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Wittig Reactions of Phosphonium Ylides Bearing the Phosphastibatriptycene Skeleton with Carbonyl Compounds

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Accepted author version posted online: 30 Oct 2014.

To cite this article: Yosuke Uchiyama, Rikiya Murakami & Jun Sugimoto (2014): Wittig Reactions of Phosphonium Ylides Bearing the Phosphastibatriptycene Skeleton with Carbonyl Compounds, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI: <u>10.1080/10426507.2014.974095</u>

To link to this article: <u>http://dx.doi.org/10.1080/10426507.2014.974095</u>

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Abstract

To investigate effects of the tridentate ligand on the reactivity of a 1,2-oxaphosphetane, an intermediate of the Wittig reaction, the reactions of phosphonium ylides **1** and **2** bearing the phosphastibatriptycene skeleton with carbonyl compounds have been conducted and compared with those of triphenyl phosphorus compounds. Non-stabilized and semi-stabilized phosphonium ylides **1** and **2** bearing the tridentate ligand were generated from the corresponding phosphonium salts **3** and **4**, which were prepared by the reactions of a phosphastibatriptycene with ethyl iodide and benzyl bromide, respectively. The reactions of ylides **1** and **2** with benzaldehyde showed high *E*-selectivity, in sharp contrast to those of triphenylphosphonium ylides **5** and **6** giving *Z*-alkenes as a major product. However, the reaction of **1** with trifluoroacetophenone gave *E/Z*-alkenes **10** in the ratio of 69:31 together with phosphine oxide **13**, which showed slightly higher selective *E*-alkene formation compared with the reaction of non-stabilized ylide **5** (*E/Z* ratio of 51:49). The results showed that the reactions did not proceed with high stereoselectivity as same as those of semi-stabilized phosphonium ylides **2** and **6**. In the VT-³¹P{¹H} NMR spectra of the reaction mixture of non-stabilized phosphonium ylide **1** with trifluoroacetophenone, the signals due to the corresponding 1,2-oxaphosphetanes were observed as multi signals in high field around –54 ppm at –80 °C, which was different from the reaction of ylide **5** showing two signals.



Keywords

Wittig Reaction, Tridentate Ligand, VT-³¹P{¹H} NMR, 1,2-Oxaphosphetane

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Introduction

Numerous studies for the Wittig reaction mechanism have revealed that a 1,2-oxaphosphetane is sole detectable and isolatable intermediate in the reaction.¹ To investigate the reactivity of a 1,2-oxaphosphetane and the selectivity of the Wittig reaction, modification of the substituted groups on the phosphorus atom is necessary because of instability of the reaction intermediate. The bidentate ligands such as fluorenyl and Martin ligands have been used to stabilize a pentacoordinated phosphorus intermediate by taking advantage of 5-membered ring around phosphorus atom, thermodynamically.¹ However, a 1,2-oxaphosphetane with a tridentate ligand has never been reported nevertheless the ligand has potentially a thermodynamic stabilization effect toward an intermediate and interesting features concerning the structure and reactivity of the intermediate are expected. We have designed phosphorus ylides bearing high symmetrical phosphastibatriptycene skeleton to investigate effects of the tridentate ligand on the reactivity of a 1,2-oxaphosphetane, an intermediate of the Wittig reaction.² In this paper, we wish to describe the Wittig reactions of phosphonium ylides **1** and **2** bearing the tridentate ligand with carbonyl compounds and observations of the intermediates by VT-³¹P{¹H} NMR spectroscopy.

Results and Discussion

Phosphastibatriptycene derivative was synthesized by the reaction of tris(bromoaryl)phosphine with *t*-BuLi followed by the addition of antimony trichloride in a 26% yield according to the previous report.^{2a} Alkylation reactions of phosphastibatriptycene with ethyl iodide and benzyl bromide were performed in CHCl₃ at 70 °C to give ethyl and benzyl phosphonium salts **3** and **4**,

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respectively. These alkylation reactions proceeded at the phosphorus atom, judging from the P– H coupling between a phosphorus nucleus and methylene protons, $J_{PH} = 13.2$ (3) and 14.4 (4) Hz, in ¹H NMR spectra and X-ray crystallographic analysis³ (Fig. 1). Non-stabilized and semistabilized phosphonium ylides 1 and 2 were obtained as yellow solutions by the reactions of corresponding phosphonium salts 3 and 4 with *n*-BuLi at 0 °C. Triphenylphosphonium ylides 5 and 6 were also generated from alkyltriphenylphosphonium salts 7 and 8 in the same reaction conditions as ylides 1 and 2.

The reactions of the ylides **1**, **2**, **5**, and **6** with benzaldehyde or trifluoroacetophenone have been conducted in THF at -90 °C in a sealed NMR tube.⁴ The reaction mixtures were allowed to warm from -90 °C to 25 °C for 2.5 hrs. The signals due to alkenes **9-12⁵⁻⁸** and phosphine oxides **13** or **14** were observed after 12 hours elapsed for decomposition of the intermediates (**Scheme 1**, **2**, and **Table 1**).⁹

The reactions of ylides **1** and **2** bearing the tridentate ligand with benzaldehyde showed *E*-selective alkene formation in the ratios of 83/17 and 70/30, whereas those of ylides **5** and **6** gave alkenes 9^5 and 11^6 in the ratios of 23/77 and 36/64 as almost same as those of the previous reports. The results showed that the tridentate ligand affected on the alkene formation because the rotation of benzene rings around the phosphorus were strongly restricted compared with the triphenylphosphonium system.

