JOC Article

Formation of P-Ylide under Neutral and Metal-Free Conditions: Transformation of Aziridines and Epoxides to Conjugated Dienes In the Presence of Phosphine

Ren-Hua Fan,[†] Xue-Long Hou,*[,†,‡] and Li-Xin Dai[‡]

State Key Laboratory of Organometallic Chemistry and Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

xlhou@mail.sioc.ac.cn

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A general approach to formation of the P-ylide from the reaction of aziridines or epoxides with organophosphine under neutral and metal-free conditions is realized. Conjugated diene derivatives based on this kind of P-ylide were prepared in a facile and convenient way.

Ever since the discovery of the Wittig reaction, one of the most important reactions in organic chemistry, about 50 years ago,[1] ylide reactions have become powerful tools in organic synthesis, especially for the synthesis of alkenes and small-ring compounds.[2] However, there are several drawbacks associated with ylide reactions. For example, difficulty is encountered sometimes in the formation of the salt and the use of strong base is necessary to form an ylide. Many efforts have been made to find new procedures to overcome the difficulties in the formation of salt.[3] Aggarwal developed an efficient salt formation procedure successfully using a metal-catalyzed carbene transfer method,[3d,f−j] and Tang realized catalytic Wittig-type reactions in an elegant way.[3k,l,n] Very recently, Lu provided an excellent example of a catalytic C−P ylide reaction.[3p] However, there is still a need to develop new ylide formation methodology under more practical conditions.

On the other hand, the conjugated dienes as subunits appeared in many natural and synthetic biologically active compounds, and they also served as the versatile intermediates in organic synthesis.[4] All of these facts have promoted many studies on their construction.[5] Wittig reactions[5a−c] or elimination reactions[5d−f] are the typical methods for the construction of conjugated dienes, but strong bases were usually necessary. The conjugated dienes could also be prepared from coupling reactions,[5g−i] but metal compounds and harsh reaction conditions were needed. Recently, small-ring heterocyclic compounds such as epoxides and aziridines have become very popular in organic synthesis not only as building blocks but also as synthetic intermediates.[6] Although a variety of transformations for epoxides or aziridines are well documented, attention focuses mainly on their direct transformations, especially the nucleophilic ring-opening reaction.[7,8] It remains a challenge to find a new transformation pattern of these three-membered heterocyclic compounds to make

* Corresponding author.
† Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis.
‡ State Key Laboratory of Organometallic Chemistry.

(1) (a) Wittig, G.; Schöllkopf, U. *Chem. Ber.* **1954**, *87*, 1318. (b) Wittig, G. *Angew. Chem.* **1956**, *68*, 505. (c) *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: London, 1979.

(2) (a) Dauben, W. G.; Kozikowski, A. P. *Tetrahedron Lett.* **1973**, 3711. (b) Dauben, W. G.; Hart, D. J.; Ipaktschi, J.; Kozikowski, A. P. *Tetrahedron Lett.* **1973**, 4425. (c) *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: London, 1979. (d) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (e) Johnson, W. A. *Ylides and Imines of Phosphorus*; John Wiley & Sons: New York, 1993. (f) Vedejs, E.; Peterson, M. J. *Top. Stereochem.* **199**4, *21*, 1. (g) Coyne, E.; Gilheany, D. G. In *Comprehensive Organic Functional Group Transform*; Katrizky, A. R., Meth-Cohn, O., Rees C. W., Eds.; Elsevier: Oxford, UK, 1995; Vol. 3. (h) Kolodiazhny, O. I. *Phosphorus Ylides*; Wiley-VCH: Weinheim, 1999. (i) Balema, V. P.; Wiench, J. W.; Pruski, M.; Pecharsky, V. K. *J. Am. Chem. Soc.* **2002**, *124*, 6244.

(3) (a) Oda, R.; Kawabata, T.; Tanimoto S. *Tetrahedron Lett.* **1964**, 1653. (b) Burnett, M. G.; Oswald, T.; Walker, B. J. *J. Chem. Soc. Chem. Commun.* **1977**, 155. (c) Shi, L.; Wang, W.; Wang, Y.; Huang, Y. Z. *J. Org. Chem.* **1989**, *54*, 2028. (d) Aggarwal, V. K. *Synlett* **1998**, 329. (e) Arisawa, K.; Yamaguchi, M. *J. Am. Chem. Soc.* **2000**, *122*, 2387. (f) Aggarwal, V. K.; Alonso, E.; Hynd, G.; Lydon, K. M.; Palmer, M. J.; Porcelloni, M.; Studley, J. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 1430. (g) Aggarwal, V. K.; Alonso, E.; Fang, G.; Ferrar, M.; Hynd, G.; Porcelloni, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1434. (h) Aggarwal, V. K.; Ferrara, M.; O'Brien, C. J.; Thompson, A.; Jones, R. V. H.; Fieldhouse, R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1635. (i) Aggarwal, V. K.; de Vicente, J.; Bonnert, R. V. *Org. Lett.* **2001**, *3*, 2785. (j) Lebel, H.; Paquet, V.; Proulx, C. *Angew. Chem., Int. Ed.* **2001**, *40*, 2887. (k) Ye, S.; Tang, Y.; Dai, L. X. *J. Org. Chem.* **2001**, *66*, 5717. (l) Huang, Z. Z.; Ye, S.; Xia, W.; Tang, Y. *Chem. Commun.* **2001**, 1384. (m) Balema, V. P.; Wiench, J. W.; Pruski, M.; Pecharsky, V. K. *J. Am. Chem. Soc.* **2002**, *124*, 6244. (n) Ye, S.; Huang, Z. Z.; Xia, C. A.; Tang, Y.; Dai, L. X. *J. Am. Chem. Soc.* **2002**, *124*, 2432. (o) Aggarwal, V. K.; Harvey, J. N.; Richardson, J. *J. Am. Chem. Soc.* **2002**, *124*, 5747. (p) Du, Y. S.; Lu, X. Y. Zhang, C. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1035.

