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Stereoselective Synthesis of P-Stereogenic Aminophosphines: Ring Opening of Bulky Oxazaphospholidines

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Supporting Information

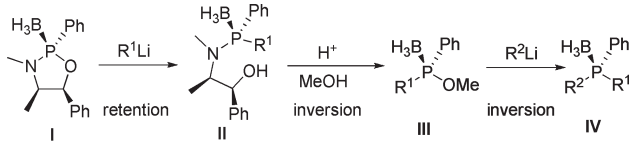
ABSTRACT: A highly diastereoselective and efficient synthesis of P-stereogenic bulky alkyl and aryl aminophosphines that relies on ring opening of *tert*-butyl-oxazaphospholidine **2** is described. Ring opening with several organometallic reagents takes place with inversion of configuration at the phosphorus center as it has been demonstrated by X-ray analysis of two ring-opened intermediates. The unprecedented reactivity observed is attributed to the presence of a free NH functionality that facilitates the attack of the organometallic reagent in an S_N2@P-type process.

Efficient and readily available chiral ligands remain a principal target in catalysis. Bulky P-stereogenic phosphines (P*) have demonstrated efficiency in myriad catalytic processes.[1] However, their synthesis in an enantiomerically pure form is often tedious.[2] The work of Evans and co-workers in 1995 represented a breakthrough in this field.[3] These authors unveiled that alkyl(dimethyl)phosphine borane complexes could be selectively deprotonated at one of their methyl groups in the presence of (−)-sparteine. This strategy was later utilized by Imamoto and others for the synthesis of C_2 symmetric bulky diphosphine ligands.[4] Its chief drawbacks are that it requires very low temperatures and that only the naturally occurring enantiomer of sparteine is available. For stereoselective synthesis of P*-compounds, the main alternative to enantioselective deprotonation is ring opening of oxazaphospholidines (Scheme 1). The pioneering work of Jugé[5a−c] showed that both the condensation of a bis(dialkylamino) phenylphosphine with (−)-ephedrine and the ring opening of the resulting oxazaphospholidine (**I**) with alkyllithium reagents to give **II** are highly diastereoselective.[5] This elegant work has been used to prepare several P-stereogenic ligands.[5] However, it is not amenable to the synthesis of bulky P*-building blocks, due to the lack of reactivity of intermediate **II** when a bulky group is attached to the phosphorus.[6]

We recently described the synthesis of bulky aminophosphines of type **V** as valuable P*-building blocks for ligand synthesis.[7] We showed that these compounds can be readily and efficiently converted into useful PnP ligands of type **VI** such as MaxPHOS (Figure 1).[8]

Compounds of type **V** were obtained via dynamic kinetic resolution (DKR) of racemic chlorophosphines with chiral amines as resolving agents, followed by reductive cleavage of the benzylic amine. Although this strategy afforded aminophosphines **V** in optically pure form (>99% ee), the synthesis was hindered by the low diastereoselectivity of the DKR step. At this point, in the search for a more efficient synthesis of P*-aminophosphine building blocks, we turned our attention to oxazaphospholidine chemistry. Herein we report the synthesis of new, bulky *tert*-butyl-oxazaphospholidines and their diastereoselective ring opening and subsequent reductive cleavage. This methodology constitutes a novel, practical, and efficient route to P*-aminophosphines and their PnP derivatives.

Scheme 1. Jugé's Strategy for Synthesizing P-Stereogenic Tertiary Phosphines



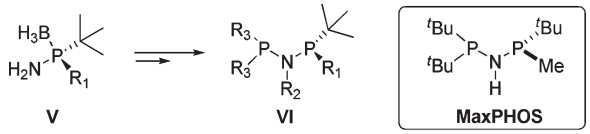


Figure 1. Bulky P-stereogenic aminophosphines and their corresponding PnP ligands.

Among the commercially available β-amino alcohols, we choose for our study the *cis*-1-amino-2-indanol **1**, which has been utilized to prepare chiral sulfoxides and sulfinamides.[9] Compound **1** contains a benzylic amine, and both of its enantiomers are equally available in bulk, characteristics essential to our strategy.[10] A possible inconvenience of amino alcohol **1** was that, to the best of our knowledge, there were no oxazaphospholidines with the free NH functionality described in the literature.[11] With this in mind, we began to screen the condensation of **1** with different *tert*-butylphosphine reagents (Table 1). Dichloro-*tert*-butylphosphine and *tert*-butyl-bis-(diethylamino)-phosphine reagents provided the desired product with good selectivity but in low yields (Table 1, entries 1 and 2). The best reagent was the racemic chloro-*tert*-butyl(diethylamino)-phosphine, which provided the corresponding condensation product in an excellent yield of 78% and with diastereomeric ratios of up to 18:1 (Table 1, entry 4). Most conveniently, the major diastereomer was separated by crystallization to afford **2** in diastereomerically pure form. As confirmed by X-ray analysis, the bulky *tert*-butyl group in **2** was positioned *trans* to the Indane fragment, thereby avoiding steric

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