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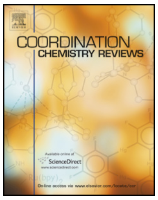

Review

Synthesis, reactivity, and coordination chemistry of secondary phosphines

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ABSTRACT

The coordination chemistry of secondary phosphines is reviewed. Although the number of secondary phosphine complexes is still relatively small, a number of important uses for these complexes have emerged. In particular, they are useful precursors in the synthesis of asymmetric tertiary phosphines, and they are important synthetic intermediates in the preparation of phosphine macrocycles. The use of secondary phosphine complexes in homogeneous catalysis is limited because the complexes are generally unstable under catalytic conditions. The physical properties of secondary phosphines are briefly discussed first, followed by a review of the synthetic routes used to prepare them. The metal complexes of secondary phosphines are then reviewed according to their group in the periodic table. A special focus of this latter section is on secondary phosphine complexes used in the preparation of phosphine macrocycles.

1. Introduction

In this review, we examine the emerging coordination chemistry of secondary phosphines. Numerous review articles have examined the coordination chemistry of phosphine ligands, but it is notable that these reviews focus almost exclusively on tertiary phosphines [1–13]. The reason for this emphasis is that complexes with secondary or primary phosphine ligands are generally unstable under catalytic conditions, and consequently there is little applied chemistry to report. Secondary phosphines and their complexes are, however, useful synthetic intermediates in a variety of reactions, and consequently new complexes with secondary phosphine ligands are slowly beginning to appear in the literature. Following a brief overview of the physical properties of secondary phosphines, including a comparison to tertiary

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phosphines and amines, the synthesis of secondary phosphines is reviewed followed by a discussion of their coordination chemistry. The emphasis is on secondary phosphine transition metal complexes where the P—H bond remains intact after coordination to metals; thus, secondary phosphine oxides, secondary phosphine chalcogenides, and phosphide complexes are not covered. In addition, pincer-type ligands containing phosphines (e.g. PNP or PCP ligands) are also not discussed because these ligands have been reviewed extensively [14–18]. The coverage is generally restricted to results from the past twenty-five years.

2. Physical properties of secondary phosphines

The C—P—H bond angle in secondary phosphines ranges from 95° to 97° [19]. In contrast, the C—P—C angle in tertiary phosphines depends on the R group and ranges from 98.6° in trimethylphosphine to 109.9° in tri-*tert*-butylphosphine (Fig. 1) [19].

Although both phosphines and amines are pyramidal, the pyramidal inversion at room temperature is rapid for amines but is slow for secondary and tertiary phosphines. The explanation for this behavior is that the energy barrier for going through an sp^2 planar transition state is higher for phosphines than for amines (~30–35 kcal/mol for phosphines compared to ~5 kcal/mol for amines). Because of the larger barrier, a phosphine has a fixed pyramidal geometry; if the phosphine has three different substituents, the molecule can be optically active (Fig. 2). The fact that phosphines can be optically active has led to many advances in organometallic asymmetric catalysis, a topic that has been extensively reviewed [20–22].

In terms of basicity, phosphines trend well with amines, with phosphines being slightly less basic. For example, the pK_b of triethylphosphine is 5.4, similar to other simple tertiary phosphines in the range 4.5–6. In comparison, triethylamine has a pK_b of 3.2. Replacing an alkyl group with a hydrogen atom in phosphines has a dramatic effect on basicity, with secondary phosphines having pK_b values around 9.5–10.5 and primary phosphines ranging from 13.5 to 14. In contrast, replacing alkyl groups on nitrogen with hydrogen has no appreciable effect. For example, diethylamine has a pK_b of 2.9 and ethylamine has a pK_b of 3.2 [23].