(4) (a) Singh, J.; Dhar, K. L.; Atal, C. K. *Tetrahedron Lett.* **1971**, 2119. (b) Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845. (c) Huang, Y. Z.; Shi, L. L.; Yang, J. H. *Tetrahedron Lett.* **1987**, *28*, 2159. (d) Shi, L. L.; Xiao, W. J.; Yang, J. H.; Wen, X. Q.; Huang, Y. Z. *Tetrahedron Lett.* **1987**, *28*, 2155. (e) Huang, Y. Z.; Shi, L. L.; Yang, J. H.; Cai, Z. W. *J. Org. Chem.* **1987**, *52*, 3558−3560.

(5) (a) Ousset, J. B.; Mioskowski, C.; Solladie, G. *Synth. Commun.* **1983**, 119. (b) Schlosser, M.; Franzini, L. *Synthesis* **1998**, 707. (c) Wang, Q.; Wei, H. X.; Schlosser, M. *Eur. J. Org. Chem.* **1999**, *3263*, 3. (d) Bartoli, G.; Dalpozzo, R.; Nino, A. D.; Procopio, A.; Sambri, L.; Tagarelli, A. *Tetrahedron Lett.* **2001**, *42*, 8833. (e) Katritzky, A. R.; Denisko, O. V. *J. Org. Chem.* **2002**, *67*, 3104. (f) Blackburn, L.; Pei, C. X.; Taylor, R. J. K. *Synlett* **2002**, 215. (g) Masuyama, Y.; Maekawa, K. *Chem. Lett.* **1988**, 1449. (h) Kurihara, T.; Kurusu, Y. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2311. (i) Trost, B. M.; Kulawiec, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 2027.

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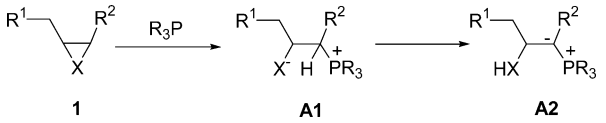
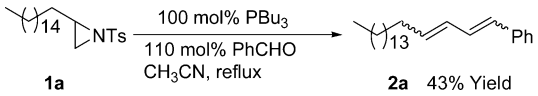
them more useful synthetic intermediates that fully deserve a prominent place in the arsenal of the organic chemist. In the course of our studies on the synthesis of aziridines and epoxides and their applications in organic synthesis,[9] we developed a novel phosphine-mediated ring-opening reaction of various aziridines and epoxides with a wide range of nucleophiles. The mechanism studies showed that the P-ylide would be a possible intermediate. We describe here the investigations on the novel ylide formation procedure from aziridines or epoxides under neutral and metal-free conditions and its use in the formation of dienes, as well as important aspects of the reaction mechanism.

In our previous publications,[9i−k] we found that organophosphine[10] could attack aziridines and epoxides to form the corresponding betaine intermediate **A1**.[10b] We supposed that an ylide intermediate **A2** might be formed from the betaine **A1** after an inter- or intra-hydrogen shift reaction (Scheme 1).[10a,11] If it is possible, an *umpolung* would occur so that the electrophilic carbon atom of aziridines or epoxides would become a nucleophilic center.

SCHEME 1. Proposed Intermediate



To prove the existence of the ylide intermediate **A2**, benzaldehyde was introduced into the mixture of aziridine **1a** with tributylphosphine in CH_3CN. After 48 h at reflux, aziridine **1a** disappeared but no corresponding expected allylic amine was obtained. To our surprise, an unexpected conjugated diene compound was isolated in 43% yield *even in the absence of any base* (eq 1). After considerable experimentation in various reaction conditions, we found that *t*-BuOH was the optimal solvent, giving the highest yield (75%). It is noted that the reaction could also proceed in water at 40 °C (48% yield) or in solvent-free conditions at 100 °C (53% yield). When PPh_3 was used instead of PBu_3, the yield of the reaction **1a** with benzaldehyde decreased to 55%.



(1)

To explore the generality of this transformation, a variety of substrates and carbonyl compounds were examined. As shown in Table 1, not only the aziridines but also the epoxides (entries 5, 8, and 10), both easily derived from acyclic or cyclic precursors, were suitable substrates. All carbonyl compounds we tested, aromatic and aliphatic, aldehydes and ketones, worked well in these diene formation reactions. The yields of dienes from the aziridines or epoxides derived from acyclic precursors are higher than those from other substrates derived from cyclic precursors. The reactions gave predominantly conjugated dienes with (*E*,*E*)- or (*E*)-configuration. The stereochemistry of products was determined by ^1H NMR.

