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Microwave-Assisted Regioselective Addition of P(O)–H Bonds to Alkenes without Added Solvent or Catalyst

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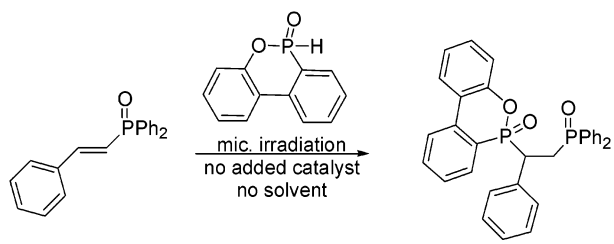
ABSTRACT



The addition of P(O)–H bonds to alkenes has been accomplished using microwave irradiation in the absence of added solvent and catalyst. In addition to single addition reactions, tandem hydrophosphinylation reactions with alkynes afforded unsymmetrical species such as phosphine oxide – phosphinates.

Atom-efficient transformations have been the subject of intense research over the past few years.[1] Recently, this technology has been applied to the bis(stannylation) of alkynes,[2] the synthesis of unsymmetrical ketones,[3] and the silylcupration of acetylenes.[4] If the desired reaction can be carried out in the absence of solvent, this process represents a powerful and practical synthetic approach.

The addition of P−H bonds across unsaturated substrates is an important transformation that is often promoted by radial initiators such as benzoyl peroxide or AIBN.[5] Strong bases also promote this transformation.[6] Knochel has recently shown that KO^{t}Bu (20 mol %) promoted the addition of secondary phosphines to alkenes.[7] Gaumont reported that a Lewis acid (BH_3) catalyzed the microwave-assisted addition of diphenylphosphine to alkenes.[8]

A number of transition-metal-catalyzed hydrophosphinylation reactions have been reported recently. Montchamp demonstrated that solid-supported palladium catalysts containing large bite-angle phosphine ligands catalyzed the addition of hypophosphorus reagents to alkenes in water,[9] and Tanaka reported the rhodium-promoted addition of diphenylphosphine oxide to alkynes,[10] as well as the palladium-catalyzed addition of a pinacol-derived hydrogen phosphonate to alkenes.[11] As part of our continuing studies on the development of new approaches for the formation of P(O)−C(sp^3) bonds,[12,13] the microwave-assisted addition of

(1) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695.
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Table 1. Addition of $HP(O)Ph_2$ to Alkenes

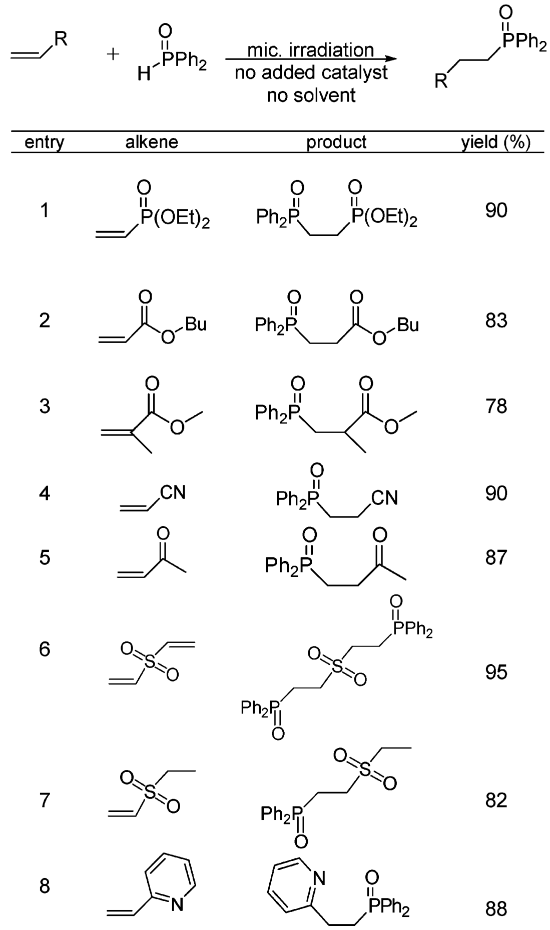
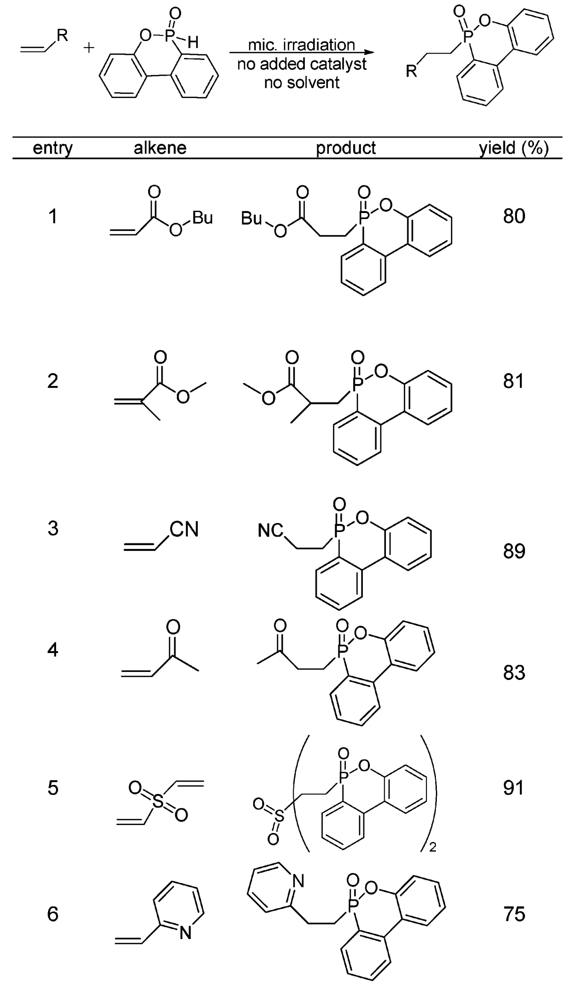


Table 2. Addition of DOPO to Alkenes



P(O)−H bonds to alkenes was investigated in the absence of solvent and added catalyst.