In general, phosphines are extremely air-sensitive compounds that are characteristically malodorous and potentially toxic. These compounds also tend to be difficult to handle and pyrophoric, especially low molecular weight primary and secondary phosphines. A recent paper by Stewart et al. [24] describes computational methods to predict the air-stability of phosphines; steric bulk or the incorporation of heteroatoms/conjugation is required to protect the phosphorus atom from oxidation by molecular oxygen.

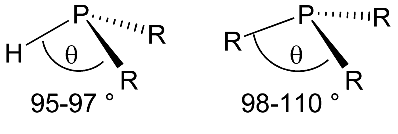

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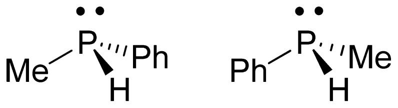
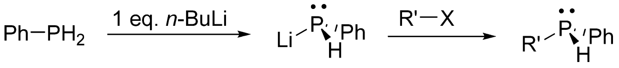
Fig. 1. C—P—H and C—P—C bond angle comparison between a generic secondary phosphine (1) and a generic tertiary phosphine (2).



R *S*

Fig. 2. The two stereoisomers of methylphenylphosphine showing the stereochemical implication of three different substituents on phosphorus.



3 (+,-) (+,-)

Scheme 1. Alkylation of a primary phosphine to yield a secondary phosphine [19].

3. Synthesis of secondary phosphines

The synthesis of secondary phosphines is well documented in the literature. Several points are noteworthy. First, significant advances in the preparation of these molecules have not been made over many years. Many of the methods discussed below were developed years ago. Second, any procedure described below for synthesizing secondary phosphines can be applied to tertiary phosphines as well [25]. Third, the common modern reason for making secondary phosphines is the ability to convert these molecules into chiral tertiary phosphines, which, once resolved, are useful ligands in asymmetric homogeneous catalysis. Finally, note that secondary phosphines are also key precursors for synthesizing a range of acyclic bidentate and multidentate tertiary phosphines, typically via metallation of the secondary phosphine, followed by coupling of the resultant phosphide anion with a range of halo-substituted organic substrates [19,20,26–31].

3.1. Alkylation

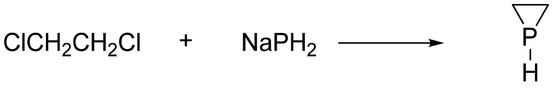
The most basic way to synthesize secondary phosphines is to start with a phosphide anion derived from a primary phosphine. For example, phenylphosphine, **3**, can be metallated with Na/NH_3, Li/THF, K, Ca, or deprotonated with *n*-BuLi to produce the phosphide, followed by alkylation with any number of electrophiles to yield the desired secondary phosphine (Scheme 1) [19]. This general reaction [32] is not stereospecific, and a mixture of stereoisomers is obtained. Stoichiometry is very important in these reactions because over-alkylation is common.

Reaction of phosphide anions with alkylene dihalides leads to either cyclic or bis(phosphino) derivatives. The first phosphorus heterocycle with three members, called a phosphirane, **4**, was prepared this way as a secondary phosphine (Scheme 2) [33].

More recently, work investigating primary and secondary phosphine-borane adducts (**5** in Scheme 3), showed that alkylation of these compounds can be more easily controlled than that of the non-adducts. A review on phosphine-borane adducts described these syntheses and reactivities extensively [34]. Another advantage of phosphine-boranes is the ability to work with air-sensitive phosphines as air-stable solids. Note that an extra deprotection step is required with a secondary amine to release the free phosphine from the adduct (Scheme 3).

3.2. Reduction

Perhaps the most common method to produce secondary phosphines is by using reduction reactions. There are many phosphorus species that can be reduced to secondary phosphines: phosphinous dichlorides **6** [35,36], secondary phosphine oxides **7** [35,37], phosphonate esters and other phosphinic species **8**–**9** [35,38], and secondary chalcogenides **10** [39]. A number of reagents and methods are capable of carrying out the reduction, but traditionally the



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Scheme 2. Alkylation with a dihalide to form a phosphirane, 4 [33].