In our reactions, the conjugated dienes were formed in a neutral and metal-free conditions. The yields in some reactions were not high but acceptable compared with those in other methods. It is worth noting that, because most of the epoxides or aziridines in Table could be

(6) (a) Padwa, A.; Woolhouse, A. D. In *Comprehensive Heterocyclic Chemistry*; Lwowski, W., Ed.; Pergamon: Oxford, 1984; Vol. 7. (b) Pattenden G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, p 223. (c) Padwa, A.; Pearson, W. H.; Lian, B. W.; Bergmeier, S. C. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: New York, 1996; Vol. 1a. (d) Jacobsen, E. N.; Wu, M. H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999.

(7) For some reviews of syntheses and reactions of activated and unactivated aziridines, see: (a) Kasai, M.; Kono, M. *Synlett* **1992**, 778. (b) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. (c) Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693. (d) Rayner, C. M. *Synlett* **1997**, 11. (e) Ibuka, T. *Chem. Soc. Rev.* **1998**, *27*, 145. (f) Li, A. H.; Dai, L. X.; Aggarwal, V. K. *Chem. Rev.* **1997**, *97*, 2341. (g) Stamm, H. *J. Prakt. Chem.* **1999**, 319. For some reviews of reactions of epoxides, see: (h) Pattenden, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, p 223. (i) Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14361. (j) Jacobsen, E. N.; Wu, M. H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999. (k) Willis, M. C. *J. Chem. Soc., Perkin. Trans. 1* **1999**, 1765.

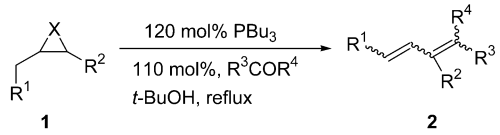
(8) For some examples, see: (a) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742. (b) Stamm, H.; Baumnn, T. *Pharmazie* **1997**, *52*, 441. (c) Muller, P.; Nury, P. *Org. Lett.* **1999**, *1*, 439. (d) Li, Z.; Fernandez, M.; Jacobsen, E. N. *Org. Lett.* **1999**, *1*, 1611. (e) Lee, W. Y.; Salvador, J. M.; Bodige, K. *Org. Lett.* **2000**, *2*, 931. (f) Nakagawa, M.; Kawahara, M. *Org. Lett.* **2000**, *2*, 953. (g) Gadikota, R. R.; Callam, C. S.; Lowary, T. L. *J. Org. Chem.* **2001**, *66*, 9046. (h) Salomon, C. J. *Synlett* **2001**, 65. (i) Fringuelli, F.; Pizzo, F.; Vaccaro, L. *Tetrahedron Lett.* **2001**, *42*, 1131−1133. (j) Ready, J. M.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2002**, *41*, 1374. (k) Yadav, J. S.; Reddy, B. V. S.; Abraham, S.; Sabitha, G. *Tetrahedron Lett.* **2002**, *43*, 1565. (l) Barluenga, J.; Vazquez-Villa, H.; Ballesteros, A.; Gonzalez, J. M. *Org. Lett.* **2002**, *4*, 2817. (m) Hoard, D. W.; Moher, E. D.; Martinelli, M. J.; Norman, B. H. *Org. Lett.* **2002**, *4*, 1813−1815. (n) Righi, P.; Scardovi, N.; Marotta, E.; ten Holte, P.; Zwanenburg, B. *Org. Lett.* **2002**, *4*, 497−500. (o) Yadav, J. S.; Reddy, B. V. S.; Premalatha, K. *Adv. Synth. Catal.* **2003**, *345*, 948. (p) Bisai, A.; Pandey, G.; Pandey, M. K.; Singh, V. K. *Tetrahedron Lett.* **2003**, *44*, 5839.

(9) (a) Li, A. H.; Dai, L. X.; Hou, X. L.; Chen, M. B. *J. Org. Chem.* **1996**, *61*, 4641. (b) Li, A. H.; Zhou, Y. G.; Dai, L. X.; Hou, X. L.; Xia, L. J.; Lin, L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1317. (c) Hou, X. L.; Yang, X. F.; Dai, L. X. *Chem. Commun.* **1998**, 747. (d) Hou, X. L.; Wu, J.; Dai, L. X.; Xia, L. J.; Tang, M. H. *Tetrahedron: Asymmetry* **1998**, *9*, 1747. (e) Hou, X. L.; Wu, J.; Dai, L.-X. *Chinese J. Chem.* **1998**, *16*, 557. (f) Wu, J.; Hou, X. L.; Dai, L. X.; Xia, L. J.; Tang, M. H. *Tetrahedron: Asymmetry* **1998**, *9*, 3431. (g) Zhou, Y. G.; Hou, X. L.; Dai, L. X.; Xia, L. J.; Tang, M. H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 77. (h) Li, B. F.; Zhang, M. J.; Hou, X. L.; Dai, L. X. *J. Org. Chem.* **2002**, *67*, 2902. (i) Hou, X. L.; Fan, R. H.; Dai, L. X. *J. Org. Chem.* **2002**, *67*, 5295. (j) Fan, R. H.; Hou, X. L. *J. Org. Chem.* **2003**, *68*, 726. (k) Fan, R. H.; Hou, X. L. *Tetrahedron Lett.* **2003**, *44*, 4411. (l) Fan, R. H.; Hou, X. L. *Org. Biomol. Chem.* **2003**, *1*, 1565.

