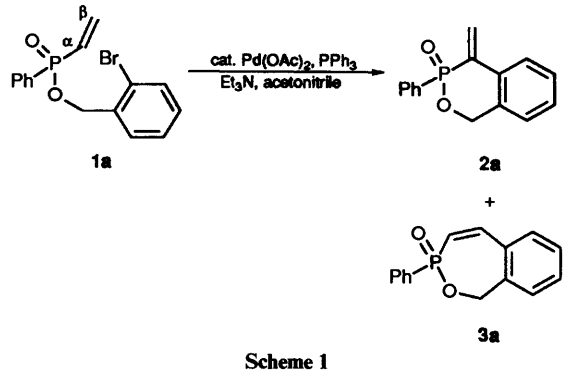
Palladium-catalysed Carbocyclization of Organophosphorus Compounds: A Novel and Effective Method for the Synthesis of Cyclic Organophosphorus Compounds Including the Phosphorus Analogues of α-Methylene Lactones

Feng Hong, Jiazhi Xia and Yuanyao Xu *
Shanghai Institute of Organic Chemistry, Laboratory of Organometallic Chemistry, Academia Sinica, 354 Fenglin Lu, Shanghai 200032, China

Cyclic organophosphorus compounds, including the phosphorus analogues of α-methylene lactones, have been synthesized in good yields by palladium-catalysed carbocyclization.

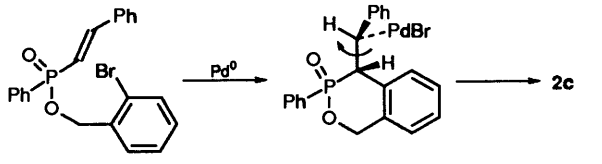
Transition metal-catalysed synthesis of heterocyclic compounds often permits the use of unconventional starting materials to prepare compounds under mild reaction conditions with high selectivity,[1-4] benzofuran,[5] indoles, oxindoles and quinolines *etc.*[6] having been so prepared by palladium-catalysed carbocyclization. Because of their potent biological activity,[7] cyclic organophosphorus compounds have received considerable attention and, recently, we described the synthesis of benzoxaphosphacycloalkane derivatives[8] and phosphorus analogues of α-methylene lactones[9a] by way of a palladium-catalysed carbon–phosphorus bond-forming reaction.[10-12] To our knowledge, however, the synthesis of cyclic organophosphorus compounds by palladium-catalysed carbocyclization has not been reported earlier. Herein we present details of a study of this reaction and provide a novel and effective method for the synthesis of cyclic organophosphorus compounds.



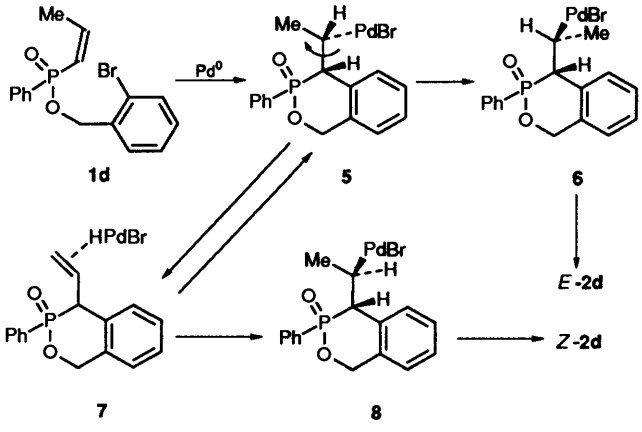
Scheme 1

The results are summarized in Table 1. The substituent attached to phosphorus had little effect on the yield and the ratio of the product (entries 1–3). Formation of the smaller-membered ring product is preferred over that of the larger.[9b] The bulkier the substituent position β to the vinyl moiety, the higher the preferred selectivity for formation of the smaller-membered ring products, although the yields are reduced (entries 1, 4, 5). Since insertion of the ArPdBr into the double bond and the elimination of the HPdBr was known to proceed in a *cis* fashion,[13] **2e** was formed stereospecifically (Scheme 2). If the same argument was followed for entry 4, only *E*-**2d** should be formed; however, in this case the elimination of HPdBr could take place in two directions, giving *E*-**2d** and **7**. The latter gave *E*-**2d** and *Z*-**2d** by migration of the terminal double bond through **5** and **8** (Scheme 3).

Isomerization of the 6-*exo-trig* cyclized product afforded the thermodynamically stable 6-*endo-trig* cyclic product **2g**. Compound **1f** gave 7-*endo-trig* cyclized product **3f** and some polymer, which was supposed to come from the 6-exo-trig



