in 2003.[10] Moreover, the use of chiral sulfoxides in enantioselective metal-catalysed asymmetric synthesis was reviewed in 2003 by Fernandez and Khiar.[11] Indeed, sulfur donor ligands have been used much less than phosphorus donor ligands in asymmetric homogeneous catalysis,[12] although, in recent decades, the number of studies with chiral sulfur-containing catalytic systems has increased considerably.[7,10] Compared to phosphorus, sulfur has less donor and acceptor character. In addition to these electronic considerations, the sulfur atom, in thioether ligands, for example, has only two substituents, which can create a less hindered environment than trivalent phosphorus. In addition, compared

to phosphorus or nitrogen, sulfur is known to have a tendency to poison heterogeneous catalysts. The formation of mixtures of diastereomeric complexes, and the difficulty to control their interconversion in solution have been regarded as a problem for asymmetric induction in catalytic reactions. Nevertheless, in recent years, chiral bidentate S-donor ligands, in particular, have proved to be as useful as other classical asymmetric ligands, especially when combined with other donor atoms.[13]

2. Allylic substitution

Carbon–carbon bond formation is one of the most important reactions in synthetic organic chemistry. One useful and popular method is the palladium-catalysed allylation,[14] e.g., the Tsuji–Trost reaction,[15] and asymmetric versions of this reaction have been extensively studied over the last decade.[16] Strategies for controlling enantioselectivity in palladium-catalysed asymmetric reactions have depended on the design and application of chiral ligands. Many of the efficient homo- and hetero-donor chiral ligands such as N/N- (e.g., bis-oxazolines[17]), P/P- (e.g., Trost's P/P ligands[18]), and N/P- (phosphinooxazolines[19]) types have been exploited. A particular efficient method of C–C bond formation was opened up by the reaction of carbon nucleophiles with allyl-palladium complexes, the generation of which is in situ accomplished, and requires only a catalytic amount of the transition metal. Considerable efforts have been devoted to study the reaction between allylic substrates and nucleophiles catalysed by chiral palladium complexes. The palladium-catalysed allylic substitution is one of the catalytic homogeneous processes that has attracted most attention in recent decades, and for which the catalytic cycle is well established (Scheme 1).[20]

L, L' = mono- or bidentate ligand
S = solvent or vacant
LG = leaving group
Nu = nucleophile
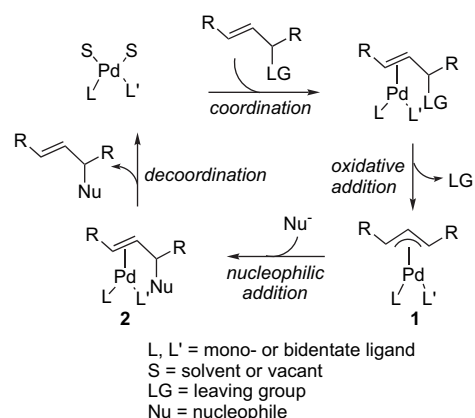
Scheme 1. Mechanism for Pd-catalysed allylic substitution with soft nucleophiles.

This is due in part to the relative ease of isolating catalytic intermediates, especially the palladium allylic species **1** (Scheme 1), although some related Pd(0) species (**2**) have also been characterised in solution.[21] The enantioselectivity of the process with soft nucleophiles (derived from conjugated acids with $pK_a < 25$) is controlled by the external nucleophilic attack on the more electrophilic terminal allylic carbon of **1**. The chemo-, regio-, diastereo- and enantioselectivities of this process have been widely analysed, and the