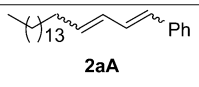
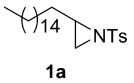
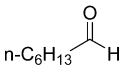
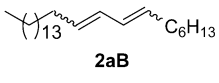
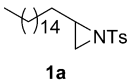
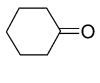
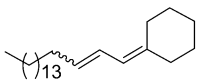
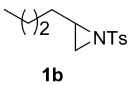
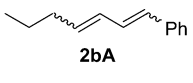
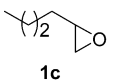
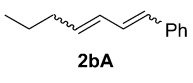
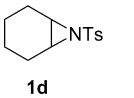
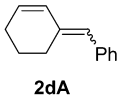
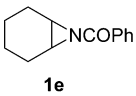
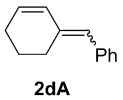
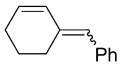
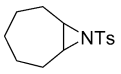
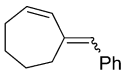
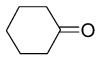
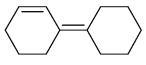
(10) (a) For reviews on the chemistry of phosphine, see: *The Chemistry of Organophosphorus Compounds*; Frank, H. R., Ed.; Wiley: West Sussex, 1990; Vol. 1. (b) Christol, H.; Grelet, D.; Darvich, M. R.; Fallouh, F.; Plenat, F.; Cristau, H.-J. *Bull. Soc. Chim. Fr.* **1989**, 477. (c) Guo, C.; Lu, X. *J. Chem. Soc., Chem. Commun.* **1993**, 394. (d) Trost, B. M.; Li, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 10819. (e) Zhang, C.; Lu, X. *J. Org. Chem.* **1995**, *60*, 2906. (f) Zhang, C.; Lu, X. *Synlett* **1995**, 645. (g) Xu, Z.; Lu, X. *Tetrahedron Lett.* **1997**, *38*, 3461. (h) Trost, B. M.; Dake, G. R. *J. Org. Chem.* **1997**, *62*, 5670. (i) Xu, Z.; Lu, X. *J. Org. Chem.* **1998**, *63*, 5031. (j) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535 and references therein. (k) Shi, M.; Xu, Y. M. *Chem. Commun.* **2001**, 1876. (l) Vedejs, E.; Rozners, E. *J. Am. Chem. Soc.* **2001**, *123*, 2428 (m) Vedejs, E.; Daugulis, O.; MacKay, J. A.; Rozners, E. *Synlett.* **2001**, 1499. (n) Shi, M.; Xu, Y. M. *Eur. J. Org. Chem.* **2002**, 696. (o) Wende, M.; Meier, R.; Gladysz, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 11490. (p) Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 2404. (q) Wang, L. C.; Luis, A. L.; Agapiou, K.; Jang, H. Y.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 2402. (r) Lumbierres, M.; Moreno-MaLas, M.; Vallribera, A. *Tetrahedron* **2002**, *58*, 4061. (s) Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 2404. (t) Wang, J. C.; Ng, S. S. Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 3682. (u) Zhu, X. F.; Lan, J. Kwon, O. *J. Am. Chem. Soc.* **2003**, *125*, 4716. (v) Jellerichs, B. G.; Kong, J. R.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 7758. (w) Vedejs, E.; Daugulis, O.; Harper, L. A.; MacKay, J. A. Powell, D. R. *J. Org. Chem.* **2003**, *68*, 5020.

(11) Dellaria, J. F.; Sallin, K. J., Jr. *Tetrahedron Lett.* **1990**, 2661.

TABLE 1. Transformation of Aziridines or Epoxides to the Conjugated Dienes in the Presence of Tributylphosphine[a]



1 2

Entry	Substrate	Carbonyl compound	Product	Yield [b]	(E, E):(E, Z) : other isomer [c]
1	 **1a**		 **2aA**	75	77 : 13 : 10
2	 **1a**		 **2aB**	82	50 : 37 : 13
3	 **1a**		 **2aC**	71	72 : 28
4	 **1b**		 **2bA**	74	84 : 15 : 1
5	 **1c**		 **2bA**	65	75 : 13 : 12
6	 **1d**		 **2dA**	44	67 : 33
7	 **1e**		 **2dA**	48	66 : 34
8	 **1f**		 **2dA**	55	69 : 31
9	 **1g**		 **2gA**	41	63 : 37
10	 **1f**		 **2fC**	64	–

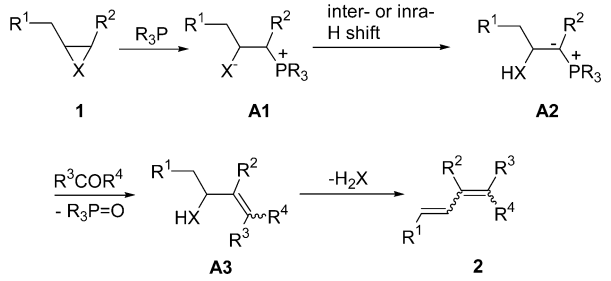
[a] Bu_3P was purified by distillation from CuI, and the reactions were carried out at reflux in *t*-BuOH under Ar. [b] Isolated yields based on aziridines or epoxides. [c] Ratios of isomers were determined at 300 MHz by ^1H NMR.

simply prepared from the corresponding alkenes in one step,[7] this approach offered a two-step transformation path from alkenes to the conjugated diene compounds in reasonable total yield. For example, compound **2aB** was a compound isolated from natural product reticulitermes flavipes[12] and can be obtained in 82% yield from the reaction of aziridine **1a** (entry 2), while aziridine **1a** was prepared from octadec-1-ene in 87% yield.

