Synthesis of Cycloheptenyldiphenylphosphine Oxides from the Reactions of a Cyclic Phosphonium Salt with α,β-Unsaturated Carbonyl Compounds

Tetsuya Fujimoto,* Yukiharu Takeuchi, Koh-ichi Kai, Yukihiko Hotei, Kazuchika Ohta and Iwao Yamamoto*

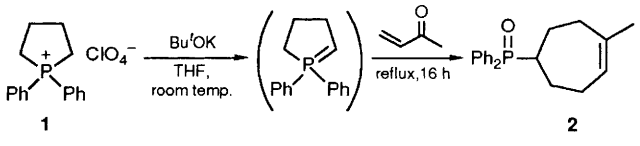
Department of Functional Polymer Science, Faculty of Textile Science and Technology, Shinshu University, Ueda, Nagano 386, Japan

The reactions of the ylide from the five-membered cyclic phosphonium salt **1** with methyl vinyl ketone, chalcone, and benzylidene acetone afforded cycloheptenyldiphenylphosphine oxides *via* a Michael-type reaction followed by an intramolecular Wittig reaction.

Cyclic phosphonium salts are versatile reagents for the synthesis of unsymmetrical unconjugated dienes[1,2] because their Wittig reactions provide alkenylphosphine oxides which can be subjected to further alkenation by the Horner–Wittig reaction. We have previously reported the applications of these tandem Wittig reactions and their modification to the syntheses of insect sex pheromones[3] and 1,4-diketones.[4]

In our continuing studies on the application of cyclic phosphonium salts to organic synthesis, reaction of the ylide generated from 1,1-diphenylphospholanium perchlorate **1**[5] in the presence of potassium *tert*-butoxide with methyl vinyl ketone was attempted (Scheme 1).† The cycloheptenyldiphenylphosphine oxide **2** and not the Wittig product was generated.

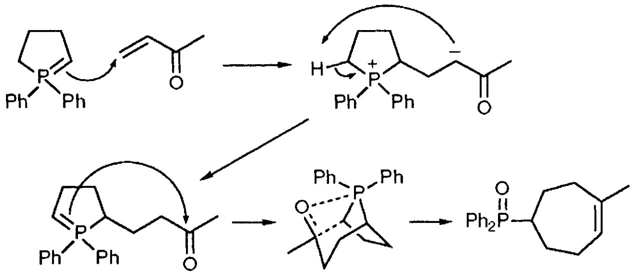
The structure of **2** was confirmed by ^{13}C NMR spectroscopy. Generally carbon atoms α, β and γ to phosphorus in diphenylphosphine oxides have characteristic J_{PC} values.[6] The α carbon atom in the ^{13}C NMR spectrum of **2** resonated at δ 41.1 (J_{PC} 78.1 Hz), the β carbon atoms at δ 25.5 (J_{PC} 1.9 Hz) and 24.4 (J_{PC} 2.0 Hz), and the γ carbon atoms at δ 33.4 (J_{PC} 15.5 Hz) and 27.3 (J_{PC} 15.7 Hz). Their coupling constants were comparable with those in acyclic diphenylphosphine oxides,[2] with a slight increase for the α atom and a decrease for the β atoms. The existence of a pair of β and γ carbon atoms in the product indicated that **2** had a cyclic structure bonded by a $Ph_2P(O)$ group. The ^1H NMR and mass spectra, and elemental analysis also supported the structure **2**.



Scheme 1

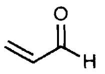
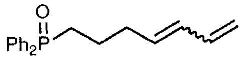
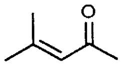
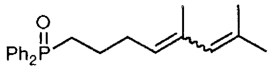
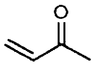
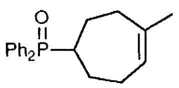
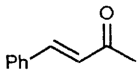
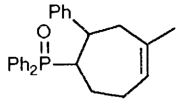
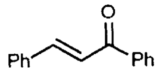
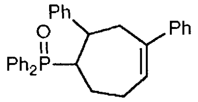
---

† *Typical procedure*: a mixture of **1** (5.87 mmol) and Bu^tOK (5.87 mmol) in dry tetrahydrofuran (THF) (25 ml) was stirred at room temperature for 1 h and a solution of methyl vinyl ketone (5.87 mmol) in dry THF (5 ml) was added dropwise. The resulting solution was refluxed for 16 h. Purification of the crude product by column chromatography gave the phosphine oxide **2** (0.74 g, 41%) as white crystals.



Scheme 2

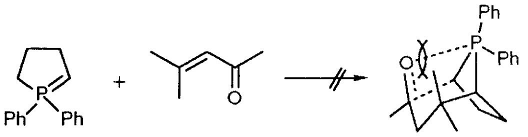
Table 1 Reactions of the phosphonium salt **1** with α,β-unsaturated aldehyde or ketones

Substrate	Product	Yield[a] (%)
		41[b]
		71[c]
		41
		49
		51

[a] Isolated yield. [b] E : Z ratio of the isolated product was 1 : 10. [c] E : Z ràtio of the isolated product was 1 : 2 (or 2 : 1).

