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The Phospha-Cope Rearrangement of 3-Phospha-1,5-hexadiene Derivatives Bearing a Hydroxyl Group†

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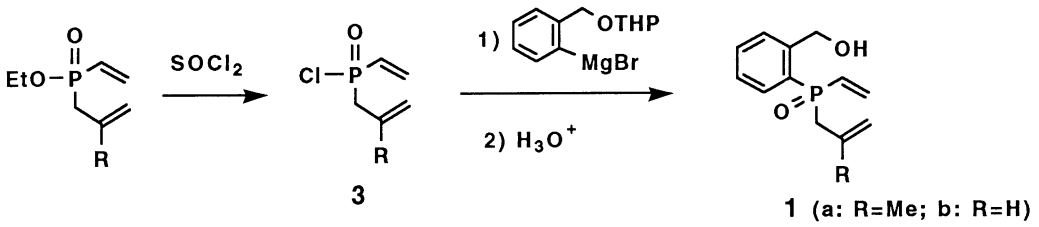
The title phospha-Cope rearrangement gives the corresponding cyclic phosphonates or phosphinates in 30 to 100% yields. Studies on solvent effects and kinetic isotope effects using the deuterated derivatives strongly support that there is a pre-equilibrium between tetracoordinate and pentacoordinate structures, followed by the rate-determining phospha-Cope rearrangement.

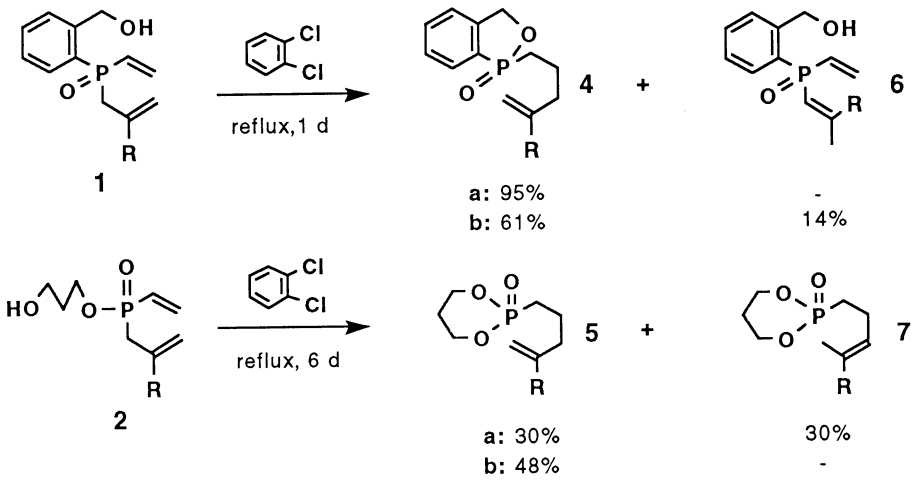
We have reported that the phospha-Cope rearrangement of 3-phospha- and 2-aza-3-phospha-1,5-hexadienes and 4-phospha-1-hexene-5-yne derivatives gives the corresponding 1-phospha-1,5-hexadiene derivatives, which have been led to the corresponding phosphonates or phosphinates by an intermolecular reaction with an alcohol.[1] The phospha-Cope rearrangement, followed by intramolecular addition reaction of hydroxyl group, is of interest from the viewpoints of not only promising the synthesis of the cyclic phosphonates or phosphinates bearing a double bond at δ-position, but also making it possible to study on solvents effects of the rearrangement. Here, we wish to report on the mechanistic study of the rearrangement.

3-(2-Hydroxymethylphenyl)-3-phospha-1,5-hexadiene 3-oxides (**1a,b**) were prepared in 58 and 32% yields, respectively, from 2-propenylvinylphosphinic chlorides (**3a,b**) as shown in the following scheme.[2,3] 3-(3-Hydroxypropyoxy)-3-phospha-1,5-hexadiene 3-oxides (**2a,b**) were prepared by the reactions of **3a,b** with 1,3-propanediol in the presence of triethylamine.



Compounds **1** and **2** (1 mmol) were heated in *o*-dichlorobenzene (3 ml) under argon atmosphere to afford the corresponding cyclic 4-methyl-4-pentenylphosphoryl derivatives (**4a,b** and **5a,b**) as shown in the following scheme. It is very interesting that the reaction of **1a** even in hexanol gives quantitatively **4a** and the intermolecular trapping product is not obtained at all. But, in the case of the reaction of **2a** there is a side reaction, which gives **7a** probably formed by double bond migration of **5a**, presumably because of long reaction time (6 d).