Treatment of a terminal alkene with 1 equiv of $HP(O)Ph_2$ (**1**) in the absence of solvent with microwave irradiation as the heating source afforded high yields of the desired phosphine oxide.[14] The addition reaction formed the 1,2-substituted species exclusively with no trace of a 1,1-adduct observed in the ^1H or ^{31}P NMR spectrum. When the alkene contained a -C(O)R unit, there was no evidence of addition to the carbonyl group. A variety of alkenes were employed in this reaction, with the best results obtained when the alkene contained an activating group. In addition to terminal alkenes, disubstituted olefins were also successfully hydrophosphinylated (Table 1 entry 3). In many cases, the crude products were >95% pure when removed from the microwave.

The addition of a hydrogen phosphinate to alkenes was also successful (Table 2). Treatment of terminal alkenes with 1 equiv of 6*H*-dibenz[*c*,*e*][1,2]oxaphosphorin, 6-oxide (DOPO) gave high yields of the desired phosphinate. Since the phosphorus center in DOPO is chiral, the product of the addition reaction between DOPO and an unsymmetrically disubstituted alkene such as methyl methacrylate produced a mixture of diastereomers. The ratio of diastereomers was readily determined by ^{31}P NMR spectroscopy.[15]

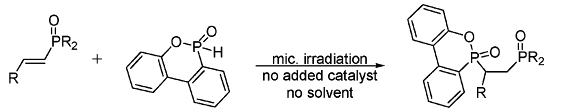
The addition of P(O)−H bonds to internal alkenes is a challenging transformation. If the alkene contains a P=O donor, carrying out the addition reaction with a different HP(O)R_2 species is an attractive way to generate unsymmetrical compounds such as phosphine oxide − phosphinates. Selective reduction of these compounds would generate a range of hemilabile ligands for transition metal catalysis.[16]

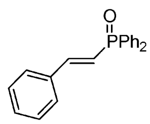
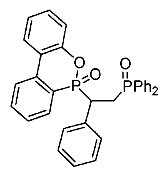
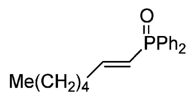
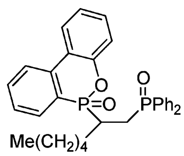
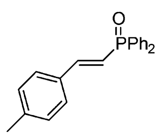
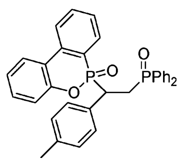
Treatment of alkenylphosphine oxides with 1 equiv of DOPO generated the desired unsymmetrical compounds in moderate yields. Both aryl- and alkyl-substituted internal alkenes were successfully hydrophosphinylated (Table 3).

(13) Stone, J. J.; Stockland, R. A., Jr.; Kovach, J.; Reyes, J. M., Jr.; Goodman, C. C.; Tillman, E. S. *J. Mol. Catal. A: Chem.* **2005**, *226*, 11.
(14) In a typical reaction, a new reactor vial (10 mL) was charged with the phosphine oxide or phosphinate (0.023−0.025 mmol) and a new magnetic stirring bar. The new equipment was used to prevent metal contamination from other reactions. The vial was evacuated and refilled with nitrogen before addition of the alkene (1 equiv). In the case of divinyl sulfone, 0.5 equiv of the alkene was used. The vial was heated in the microwave for the desired time at 120−140 °C. After cooling to room temperature, the purity of the product was determined by GC and multinuclear NMR spectroscopy. When needed, the products were purified by trituration with an appropriate solvent or by column chromatography.

(15) Nelson, J. *Coord. Chem. Rev.* **1995**, *139*, 245.
(16) Gloede, J.; Ozegowski, S.; Kockritz, A.; Keitel, I. *Phosphorus, Sulfur Silicon Relat. Elem.* **1997**, *131*, 141.

Table 3. Addition Reactions Involving Internal Alkenes



entry	alkene	product	yield (%)
1			68
2			80
3			71

The unsymmetrical compounds were isolated as a mixture of diastereomers with the diastereomeric ratio determined by ^{31}P NMR spectroscopy.[15]

In some cases, increasing the reaction temperature and decreasing the time in the microwave was found to be an efficient way to carry out a desired transformation while minimizing the formation of side products. In all cases, when the reaction temperature was increased to 200 °C for 2 min, a mixture of products was obtained. This mixtured contained less than 60% of the desired product.

In summary, the microwave-assisted addition of P(O)−H bonds to activated alkenes proceeds smoothly without solvent or added catalyst. In many cases, the resulting compounds are isolated (>95% pure) directly from the reactor vial. We are currently investigating the addition of P(O)−H bonds to unactivated alkenes and will report these data in due course.

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Supporting Information Available: Experimental procedures, spectroscopic data, and selected ^{1}H, ^{13}C, and ^{31}P NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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