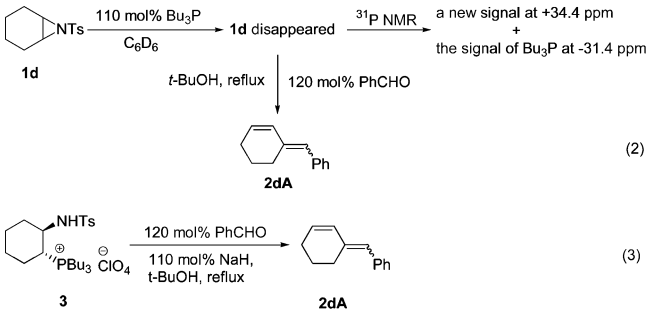
To understand the reaction pathway, aziridine **1d** and Bu_3P were mixed in a 1:1.1 ratio in C_6D_6, and the mixture

(12) Howard, R. W.; McDaniel, C. A.; Blomquist, G. J. *J. Chem. Ecol.* **1978**, *4*, 233.

SCHEME 2. Porposed Mechanism of Formation of Conjugated Diene Compounds from Aziridines or Epoxides in the Presence of Phosphine

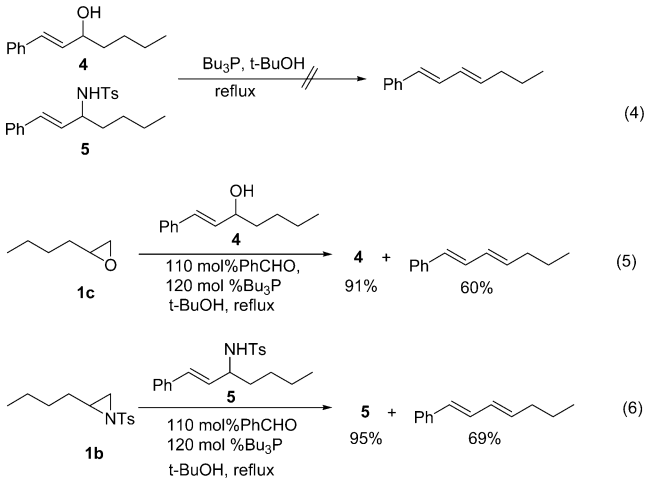


was stirred at room temperature until the disappearance of aziridine **1d**. The ^{31}P NMR spectrum showed a new signal at +34.4 ppm, in addition to the signal of Bu_3P at −31.4 ppm. The new signal was consistent with those of similar phosphonium salts.[13] With the addition of 120 mol % PhCHO, the mixture was stirred at reflux for 48 h and gave rise to the conjugated diene **2dA** in 30% yield (eq 2). On the other hand, a phosphonium salt **3**, which is prepared from the reaction of aziridine **1d** with tributylphosphine, was subjected to PhCHO in the presence of 110 mol % NaH under the same reaction conditions to give **2dA** in 32% yield (eq 3). When PPh_3 was used instead of PBu_3 in the reaction of aziridine **1a** with benzaldehyde, Ph_3PO and $TsNH_2$ were separated from the reaction mixture. These experiments showed that a phosphonium salt should be an intermediate in the reaction and that the diene product might be formed via a Wittig reaction and elimination.

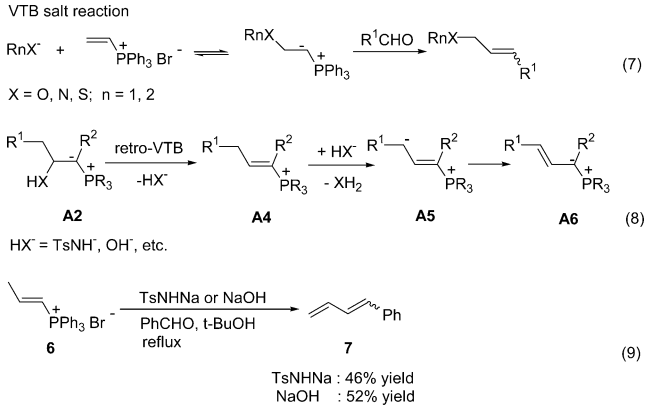


On the basis of the above results, we supposed that the reaction might proceed via the route depicted in Scheme 2: phosphine attack on the aziridine or epoxide to form phosphonium salt **A1**, followed by conversion into ylide intermediate **A2** after an inter- or intra-hydrogen shift reaction.[11] The ylide intermediate then reacts with carbonyl compound followed by elimination of H_2X to form the final diene product.

If this mechanism were correct, allylic alcohol **4** and amine **5**, structurally similar to the intermediate **A3**, would provide the corresponding diene product under the reaction conditions. However, allylic alcohol **4** and amine **5** failed to be converted into the desired product (eq 4) even when they were added to the reaction system containing epoxide **1c** or aziridine **1b** and benzaldehyde under appropriate conditions (eq 5 and 6).



