1 Introduction

1.1 Book Structure and Notation

The field of asymmetric Brønsted acid catalysis is known to contain a diverse array of catalyst architectures, but by far the most dominant within these are BINOL-derived acids [1-11]. They have become so strongly associated with the term *asymmetric Brønsted acid* that it is not unusual to see this key descriptor omitted in abstracts of recent literature. To complicate the definition, several classes of hydrogen-bond donors such as BINOLs are sometimes referred to as *Brønsted acids*. While they may certainly be involved in hydrogen-bonding interactions, their complete dissociation to the conjugate base by loss of a proton is not a prevalent mechanistic pathway. The pKa values of common Brønsted acid catalysts have been measured by several groups [12-15] in a variety of solvents. Since the comparison of different acids is difficult across different solvents, we will not endeavor to formalize a pH range for the catalysts included in this book. Instead, in general, we have curtailed our coverage to only include BINOL-derived phosphoric acids (and derivatives), carboxylic acids, and sulfonamides.

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In order to circumvent the repetitive reproduction of the most commonly employed catalysts within this book, we have opted to use a logical abbreviation formatting for the schemes (Figure 1.1).

BINOL-derived phosphoric acids will be defined as **PA**, the corresponding *N*-phosphoramides will be denoted as **NPA**, and finally, spirocyclic phosphoric acids will be referred to as **SPA**. All other catalysts will simply be denoted as **BA**. In each case, a number will follow the descriptor and these numbers will be consistent throughout the whole book. The nature of the aryl (or R-group) will be shown with the catalyst, and all **BA** catalysts will be embedded within the scheme. In most cases, the (*R*)-enantiomer is employed but wherever this differs, it will be noted appropriately, for example, (*S*)-**PA 1** would be the (*S*)-enantiomer. Finally, the partially dehydrogenated catalysts of BINOL will be referred to as $[H_8]$ -, and this should be assumed as always being the distant aromatic rings.



Figure 1.1 Commonly employed catalysts and their notation within this book.

1.2 Catalyst Preparation

This book will cover a range of Brønsted acid catalysts, so we will not endeavor to try and cover all the synthetic processes involved for every catalyst employed. However, since BINOL-derived phosphoric acids are featured in a large majority of research papers, we feel it would be beneficial to show the most commonly used route toward preparing them (Scheme 1.1) [16].



Scheme 1.1 Common synthetic route to BINOL phosphoric acid catalysts.

The process would normally commence from commercially available BINOL, which would be appropriately protected with either a methyl or a MOM group (**1a**). The next stage is to install boronic esters at the 3,3'-positions. This requires a three-step procedure, which involves lithiation, followed by electrophilic quenching with a boronate, and finally, hydrolysis to yield **1b**. The installation of aromatic groups is performed via a Suzuki reaction and then the protecting group can be removed to yield **1c**. Lastly, condensation of POCl₃ with BINOL **1c** leads after hydrolysis to the phosphoric acid catalyst **PA**. The overall route is highly reliable and works well for a range of aromatic partners. On a critical note, the route makes use of two wasteful protecting group steps, and to circumvent this flaw, several groups have reported protecting-group-free strategies [17, 18].

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For the remaining common catalysts, the *N*-phosphoramide catalysts can be easily prepared in a single step from the corresponding phosphoric acid catalyst by a simple amidation reaction [19]. The spirocyclic phosphoric acid catalysts are prepared in a similar manner but starting from the corresponding spirobiindane diol precursor. This is, however, not commercially available and can be prepared as described by Birman *et al.* [20].

1.3 Metal Impurities

Although beyond the scope of this book, chiral phosphate anions combined with metal cations are well known to be suitable for catalyzing a whole host of asymmetric transformations [21-23]. Metal cations can enhance the catalytic behavior of a catalyst in a number of ways, and therefore, sometimes its role is difficult to determine. The issue of metal impurities is an even more difficult subject to address. Chiral phosphoric acids are now well known to chelate to metal cations during purification techniques, particularly so on silica gel. This usually leads to the isolation of a catalyst that contains a highly variable amount of metal content, which results in large deviations in catalytic performance from batch to batch. This phenomenon has been reported by several groups [24-28] and most likely has been experienced by many groups too. The solution to avoid such issues is simply to wash the purified catalyst with a strong acidic solution [25, 29]. Although researchers in the field are all conscious of this issue now, this was not always the case, and, therefore, it should be taken into account that some earlier reports may have involved metal impurities of which the authors were completely unaware . It is impossible to suggest which reports may suffer from this; therefore, we have adopted to include all the reports as reported originally.

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