



One-Pot Synthesis of Phosphine Oxide Derivatives from a Phosphine, an Acetylenic Ester and Water

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Abstract

Protonation of the highly reactive intermediates, produced in the reaction between triphenylphosphine and alkyl acetylenecarboxylates by water leads to vinyltriphenylphosphonium salts, which undergo coupling reaction with conjugate base to produce corresponding pentavalent phosphorus intermediates. The pentavalent phosphorus intermediates are unstable and rearrange to stable diphenylphosphine oxide derivatives under reaction conditions.

Keywords: *Triphenylphosphine, Acetylenic ester, Synthesis, Phosphine oxide.*

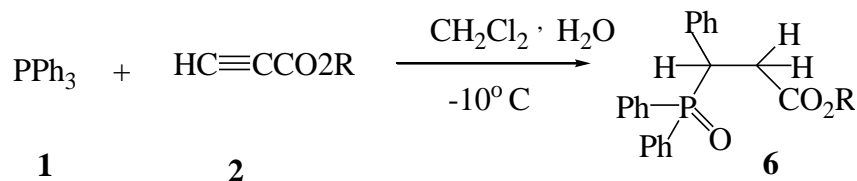
Introduction

Due to the unique chemical properties of phosphorus, phosphorus-containing monomers and polymers have been the subject of extensive research in the last decade. Phosphorus-containing materials have vast applications, for example metals binders, flame retardants and due to their proven biocompatibility also in the biomedical field [1]. Phosphorus chemistry might play an important role in origins of life on earth. Organophosphorus reagents operating by the P(III)→P(V) redox couple drive numerous valuable organic transformations [2]. Trialkylphosphines have found utility in a range of applications owing to their diversity of structure and properties. In organic synthesis, they find use as reagents for protocols such as Wittig [3,4], Staudinger [5] and Mitsunobu [6] reactions. The ylides are usually prepared by treatment of a phosphonium salt with a base, and phosphonium salts are usually obtained from a phosphine and an alkyl halide. Phosphorus ylides are a class of a special type of zwitterion, which bear strongly nucleophilic, electron-rich carbanions. Proton affinity of these ylides can be used as a molecular guide to assess their utility as synthetic reagents and their function as ligands in coordination and organometallic chemistry [7,8]. The stabilized phosphorus ylides are able to take part in the intramolecular Wittig reactions, but they are not generally able to participate in the intermolecular Wittig reactions [9-23]. The intermolecular Wittig reactions of the ylides

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are observed only with highly electron-poor carbonyl groups such as indane-1,2,3-trione. Wittig reactions of short-chain trialkylphosphine derived ylides will be presented under aqueous and non-aqueous conditions as well as applications in natural product and fine chemicals synthesis [24-27]. In this paper, we wish to describe a simple, one-pot method for the preparation of phosphine oxide (6) derivatives from phosphines (1) and acetylenic esters (2) (Scheme 1).



Scheme 1: Synthesis of phosphinoxide derivatives.

Experimental

Starting materials and solvents were obtained from Merck (Darmstadt, Buchs, Germany) and Fluka (Switzerland) and were used without further purification. The methods used to follow the reactions were TLC and NMR. Melting points were measured with an Electrothermal 9100 apparatus (LABEQUIP LTD., Markham, Ontario, Canada) and are uncorrected. IR spectra were measured on a Jasco 6300 FTIR spectrometer (JASCO Ltd., Easton, MD). ¹H and ¹³C NMR spectra were measured (CDCl₃ solution) with a Bruker DRX-250 Avance spectrometer (Bruker Ltd., Ettlingen, Germany) at 250.0 and 62.5 MHz, respectively.

General procedure for the preparation of phosphinoxide derivatives

To a magnetically stirred solution of trialkylphosphine (1.00 mmol) in CH₂Cl₂ (10 mL) was added dropwise a mixture of dialkylacetylenedicarboxylate (1.0 mmol) in CH₂Cl₂ (5 mL) at -10 °C over 20-25 min. The mixture was allowed to warm up to room temperature and stirred for 24 hours. The solvent was removed under reduced pressure. Then the product was washed with acetone for several times and drying at 40 °C for 1h and the products were obtained as white crystals.