Vedejs observed the formation of vinyl phosphonium salt in the reaction of cycloheptene oxide and PPh_2Me.[14] Schweizer and co-workers reported some reactions of VTB salt (VTB: vinyl triphenylphosphonium bromide), in which an equilibrium between VTB salt and ylide intermediate was observed (eq 7).[15] It seems that the structure of the possible intermediate **A2** is similar to that of the ylide intermediate in VTB salt reaction. It is possible that intermediate **A2** might convert into intermediate **A4** *via a retro-VTB salt reaction* and provide an anion HX^-, acting as base in formation of **A5** (eq 8), which then reacts with carbonyl compound to give diene as the final product.[3e] To prove this possibility, phosphonium salt **6**, structurally similar to intermediate **A4**, was treated with PhCHO in *t*-BuOH in the presence of 100 mol % TsNHNa or NaOH. Indeed, diene **7** was obtained in moderate yield (eq 9).



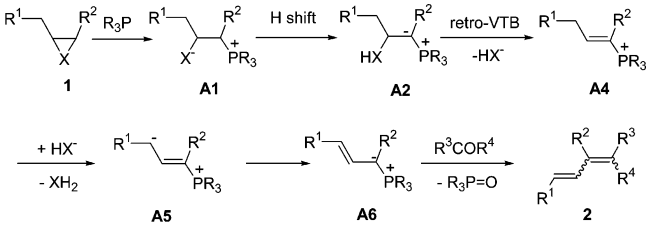
According to the clues we have found, a plausible reaction mechanism is proposed (Scheme 3). Phosphine attacked the aziridine or epoxide to form a phosphonium salt intermediate **A1**, which followed a hydrogen shift to give rise to ylide **A2**. Then, a retro-VTB reaction occurred to produce **A4** and a HX^- ion. HX^- acted as a base to deprotonate **A4** to form **A5** and the corresponding XH_2. **A5** would isomerize to an allyl ylide intermediate **A6**,

(13) Albright, T. A.; Freeman, W. J.; Schweizer, E. E. *J. Am. Chem. Soc.* **1975**, *97*, 2942.

(14) Vedejs, E.; Snoble, K. A. J.; Fuchs, P. L. *J. Org. Chem.* **1973**, *38*, 1178.

(15) Schweizer, E. E.; Smucker, L. D.; Votral, R. J. *J. Org. Chem.* **1966**, *31*, 467.

SCHEME 3. Plausible Mechanism of Formation of Dienes from Aziridines or Epoxides via an Allyl Ylide Route



which reacted with carbonyl compound to produce conjugated diene as the final product.[3e]

From the above studies on the mechanism of the transformation of aziridines or epoxides into the conjugated dienes, we found a novel ylide formation procedure under metal-free and neutral conditions. And because the phosphonium salt is formed in situ, it would provide a chance to realize the ylide reaction in a catalytic mode.

In conclusion, a general approach to formation of P-ylide under metal-free and neutral conditions is realized. Conjugated diene derivatives were prepared from aziridines or epoxides in the presence of organophosphine based upon this kind of P-ylide in a facile and convenient way. Studies on the further applications of this novel methodology to ylide and its catalytic and asymmetric version are in progress.

Experimental Section

General Experimental Conditions. All reactions were performed under an atmosphere of either dry argon or nitrogen using oven-dried glassware. Solvents were distilled under an atmosphere of nitrogen before use. The commercially available reagents were used as received without further purification. Melting points are uncorrected. ^{1}H NMR spectra were recorded on a 300 MHz spectrometer, and the chemical shifts were referenced to $CHCl_3$ (δ 7.27) in $CDCl_3$. Chemical shifts are given in parts per million relative to tetramethylsilane as an internal standard. IR spectra were measured in cm^{-1}.

General Procedure for Reaction of Aziridine or Epoxide with Carbonyl Compound in the Presence of Phosphine. To a stirred solution of aziridine or epoxide **1** (0.5 mmol) and carbonyl compound (0.55 mmol) in corresponding solvent (2.0 mL) was added phosphine (0.6 mmol) under argon, and the resulting mixture was stirred at corresponding temperature for 48−60 h. The solvent was removed in a vacuum, and the crude product was purified by flash column chromatography to provide the corresponding product.

1-Phenylnonadeca-1,3-diene (2aA). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.81 0.95 (m, 3H), 1.06−1.44 (m, 26H), 2.10−2.18 [m, 2H, (E, E)], 2.25−2.30 [m, 2H, (E, Z)], 5.52 [dt, J = 10.5, 7.6 Hz, 1H, (E, Z)], 5.83 [dt, J = 14.8, 7.0 Hz, 1H, (E, E)], 6.12−6.25 (m, 1H), 6.44 [d, J = 15.9 Hz, 1H, (E, E)], 6.53 [d, J = 15.6 Hz, 1H, (E, Z)], 6.76 [dd, J = 15.4, 10.6 Hz, 1H, (E, E)], 7.07 [dd, J = 15.6, 11.2 Hz, 1H, (E, Z)], 7.16−7.29 (m, 5H). IR (film): $\tilde{\nu}$ = 3025, 2955, 1596, 1496, 1378, 985, 945 cm^{-1}. EI-MS: *m*/*z* (%) 340 (20) [M^+], 143 (49), 129 (100). Anal. Calcd for $C_{25}H_{40}$: C, 88.16; H, 11.65. Found: C, 87.93; H, 11.44.