On the other hand, when trifluoroacetophenone was used as a carbonyl compound in the Wittig reaction, the alkene formation showed the similar selectivity in both reactions of ylides 1 and 2 bearing the tridentate ligand and those of triphenylphosphonium ylides 5 and 6. The fluorinated

alkenes 10^7 and 12^8 were obtained in the ratios of 69/31 and 89/11, respectively, in the reactions of ylides 1 and 2 and in 51/49 and 97/3 in the cases of those of triphenylphosphonium ylides 5 and 6, respectively. The results showed almost no effect of the tridentate ligand on the selectivity of the alkene formation, judging from the results obtained in the corresponding triphenylphosphonium ylides.



The VT-³¹P{¹H} NMR spectra of the reaction mixtures of semi-stabilized phosphonium ylide **2** bearing the tridentate ligand with benzaldehyde or trifluoroacetophenone did not show any signals assigned to the corresponding 1,2-oxaphosphetanes around -40 to -60 ppm, although the signal due to phosphonium ylide **2** was observed during the NMR measurements after the addition of carbonyl compounds.¹⁰ As raising temperature from -90 °C, the signal due to **2** gradually disappeared and the signal due to phosphine oxide **13** was observed at -90 °C in the case of benzaldehyde and at -40 °C in that of trifluoroacetophenone, respectively. The results suggested that the 1,2-oxaphosphetanes with the phenyl group at the 3-position decomposed at low temperature. The intermediates were not observed in the reaction of non-stabilized ylide **1**

and benzaldehyde. However, the intermediates could be observed around -55 ppm as four singlets in the ratio of 1.0/0.3/0.2/0.9 at -80 °C in the reaction of **1** with trifluoroacetophenone, suggesting that 1,2-oxaphosphetanes with the methyl group at the 3-position and the trifluoromethyl group at the 4-position bearing the tridentate ligand were stable at low temperatures. In contrast to the results of the reactions of ylides bearing the tridentate ligand with trifluoroacetophenone, that of non-stabilized triphenylphosphonium ylide **5** showed only two signals of the intermediates at -57.1 and -59.7 ppm at -80 °C in the ³¹P{¹H} NMR spectra, which were considered to be the signals due to two diastereomers with the methyl group at the 3position and the phenyl and trifluoromethyl groups at the 4-position. The observation of four singlets in the reaction of **1** suggests the existence of 1,2-oxaphosphentanes other than *O*-apical pseudorotamers. The different results between ylide **1** bearing the tridentate ligand and triphenylphosphonium ylide **5** in their VT-³¹P{¹H} NMR spectra strongly suggest that the stability and reactivity of intermediary 1,2-oxaphosphetanes depend on the stereochemistry around the pentacoordinated phosphorus atom.

Conclusions

In this paper, phosphonium ylides **1** and **2** bearing the tridentate ligand were reacted with benzaldehyde to give *E*-alkenes **9** and **11** with high selectivity, in contrast to the reactions of triphenylphosphonium ylides **5** and **6** showing *Z*-selectivity. On the other hand, the reactions of ylides **1** and **2** with trifluoroacetophenone gave alkenes **10** and **12** respectively in the ratios similar to those obtained in the reactions of triphenylphosphonium ylides **5** and **6**. In the VT- ${}^{31}P{}^{1}H$ NMR spectra of the reaction mixture of non-stabilized ylide **1** bearing the tridentate

ligand with trifluoroacetophenone, four singlets assigned to the corresponding 1,2oxaphosphetanes were observed around –45 and –60 ppm, suggesting the existence of *O*-apical and *O*-equatorial 1,2-oxaphosphentanes, which is caused by difference in the stereochemistry around the pentacoordinated phosphorus atom of the intermediates in the Wittig reaction.

Acknowledgements

This study was partially supported by a Grant-in-Aid for Encouragement of Young Scientists (B) to Y. U. (No.16750041 and No.18750037) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan, Ogasawara Foundation for Oversea Visiting Researchers, and Kitasato University Research Grant for Young Researchers.

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[3] Single crystals of **3** and **4** were obtained by recrystallization from chlorobenzene and toluene, respectively. CCDC: 1019728 for **3**, 1019729 for **4**.

[4] THF as a reaction solvent in a NMR tube has been used together with acetone- d_6 as a NMR lock solvent in a capillary tube.

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[9] Yields were estimated by using a singlet signal due to the methylene protons of $Ph_2C=CH_2$ as an internal standard.

[10] The VT- ${}^{31}P{}^{1}H$ NMR spectra were measured at each 10 °C from -90 °C to 25 °C.



Figure 1: ORTEP drawings of Ethyl Phosphonium Iodide 3 and Benzyl Phosphonium Bromide
4. The counter anions, I⁻ for 3 and Br⁻ for 4, were omitted for clarity.

¹⁰ ACCEPTED MANUSCRIPT

 Table 1: E/Z Ratios and Yields of Alkenes for the Wittig Reactions of 1, 2, 5, or 6 with

PhR'C=O°

Ylide (R)	PhR'C=O	Alkene (yield)	E/Z ratio	Ylide (R)	PhR'C=O	Alkene (yield)	E/Z ratio
1 (Me)	Н	9 (13%)	83/17	5 (Me)	Н	9 (20%)	23/77
1 (Me)	CF_3	10 (80%)	69/31	5 (Me)	CF_3	10 (61%)	51/49
2 (Ph)	Н	11 (90%)	70/30	6 (Ph)	Н	11 (62%)	36/64
	~~				~~		
2 (Ph)	CF_3	12 (25%)	89/11	6 (Ph)	CF_3	12 (34%)	97/3

¹¹ ACCEPTED MANUSCRIPT