The characterization data of the compounds are given below:

Methyl-3-diphenylphosphoril-3-phenylpropanoate

White crystals; m.p. : 178-180 °C. Yield: 87%. ¹H NMR (CDCl₃) δH: 2.83 - 2.95 and 3.05 - 3.18 (2 H, 2 m, (CHAHB)); 3.44 (3 H, s, OCH₃); 4.03 - 4.12 (1 H, m, CH); 7.14 - 7.98 (15 H, m, arom). ¹³C NMR (CDCl₃) δC: 34.71 (CH₂); 42.78 (CH, d, 1JCP = 67.9 Hz); 51.92 (OCH₃); 127.28 - 134.96 (arom); 135.05 (C, arom); 171.85 (d, 3JCP = 17.6 Hz, CO, ester); ³¹P NMR (CDCl₃) □P: 33.43 (P=O). IR (KBr) (ν_{max}, cm⁻¹): 3062 (C-H, arom); 2954 (C-H, aliph); 1739 (C=O, ester); 1443 (arom); 1200 (P=O and C-O).

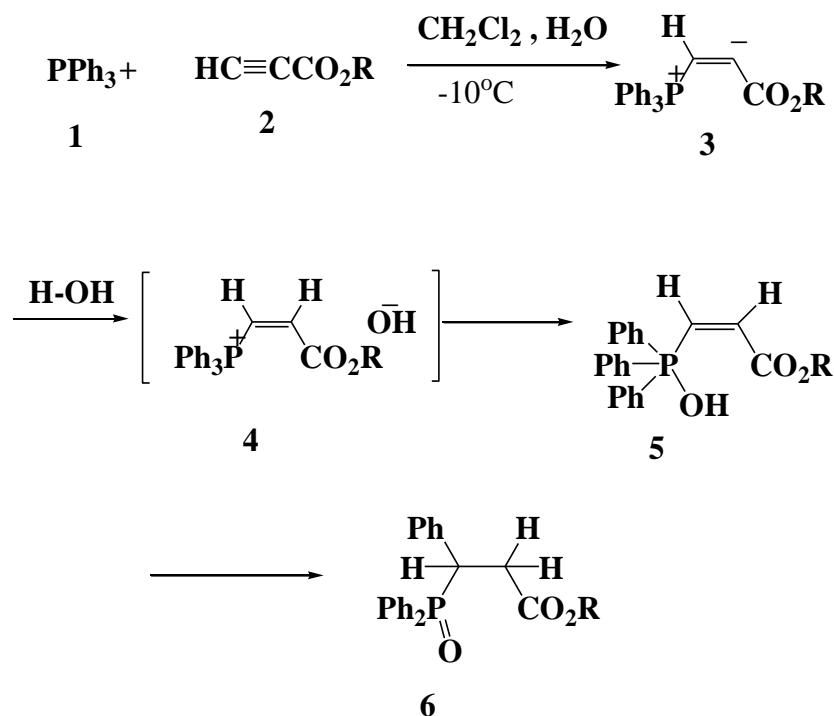
Ethyl-3-diphenylphosphoril-3-phenylpropanoate

White crystals; m.p.: 190-192 °C. Yield 86%. ¹H NMR (CDCl₃) δH: 1.01(3H, t, 3JHH = 7.0 Hz, CH₃ of OEt); 2.81-2.92 and 3.02-3.16 (2 H, 2 m, (CHAHB)); 3.90 (2H, q, 3JHH = 7.0 Hz, CH₂ of OEt); 4.02-4.09 (1 H, m, CH); 7.14 - 7.98 (15 H, m, arom). ¹³C NMR (CDCl₃) δC: 13.94 (CH₃); 34.86 (CH₂); 42.88 (CH, d, 1JCP = 67.9 Hz); 60.81(OCH₂); 127.28-135.03

(arom); 135.03 (C, arom); 171.38 (d, 3JCP = 17.6 Hz, CO, ester); 31P NMR (CDCl₃) \square P: 33.26 (p=O). IR (KBr) (vmax, cm⁻¹): 3046 (C–H, arom); 2985 and 2915 (C–H, aliph); 1739 (C=O, ester); 1439 (arom); 1185 (P=O and C–O).