†Dedicated to Professor Emeritus Osamu Simamura of The University of Tokyo on the occation of his 80th birthday.



The yields of the desired products **4** or **5** (**5**+**7**) are higher in the reactions of 5-methyl derivatives than those of 5-unsubstituted ones, indicating that the methyl group at 5-position stabilizes a transition state of the phospha-Cope rearrangement.[2] Therefore, a kinetic study was carried out using **1a**, because the reaction was the cleanest without side reaction. The reactions in *o*-dichlorobenzene, hexanol, and nitrobenzene were monitored by GLC using triphenylphosphine oxide as internal standard to give the first order rate constants as shown in Tabel 1.

Table 2 shows activation parameters obtained from the Eyring equation. These values are similar in comparison with those of typical Cope and Claisen rearrangements.[4] The values of $\Delta G^{\neq}$ are equal within experimental error in each solvent. The activation parameters obtained in hexanol are quite similar to those reported previously in the phospha-Cope rearrangements trapped by hexanol, indicating that both the intermolecular and intramolecular trapping reactions proceed via the same mechanism.[1] The solvent effect unexpectedly smaller than those of the ortho-Claisen[5] and aza-Cope[6] rearrangements can be reasonably interpreted as follows: The reactant **1** is slightly more polar than those of the above rearrangements, so that both the reactant and the transition state are similarly stabilized by the polar solvent, thus making the energy gap between them almost equal in all solvents.

Table1. Rate Constants at Various Temperature [a]

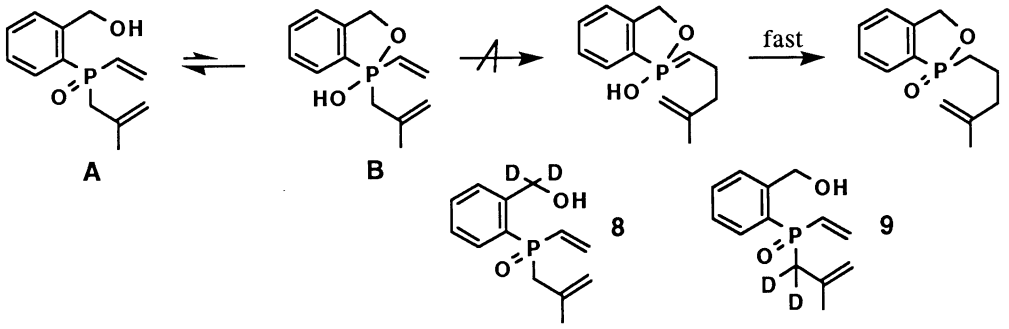
	$k/10^{-5}$ s^{-1}		
T/°C	*o*-$C_6H_4Cl_2$	*n*-$C_6H_{13}OH$	$C_6H_5NO_2$
154.5	9.97	-	9.05
150.0	8.65	5.89 [b]	6.50
145.5	6.11	4.43	4.57
140.5	5.18	2.52	2.42
135.0	2.20	1.80	-

a) By GLC (column: 1% Silicone DC QF-1 on 80/100 mesh chromosorb W-AW-DMCS). b) Measured at 149.8 °C.

Table 2. Activation Parameters

Solvent	$\Delta H^{\neq}$/kcal mol^{-1}	$\Delta S^{\neq}$/e.u.	$\Delta G^{\neq}$/kcal mol^{-1}
$C_6H_5NO_2$	27.0 ± 2.3	-14.2 ± 5.4	32.9 ± 4.5
n-$C_6H_{13}OH$	28.0 ± 2.2	-12.4 ± 5.4	33.2 ± 4.4
o-$C_6H_4Cl_2$	30.8 ± 1.8	-5.6 ± 4.2	33.1 ± 3.6