Pentacosa-7,9-diene (2aB). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.81−0.91 (M, 6H), 1.05−1.19 (M, 34H), 2.00−2.16 (m, 4H), 5.29 [dt, J = 11.1, 7.6 Hz, 1H, (E,Z)], 5.39−5.49 [m, 1H, (Z, E and Z, Z)], 5.51−5.59 (m, 1H), 5.65 [dt, J = 14.4, 6.6 Hz, 1H, (E,E)], 5.90−5.98 (m, 1H), 6.00−6.04 [m, 1H, (E, E)], 6.23−6.34 [m, 1H, (E, Z; Z, E and Z, Z)]; IR (film): $\tilde{\nu}$ = 3016, 2957, 1466, 1378, 953, 946 cm^{-1}. EI-MS: *m*/*z* (%) 348 (M^+, 0.7), 264 (5), 242 (12), 91 (100). Anal. Calcd for $C_{25}H_{48}$: C, 86.12; H, 13.88. Found: C, 86.17; H, 13.89.

1,1-Pentamethylene-1,3-nonadecadiene (2aC). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.82−0.91 (m, 3H), 1.06−1.45 (m, 26H), 1.54−1.57 (m, 6H), 2.04−2.27 (m, 6H), 5.35 [dt, J = 10.5, 7.3 Hz, 1H, (Z)], 5.59 [dt, J = 14.5, 7.1 Hz, 1H, (E)], 5.74 [d, J = 10.9 Hz, 1H, (E)], 6.02 [d, J = 11.2 Hz, 1H, (Z)], 6.17−6.32 (m, 1H). IR (film): $\tilde{\nu}$ = 3026, 2955, 1465, 1447, 963 cm^{-1}. EI-MS: *m*/*z* (%) 332 (27) [M^+], 189 (40), 135 (60), 92 (100). Anal. Calcd for $C_{25}H_{44}$: C, 86.67; H, 13.33. Found: C, 86.39; H, 13.59.

1-Phenylhept-1, 3-diene (2bA).[16] ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.84−0.95 (m, 3H), 1.41−1.54 (m, 2H), 2.10−2.18 [m, 2H, (E, E)], 2.25−2.33 [m, 2H, (E, Z)], 5.55 [dt, J = 10.9, 7.7 Hz, 1H, (E, Z)], 5.84 [dt, J = 14.7, 7.0 Hz, 1H, (E, E)], 6.14−6.27 (m, 1H), 6.45 [d, J = 15.6 Hz, 1H, (E, E)], 6.54 [d, J = 15.4 Hz, 1H, (E, Z)], 6.77 [dd, J = 15.7, 10.4 Hz, 1H, (E, E)], 7.09 [dd, J = 15.6, 11.1 Hz, 1H, (E, Z)], 7.17−7.32 (m, 5H). IR (film): $\tilde{\nu}$ = 3061, 3026, 2960, 1598, 1493, 1379, 987, 964 cm^{-1}. EI-MS: *m*/*z* (%): 172 (57) [M^+], 143 (49), 129 (100).

3-Benzylidene-cyclohexene (2dA).[17] ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.69−1.88 (m, 2H), 2.16−2.25 (m, 2H), 2.43−2.48 (m, 1H), 2.65−2.70 (m, 1H), 5.89−5.97 (m, 1H), 6.20−6.22 [m, 1H, (E)], 6.23−6.25 [m, 1H, (Z)], 6.28 [br, 1H, (E)], 6.64 [dt, J = 10.2, 2.0 Hz, 1H, (Z)]. EI-MS: *m*/*z* (%) 170 (M^+, 100), 155 (34), 141 (37), 91 (45).

Benzylidencyclohept-2-en (2gA).[18] ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.76−1.84 (m, 4H), 2.26−2.35 (m, 2H), 2.47−2.52 [m, 2H, (E)], 2.61−2.65 [m, 2H, (Z)], 5.78 [dt, J = 11.1, 5.7 Hz, 1H, (Z)], 5.91 [dt, J = 11.1, 5.1 Hz, 1H, (E)], 6.20 [dd, J = 12, 1.2 Hz, 1H, (Z)], 6.30 [s, 1H, (E)], 6.30−6.37 [m, 1H, (Z)], 6.39−6.41 [m, 1H, (E)], 7.15−7.35 (m, 5H).

3-Cyclohexylidene-cyclohexene (2fC). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.48−1.76 (m, 8H), 2.15−2.35 (m, 8H), 5.86−5.89 (m, 1H), 6.62 (s, 1H); $\tilde{\nu}$ = 3073, 3040, 2972, 1623, 1443 cm^{-1}. EI-MS: *m*/*z* (%) 162 (0.4) [M^+], 131 (14), 117 (10). Anal. δ = $C_{12}H_{18}$: C, 88.89; H, 11.11. Found: C, 88.93; H, 10.82.

Mechanism Study: Preparation of Phosphonium Salt 3. To a suspension of Bu_3P (0.28 mL, 1.1 mmol) in ethanol (10 mL) was added **1d** (252 mg, 1 mmol), giving a clear solution after a few minutes. The mixture was then stirred for 36 h at room temperature after which addition of 60% aqueous perchloric acid (3 mL) and cooling at 0 °C gave a solid product. After a recrystallization from CH_2Cl_2, a good crystal was obtained in 46% yield.