Results and Discussion

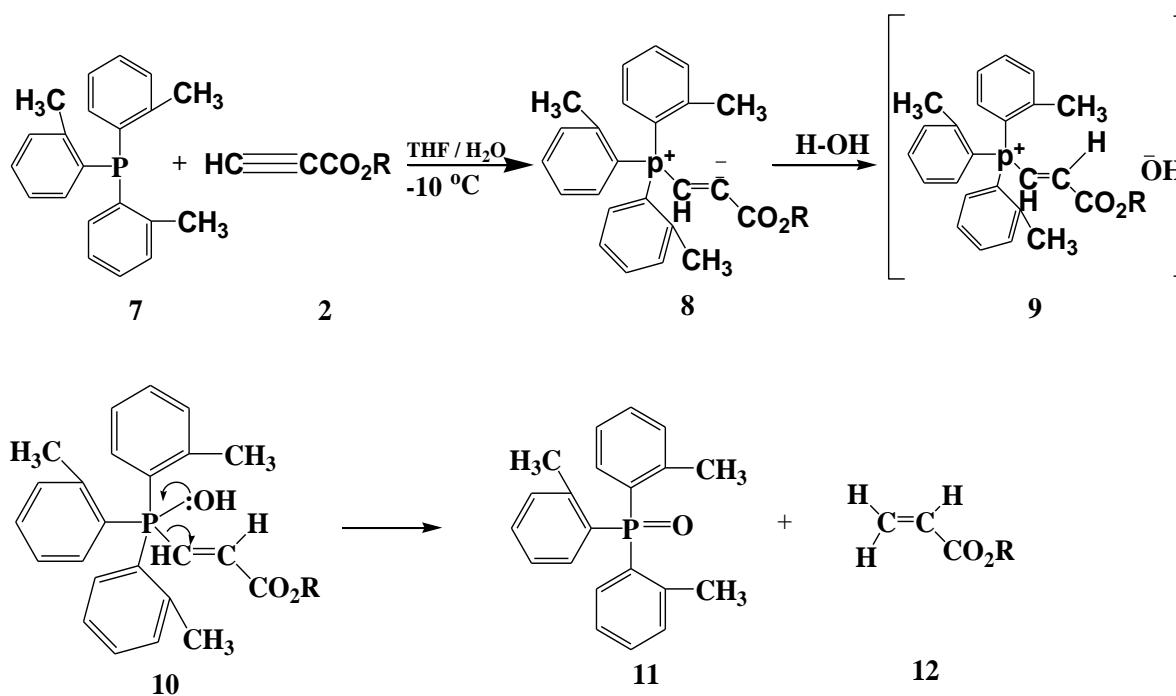
Triphenylphosphine (1) and alkyl acetylenecarboxylates (2) were reacted in a 1:1 ratio in acetone at room temperature to give alkyl 3-diphenylphosphoril-3-phenylpropanoate (6) (Scheme 2). The reactions were monitored with using of TLC technique. The reaction proceeded smoothly and cleanly under mild conditions, and no side reactions were observed. Reactions are known in which an organophosphorus compound is produced from an acetylenic ester, and a phosphine such as triphenylphosphine. Thus, protonation of the highly reactive 1:1 intermediates (3), produced in the reaction between triphenylphosphine (1) and alkyl acetylenecarboxylates (2) by water leads to vinyltriphenylphosphonium salts (4), which undergo coupling reaction with conjugate base to produce corresponding pentavalent phosphorus intermediates (5). The pentavalent phosphorus intermediates (5) are unstable and rearrange to stable diphenylphosphine oxide derivatives (6) under reaction conditions.



Scheme 2: Proposed mechanism for the formation of phosphinoid derivatives.

We also studied reaction of tri(*o*-tolyl)phosphine (7) and alkyl acetylenecarboxylates (2) in the presence of water under above conditions in THF. This reaction leads to vinyltriphenylphosphonium salts (9), which undergo coupling reaction with conjugate base to produce corresponding pentavalent phosphorus intermediates (10). The pentavalent phosphorus intermediates (10) are unstable and fragment to tri(*o*-tolyl)phosphine oxide (11) and alkene (12) (Scheme3). The structure of products (11) was proven by their ¹H NMR and ¹³C NMR spectral data:

White crystals; m.p.: 153-156 °C. Yield: 98%. ¹H NMR (CDCl₃) δ H: 2.39 (9H, s, CH₃); 7.05-7.46 (12H, m, arom). ¹³C NMR (CDCl₃) δ C: 21.98 (d, 3JCP = 3.7 Hz, CH₃); 125.37-143.58(18C, arom). ³¹P NMR (CDCl₃) \square P: 37.83 (P=O).



Scheme 3: Proposed mechanism for the formation of tri(o-tolyl)phosphine oxide.

Conclusion

In summary, we have reported preparation of phosphine oxide derivatives from phosphines and acetylenic esters in CH₂Cl₂ at room temperature in high yields. We believe that the reported method offers a mild and simple route for the preparation of these derivatives. Its ease of work-up and reaction conditions make it a useful addition to modern synthetic methodologies. Other aspects of this process are under investigation.

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