In order to clarify the mechanism furthermore, secondary kinetic isotope effects were studied using two deuterated derivatives **8** and **9** in *o*-dichlorobenzene at 419.8 K.[7] The ratio k_H/k_D were given to be 1.06 and 1.17 for **8** and **9**, respectively.[8] When the observation of secondary kinetic isotope effects in both cases is taken into consideration, the most reasonable mechanism seems as follows: There is a pre-equilibration between teracoordinate structure **A** and pentacoordinate one **B**, and the rate determinating step is the phospha-Cope rearrangement from the pentacoordinate structure **B**, followed by fast prototropy. To our knowledge, this is the first example for the phospha-Cope rearrangement on a pentacoordinate phosphorus center. This pre-equilibrium was also suggested by higher field shift in ^{31}P-NMR spectrum upon increasing measurement temperature.[9]



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References

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2) T. Kawashima, Y. Miki, and N. Inamoto, "Physical Organic Chemistry 1986, A Collection of the Invited Lectures Presented at the 8th IUPAC Conference on Physical Organic Chemistry, Tokyo, Japan, 24-29 August 1986," ed by M. Kobayashi, Elsevier Science Publishers B. V., Amsterdam (1987), pp. 181-186.

3) Spectral data of **1a**, **4a**, **8**, and **9** are shown as typical examples. **1a**: colorless oil. HRMS (70 eV): *m/z* Found: 236.0980. Calcd for $C_{13}H_{17}O_2P$: 236.0976. ^{1}H NMR ($CDCl_3$): δ 1.81 (3H, t, *J*=*J*=1.4 Hz, C($C\underline{H}_3$)=CH_2), 2.85-2.97 (2H, m, P$C\underline{H}_2$-), 4.70 (1H, d, *J*=12.8 Hz, C$\underline{H}$H'OH), 4.75 (1H, d, *J*=4.2 Hz, C(CH_3)=C$\underline{H}$H'), 4.83 (1H, d, *J*=12.8 Hz, CH$\underline{H}$'OH), 4.95 (1H, dq, *J*=1.4 Hz, J=4.2 Hz, C(CH_3)=CH$\underline{H}$'), 5.65 (1H, br s, O$\underline{H}$), 6.12-6.50 (2H, m, CH=C$\underline{H}_2$), 6.50-6.59 (1H, m, C$\underline{H}$=CH_2), and 7.32-7.50 (4H, m,

aromatic protons). ^{13}C NMR ($CDCl_3$): δ= 24.31 (d, *J*=1.9Hz), 40.57 (d, *J*=68.5 Hz), 64.93 (d, *J*=3.8 Hz), 116.32 (d, *J*=10.1 Hz), 127.39 (d, *J*=12.5 Hz), 130.50 (d, *J*=94.5 Hz), 131.18 (d, *J*=3.8 Hz), 131.27 (d, *J*=5.9 Hz), 132.20 (d, *J*=2.6 Hz), 132.52 (d, *J*=115.7 Hz), 137.80 (s), 135.78 (d, *J*=9.9 Hz), 146.60 (d, *J*=6.8 Hz). ^{31}P NMR ($CDCl_3$): δ= 31.70.

4a: colorless oil. HRMS (70 eV): *m/z* Found: 236.0953. Calcd for $C_{13}H_{17}O_2P$: 236.0976. ^1H NMR ($CDCl_3$): δ=1.66 (3H, s, $C(C\underline{H}_3)=CH_2$), 1.60-1.80 (2H, m, $PCH_2C\underline{H}_2CH_2$), 2.00-2.15 (4H, m, $PC\underline{H}_2CH_2C\underline{H}_2$), 4.64 (1H, s, $C(CH_3)=C\underline{H}H'$), 4.73 (1H, s, $C(CH_3)=CH\underline{H}'$), 5.27 (1H, dd, *J*=13.8 Hz, *J*=10.8 Hz, $C\underline{H}H'OP$), 5.49 (1H, dd, *J*=13.8 Hz, *J*=3.0 Hz, $CH\underline{H}'OP$), 7.30-7.39 (1H, m), 7.46-7.51 (1H, m), 7.58-7.63 (1H, m), and 7.75-7.82 (1H, m). ^{13}C NMR ($CDCl_3$): δ= 19.95 (d, *J*=3.0 Hz), 15.71 (s), 29.38 (d, *J*=97.3 Hz), 38.16 (d, *J*=17.0 Hz), 72.31 (s), 111.12 (s), 122.23 (d, *J*=10.5 Hz), 127.54 (d, *J*=116.4 Hz), 127.82 (d, *J*=12.5 Hz), 128.69 (d, *J*=11.6 Hz), 132.64 (d, *J*=2.8 Hz), 143.93 (d, *J*=14.0 Hz), and 144.04 (s). ^{31}P NMR ($CDCl_3$): δ=63.88.