Scheme 2



Scheme 3

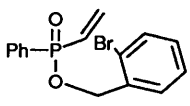
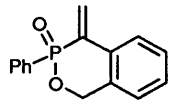
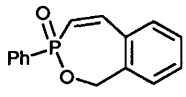
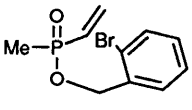
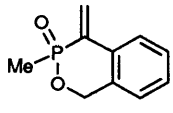
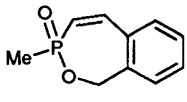
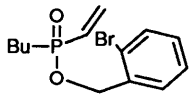
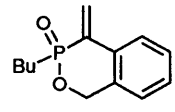
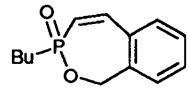
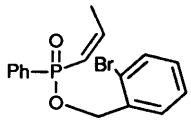
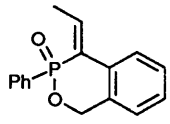
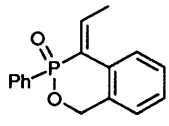
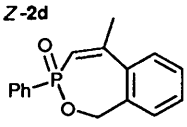
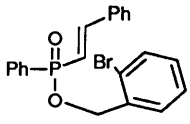
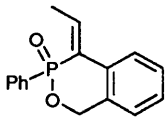
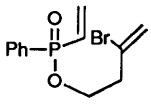
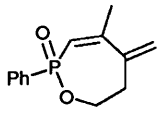
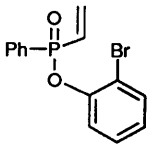
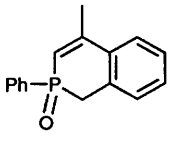
cyclized product. Moreover, the cyclization could also proceed under the effect of dichlorobis(triphenylphosphine)palladium and tetrakis(triphenylphosphine)palladium catalysis, although the yields and the selectivity of forming the smaller-membered ring product were lower.

Typical Experiment.—*o*-Bromobenzyl phenylvinylphosphinate (3.0 mmol), palladium acetate (0.15 mmol), triphenylphosphine (0.3 mmol) and triethylamine (1.5 cm^3, 10 mmol) in acetonitrile (10 cm^3) were placed in a thick-wall tube. This tube was flushed with nitrogen, capped and heated to 110 °C. After 30 min, the reaction was completed as monitored by TLC. Ethyl acetate was added to the reaction mixture which was then filtered. The filtrate was concentrated and the residue was chromatographed on a column of silica gel, eluting with ethyl acetate–light petroleum (1:1) to give 6-*exo-trig* cyclized product **2a** and 7-*endo-trig* product **3a** in 95% yield with a 79:21 ratio of **2a** to **3a**.

Acknowledgements

We thank the National Natural Science Foundation of China and Academia Sinica for their financial support.

Table 1 Synthesis of cyclic organophosphorus compounds *via* palladium-catalysed carbocyclizations[a]

Entry	Substrate	Temp. (°C)/Time (h)	Products[b]	Yield (%)[c]	Ratio[d]
1	 **1a**	100/0.5	 **2a**  **3a**	95	79:21
2	 **1b**	100/3	 **2b**  **3b**	89	71:29
3	 **1c**	100/5	 **2c**  **3c**	88	72:28
4	 **1d**	100/5	 *Z*-**2d**  *E*-**2d**  **3d**	53	85:15[e]
5	 **1e**	120/20	 **2e**	30	100:0
6	 **1f**	100/8	 **3f**	18	0:100[f]
7	 **1g**	100/1	 **2g**	83	100:0

[a] Reaction conditions: 1 equiv. of **1a–g**, 5 mol% of palladium acetate, 10 mol% of triphenylphosphine and 3 equiv. of triethylamine in acetonitrile at 100–120 °C for 0.5–20 h under nitrogen. [b] All products were isolated and fully characterized on the basis of mass spectral, IR, ^{1}H NMR and microanalytical or HRMS data. [c] Isolated yield. [d] Ratio of 6-*exo* to 7-*endo* product. [e] Ratio of *Z*-**2d** to *E*-**2d** is 44:56. [f] Ratio based on the isolated product.

References

1 J. L. Davidson and P. N. Preston, in *Adv. Heterocycl. Chem.*, 1982, **30**, 319.
2 J. Y. Lai, X. X. Shi, Y. S. Geng and L. X. Dai, *J. Org. Chem.*, 1993, **58**, 4775 and references cited therein.
3 R. C. Larock and M. Y. Kuo, *Tetrahedron Lett.*, 1991, **31**, 569–572.
4 S. M. Ma, G. X. Zhu and X. Y. Lu, *J. Org. Chem.*, 1993, **58**, 3692, and references cited therein.
5 R. C. Larock and D. E. Stinn, *Tetrahedron Lett.*, 1988, **29**, 4687, and references cited therein.
6 R. C. Larock and S. Babu, *Tetrahedron Lett.*, 1987, **28**, 5291, and references cited therein.
7 L. D. Quin, *The Heterocyclic Chemistry of Phosphorus*, Wiley, New York, 1981.
8 Y. Xu and J. Zhang, *Tetrahedron Lett.*, 1985, **26**, 4771.
9 (*a*) Y. Xu and Z. Li, *Tetrahedron Lett.*, 1986, **27**, 3017; (*b*) R. Grigg, V. Sridharan, P. Stevenson, S. Sukirthalingar and T. Worakun, *Tetrahedron Lett.*, 1990, **46**, 4003.
10 T. Hirao, T. Masunaga, N. Yamada, Y. Ohshiro and T. Agawa, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 909.
11 Y. Xu, Z. Li, J. Z. Xia, H. J. Gu and Y. Z. Huang, *Synthesis*, 1983, 377.
12 Y. Xu and J. Zhang, *Synthesis*, 1984, 778.
13 R. F. Heck, *Org. React., (New York)*, 1982, **27**, 345.

Paper 4/02449D
Received 26*th April* 1994
Accepted 16*th May* 1994