The reaction of phosphorus ylides with carbon–carbon double bonds activated by electron-withdrawing groups such as CN, C(O)R, or CO_2R is known to form an intermediate zwitterion *via* a Michael-type reaction which decomposes in one of three ways depending upon the substituents to give phosphorane, vinylphosphorane, or cyclopropane derivatives.[7] Therefore, the formation of **2** may be rationalized by proton migration in the zwitterion derived from a Michael-type reaction between the ylide of **1** and methyl vinyl ketone. The regenerated ylide would participate in an intramolecular Wittig reaction to lead to the phosphine oxide **2** *via* a six-membered cyclic transition state (Scheme 2).

Intramolecular Wittig reactions are useful for the formation of cycloalkenes[8] and heterocyclic compounds.[9] The present reaction should enhance the usefulness of such reactions and provide a convenient method for construction of the cycloheptene skeleton. Carbon–carbon bond and cyclization occur in one pot; participation of the $Ph_2P(O)$ group in the product in the Horner–Wittig reaction would provide substituted cycloheptene derivatives. The reactions of the ylide of **1** with other α,β-unsaturated carbonyl compounds under the same conditions were studied in order to establish the scope of the reaction (Table 1).



Scheme 3

The Wittig reaction of the ylide of **1** with acrolein and mesityl oxide gave the corresponding dienes in 41 and 71% yield. However, the reactions of the ylide with benzylidene acetone and chalcone, which have a bulky substituent on the β-carbon atom, gave the cycloheptenyldiphenylphosphine oxides in 49 and 51% yield respectively.

These results indicated that the course of these reactions was strictly controlled by the substitution pattern in the α,β-unsaturated carbonyl compounds; the Michael–intramolecular Wittig reactions proceeded for α,β-unsaturated ketones which are unsubstituted or singly substituted in the β-position. The failure of the reaction of **1** with mesityl oxide, a β,β-disubstituted enone, to afford the corresponding cycloheptene derivative may be rationalized by considering the six-membered cyclic transition state (Scheme 3). One of the two methyl groups in the β-position occupies an axial position, leading to a 1,3-diaxial interaction between it and oxygen. Consequently, the Wittig reaction which affords the diene would be preferred to the formation of the cycloheptene derivative.

The tandem Michael–intramolecular Wittig reactions of cyclic phosphorus ylides with easily available α,β-unsaturated ketones should thus provide a convenient method for construction of the cycloheptene skeleton.

We thank Professor R. Irie of the Faculty of Agriculture, Shinshu University, for 250 MHz NMR measurements, and Kissei Pharmaceutical Co., Ltd. for 400 MHz NMR measurements. We are grateful to Ihara Chemical Co., Ltd. for a gift of triphenylphosphine. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture of Japan (No 03650695).

Received, 6th March 1992; Com. 2/01243J

References

1 J. M. Muchowski and M. C. Venuti, *J. Org. Chem.*, 1981, **46**, 459.
2 I. Yamamoto, T. Fujimoto, K. Ohta and K. Matsuzaki, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1537.
3 I. Yamamoto, S. Tanaka, T. Fujimoto, K. Ohta, and K. Matsuzaki, *Nippon Kagaku Kaishi*, 1987, 1227; I. Yamamoto, S. Tanaka, T. Fujimoto and K. Ohta, *J. Org. Chem.*, 1989, **54**, 747.
4 T. Fujimoto, Y. Hotei, H. Takeuchi, S. Tanaka, K. Ohta and I. Yamamoto, *J. Org. Chem.*, 1991, **56**, 4799.
5 G. Märkl, *Angew. Chem., Int. Ed. Engl.*, 1963, **2**, 620; W. R. Purdum and K. D. Berlin, *J. Org. Chem.*, 1975, **40**, 2801.
6 T. A. Albright, W. J. Freeman and E. E. Schweizer, *J. Org. Chem.*, 1975, **40**, 3437.
7 D. J. H. Smith, in *Organophosphorus Reagents in Organic Synthesis*, ed. J. I. G. Cadogan, Academic Press, New York, 1979, ch. 4; J. Emsley and D. Hall, *The Chemistry of Phosphorus*, Harper & Row, London, 1976, ch. 7.
8 F. Bohlmann and Ch. Zdero, *Chem. Ber.*, 1973, **106**, 3779; A. Padwa and L. Brodsky, *J. Org. Chem.*, 1974, **39**, 1318; K. B. Becker, *Helv. Chim. Acta.*, 1977, **60**, 68.
9 E. E. Schweizer, *J. Am. Chem. Soc.*, 1964, **86**, 2744; E. E. Schweizer and K. K. Light, *J. Am. Chem. Soc.*, 1964, **86**, 2963; E. E. Schweizer, J. Liehr and D. J. Monaco, *J. Org. Chem.*, 1968, **33**, 2416; E. E. Schweizer and C. M. Kopay, *J. Org. Chem.*, 1972, **37**, 1561.