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# Palladium-catalyzed synthesis of vinyl phosphines from ketones

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## Abstract

The palladium-catalyzed conversion of vinyl triflates to vinyl phosphines is reported. This process allows for the synthesis of vinyl phosphines from ketones. Selective enolization of a variety of ketones followed by trapping of the enolate as the vinyl triflate is reported. The vinyl triflates are then converted to the corresponding vinyl phosphine through palladium catalysis. The resulting vinyl phosphines can then be reduced to give alkyl phosphines. © 1999 Elsevier Science Ltd. All rights reserved.

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Over the last few years we have been involved in the development of new phosphine ligands for catalysis.<sup>1–6</sup> One of the difficulties encountered in the synthesis of new phosphine ligands is the lack of methods available for the formation of carbon phosphorus bonds. Typically, such connections are made either through displacement by the phosphide anion on an appropriate halide or addition of a Grignard or organolithium reagent to a phosphine chloride.<sup>7</sup> Both of these routes tend to be incompatible with sensitive functionality. An alternate approach developed by Stille is the palladium-catalyzed addition of (trimethylstannyl)diphenylphosphine or (trimethylsilyl)diphenylphosphine to aryl halides.<sup>8</sup> A group from Merck Process Research as well as our group have published a similar reaction between phosphines and aryl triflates.<sup>4,9,10</sup> Recently, Lipshutz et al. has reported the synthesis of triarylphosphine-boranes by palladium-catalyzed coupling between phosphine-boranes and aryl nonaflates or triflates.<sup>11</sup> Additionally, that paper contains an example of the conversion of an activated vinyl triflate to a vinylogous acyl phosphine. Recently, Kazankova and co-workers have reported that vinyl phosphines are accessible from vinyl bromides through palladium-catalyzed addition.<sup>12</sup> These studies have prompted us to report the palladium-catalyzed coupling of vinyl triflates with diphenylphosphine. This reaction gives vinyl phosphine products, which can then be reduced to give the corresponding alkyl phosphine (Fig. 1).





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Table 1
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\*Compounds are characterized by <sup>1</sup>H, <sup>13</sup>C, <sup>31</sup>P NMR, IR and HRMS. <sup>b</sup>The triflates were synthesized by the method of McMurry and Scott. <sup>13</sup> c.) All yields are isolated yields.

One of the useful aspects of this approach is that since vinyl triflates are readily available from ketones there are hundreds of structures readily accessible.<sup>13,14</sup> In theory any ketone possessing an  $\alpha$ -hydrogen can be converted to a phosphine. Additionally, this chemistry will tolerate a variety of functionalities making it possible to synthesize structurally complicated phosphines.

Table 1 contains a number of examples of this conversion. One of the useful features of this chemistry is illustrated in the selective formation of the two regioisomeric triflates 8 and 9.15,13,16 Subsequent palladium catalysis then gives each of the corresponding regioisomeric vinyl phosphines (14 and 15). The vinyl phosphines obtained from (-)-methone (16) and camphor (18) are two examples of chiral phosphines that are readily available from the pool of chiral ketones through this methodology.

After catalysis the phosphine was converted to the phosphine oxide, sulfide or borane complex to facilitate purification and characterization. In general, the conversion of vinyl triflate to vinyl phosphine is sufficiently clean so that, if desired, it is possible to use the vinyl phosphine without purification. Attempts



#### Figure 2.

to react either diphenylphosphine-borane or diphenylphosphine-sulfide directly with cyclohexenyltriflate under the standard reaction conditions provided only unreacted starting material.

We have found that the vinyl phosphine sulfides can be reduced to alkyl phosphine sulfides by reaction with lithium aluminum hydride and cobalt dichloride (Fig. 2). Vinyl phosphine sulfide **19** can also be reduced with toluenesulfonylhydrazide to give the alkyl phosphine sulfide **20**. In both of these cases, even using excess reagents, the reactions did not go to completion. This proved not to be a problem in the reduction of phosphine oxides, which proceeds with lithium aluminum hydride in good yield (**22** and **24**).

The results reported here demonstrate that this is a viable route to vinyl and alkyl phosphines given that phosphine borane complexes, phosphine sulfides and phosphine oxides have all been converted to the corresponding phosphine.<sup>4,5,17-20</sup>

Sample procedure: Cyclohexenyl triflate (500 mg, 2.57 mmol), diphenylphosphine (570 mg, 3.06 mmol), and *N*,*N*-diisopropylethylamine (1.34 mL, 7.70 mmol) were dissolved in 10 mL of degassed toluene. Palladium(II)acetate (29 mg, 5 mol %) and 1,4-bis(diphenylphosphino)butane (55 mg, 0.13 mmol) were added and the mixture was stirred at 40°C. The reaction was monitored by TLC and <sup>19</sup>F NMR until the triflate was consumed. A 2M solution of borane-dimethylsulfide (1.67 mL) was added and the resulting mixture was stirred 2 h at room temperature. The mixture was diluted to 100 mL with ethyl acetate and washed with 2N HC1, water and brine. The solution was dried over magnesium sulfate, filtered, and the solvent removed in vacuo leaving a dark red oil. Purification by flash chromatography ( $R_{\rm f}$ : 0.20, 5:95 ethyl acetate:hexane) yielded a clear oil (690 mg g, 95%) that solidified upon standing.

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