8: colorless oil. HRMS (70 eV): *m/z* Found: 238.1112. Calcd for $C_{13}H_{15}D_2O_2P$: 238.1107. ^1H NMR ($CDCl_3$): δ=1.79 (3H, d, *J*=1.2 Hz, $C\underline{H}_3$), 2.87-2.96 (2H, m, $PC\underline{H}_2$), 4.73-4.76 (1H, m, $CMe=C\underline{H}H'$), 4.92-4.94 (1H, m, $MeC=CH\underline{H}'$), 5.67 (1H, s, $O\underline{H}$), 6.21-6.36 (2H, m, $CH=C\underline{H}_2$), 6.57 (1H, ddd, *J*=26.5 Hz, *J*=18.5 Hz, *J*=12.5 Hz, $C\underline{H}=CH_2$), and 7.35-7.50 (4H, m, aromatic protons). ^{13}C NMR ($CDCl_3$): δ= 24.08 (s, J=1.9 Hz), 40.25 (d, *J*=67.9 Hz), 63.83 (m), 116.53 (d, *J*=9.9 Hz), 127.20 (d, *J*=12.4 Hz), 130.19 (d, *J*=95.4 Hz), 130.34 (d, 94.8 Hz), 130.76 (d, *J*=11.1 Hz), 131.11 (d, *J*=12.0 Hz), 131.95 (d, *J*=2.7 Hz), 134.49 (s), 135.54 (d, *J*=9.6 Hz), and 146.51 (d, *J*=6.8 Hz). ^{31}P NMR ($CDCl_3$): δ= 31.97.

9: colorless oil. HRMS (70 eV): *m/z* Found: 238.1103. Calcd for $C_{13}H_{15}D_2O_2P$: 238.1107. ^1H NMR ($CDCl_3$): δ=1.80 (3H, d, *J*=1.3 Hz, $C\underline{H}_3$), 2.87-2.94 (0.19H, m), 4.65-4.97 (4H, m, $PC\underline{H}_2$, $C\underline{H}_2OH$), 5.68 (1H, br s, $O\underline{H}$), 6.22-6.38 (2H, m, $CH=C\underline{H}_2$), 6.56 (1H, ddd, *J*=26.5 Hz, *J*=18.5 Hz, *J*=12.5 Hz, $C\underline{H}=CH_2$), 7.35-7.52 (4H, m, aromatic protons). ^{13}C NMR ($CDCl_3$): δ=24.24 (d, *J*=1.8 Hz), 39.77-40.80 (m), 64.89 (d, *J*=3.7 Hz), 116.26 (d, *J*=9.9 Hz), 127.36 (d, *J*=12.6 Hz), 130.46 (d, *J*=94.6 Hz), 131.16 (d, *J*=10.2 Hz), 131.22 (d, *J*=12.2 Hz), 132.17 (d, *J*=2.8 Hz), 134.77 (s), 135.68 (d, *J*=9.6 Hz), 146.55 (d, *J*=6.9 Hz). ^{31}P NMR ($CDCl_3$): δ=32.11. Multiplets in the ^{13}C NMR spectra show coupling modes with ^{31}P nuceleus.

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5) W. N. White and E. F. Wolfarth, *J. Org. Chem.*, **35**, 3585 (1970).

6) T. Mitsuhashi, *J. Am. Chem. Soc.*, **108**, 2400 (1986).

7) The deuterated compounds **8** and **9** were prepared from α,α'-dideutero-*o*-bromobenzyl alcohol and α,α'-dideuteromethallyl chloride, respectively. D-Contents are 100% and 86% for **8** and **9**, respectively.

8) A similar value of k_H/k_D for **9** was reported for the Cope rearrangement: K. Humski, R. Malojcic, S. Borcic, and D. E. Sunko, *J. Am. Chem. Soc.*, **92**, 6534 (1970).

9) The values of δ_P were 30.36, 30.09, 29.68, and 29.4 at 32.2, 66.9, 103.6, and 128.7 °C, respectively, indicating the larger contribution of structure **B** at higher temperatures, because **B** is expected to have minus chemical shift.

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