Characterization of 3. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.99−1.03 (m, 11H), 1.10−1.37 (m, 3H), 1.55−1.63 (m, 13H), 1.74−1.77 (m, 1H), 1.91−1.93 (m, 1H), 2.30−2.40 (m, 6H), 2.42 (s, 3H), 2.93−2.98 (m, 1H), 3.41−3.46 (m, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H). ^{31}P NMR (162 MHz, $CDCl_3$, 25 °C, 85% H_3PO_4): δ = 35.46. EI-MS *m*/*z* (%): 283 (100), 253 (6). Anal. Calcd for $C_{25}H_{45}NO_6PS$: C, 54.19; H, 8.19; N, 2.53. Found: C, 54.13; H, 7.93; N, 2.38.

Reaction of Phosphonium Salt 3 with PhCHO. To a stirred solution of **3** (224 mg, 0.4 mmol) in *t*-BuOH (2.0 mL) was added PhCHO (0.05 mL, 0.5 mmol) under argon, and the resulting mixture was stirred at reflux for 24 h. No reaction took place as detected by TLC.

Reaction of Phosphonium Salt 3 with PhCHO in the Presence of NaH. To a stirred solution of **3** (224 mg, 0.4 mmol) in *t*-BuOH (2.0 mL) was added NaH (11 mg, 0.5 mmol) under argon, and the resulting mixture was stirred at room temperature for 1 h. Then, PhCHO (0.05 mL, 0.5 mmol) was added, and the mixture was stirred at reflux for 24 h. Compound **2dA** was isolated in 32% yield.

(16) Ousset, J. B.; Mioskowski, C.; Solladie, G. *Synth. Commun.* **1983**, *13*, 1193.

(17) Takaki, K.; Yasumura, M.; Negoro, K. *J. Org. Chem.* **1983**, *48*, 54.

(18) Vedejs, E.; Fuchs, P. L. *J. Am. Chem. Soc.* **1971**, *93*, 4070.

Test of Elimination Reaction of Allylic Alcohol 4 and Amine 5. To a stirred solution of **4** or **5** (1 mmol) in *t*-BuOH (2.0 mL) was added Bu_3P (0.28 mL, 1.1 mmol) under argon, and the resulting mixture was stirred at reflux for 24 h. No reaction took place as detected by TLC.

Test of Elimination Reaction of Allylic Alcohol 4 and Amine 5 in the Reaction System of Epoxide 1c or Aziridine 1b with PhCHO in the Presence of Bu_3P. To a mixture of **1c** or **1b** (1 mmol) with PhCHO (0.11 mL, 1.1 mmol) and Bu_3P (0.28 mL, 1.1 mmol) in *t*-BuOH (2.0 mL) was added **4** or **5** (1 mmol) under argon, and the resulting mixture was stirred at reflux for 24 h. The corresponding diene compound **2bA**, **4**, or **5** was recovered in >90% yield.

Preparation of Phosphonium Salt 6.[19] 2-Methylvinyltriphenylphosphonium bromide **6** was prepared by stirring a solution of 5 g of salt allyltriphenylphosphonium bromide in40 mL of dry pyridine containing 6 drops of triethylamine at room temperature for 18 h. After removal of solvent, purification was effected by adding 50 mL of boiling benzene, adding enough methylene chloride to effect solution, cooling to room temperature, and precipitating the salt with 20 mL of ethyl acetate. Yield: 88%. ^{1}H NMR of **6** (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.35−2.39 (m, 3H), 2.58 (br, 1H), 6.59−6.75 (m, 1H), 7.56−7.90 (m, 15H). ^{31}P NMR: δ = 19.36.

Reaction of Phosphonium Salt 6 with PhCHO in the Presence of TsNHNa or NaOH. To a stirred solution of **6** (392 mg, 1 mmol) in *t*-BuOH (2.0 mL) was added TsNHNa or NaOH (1.1 mmol) under argon, and the resulting mixture was stirred at room temperature for 1 h. Then, PhCHO (0.1 mL, 1 mmol) was added, and the mixture was stirred at reflux for 24 h. 1-Phenyl-1,3-butadiene **7** was isolated in 46 and 52% yields, respectively. ^{1}H NMR of **7** (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 5.18 (d, J = 10.8 Hz, 1H), 5.34 (d, J = 16.9 Hz, 1H), 6.44−6.58 (m, 2H), 6.78 (dd, J = 15.7, 10.7 Hz, 1H), 7.21−7.45 (m, 5H).[20]

Acknowledgment. We are grateful for the financial support from National Natural Sciences Foundation of China, the Major Basic Research Development Program (Grant G2000077506), National Outstanding Youth Fund, Chinese Academy of Sciences and Science and Technology Commission of Shanghai Municipality. R.H.F. gratefully acknowledges Hong Kong Croucher Foundation for a Studentship.

JO0354286

(19) Tsukamoto, M.; Iio, H.; Tokoroyama, T. *Tetrahedron Lett.* 1987, *28*, 4561.

(20) Avery, T. D.; Taylor, D. K.; Tiekink, E. R. T. *J. Org. Chem.* **2000**, *65*, 5531.