Reaction of Allyl Diphenyl Phosphates with Soft Bases

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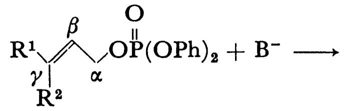
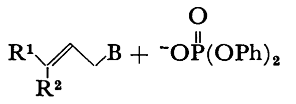
Synopsis. The title phosphates were found to react with a variety of soft bases to give nucleophilic substitution products in high yields. The reaction proceeded regiospecifically under mild reaction conditions with preservation of the double bond geometry.

It was first reported in 1958 that soft nucleophiles attack the alkyl group of trialkyl phosphates while hard bases attack the hard phosphorus atom.[1)] However, the reaction of allylic phosphates with various nucleophiles has received relatively little attention. In 1968, Miller and Wood synthesized a series of allyl diphenyl phosphates (**1**) and examined their reactions with phenols[2)] and β-diketones[3)] as a model for the biosynthesis of phenolic isoprenoids. Kitagawa *et al.* reported the regio- and stereospecific substitution of allylic phosphates using organoaluminum reagents.[4)] In the present paper, we describe the reaction of **1** with a variety of soft nucleophiles which involves the regio- and stereospecific substitutions of the diphenoxyphosphinyloxy group leading to good yields of allylic products (**2**).



1A: $R^1 = R^2 = H$
B: $R^1 = Me_2C{=}CH(CH_2)_2$, $R^2 = Me$
C: $R^1 = Me$, $R^2 = Me_2C{=}CH(CH_2)_2$



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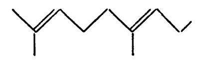
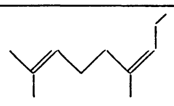
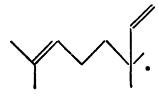
The reactions were carried out as follows. The phosphates **1** were stirred with a slight excess (1.0—1.5 eq) of nucleophiles in *N,N*-dimethylformamide at room temperature for 3 h. The reaction mixtures were poured into water, and the products were extracted with ether or collected by filtration. Analytically pure materials were obtained after distillation, column chromatography on silica gel, or recrystallization. Products were identified by their analytical and spectral properties and, in the case of known materials, by comparison of these physical constants with those of the reported ones.[5)] Treatment of **1** with soft bases such as iodide, cyanide, benzenethiolate and sulfide anions resulted in smooth displacement of the diphenoxyphosphinyloxy group to yield the corresponding allylated products in high yields. The results are given in Table 1. The phosphates **1B** and **1C** reacted with thiourea to give *S*-geranyl- and *S*-nerylisothiuronium salts (**2f** and **2j**), respectively, as colorless crystals. The reaction of **1B** with sodium thiocyanate gave an equilibrium mixture (**2g**) of linalyl isothiocyanate and geranyl thiocyanate. The ratio (81/19) estimated by ^{1}H-NMR analysis (in CCl_4 at 31.5 °C) is in good agreement with the reported one[6)] (80.56/19.44, in CCl_4 at 36 °C). The reaction of **1** with carbanionic reagents such as Grignard reagents and organolithium reagents is of special interest in view of a carbon–carbon bond formation.[7)] In fact, it has been demonstrated that the treatment of allyl diphenyl phosphates **1** with aryl Grignard reagents gives allylbenzenes in high yields.[8)] In contrast, we have found that excess (5 eq) phenyllithium, a carbanion harder than aryl Grignard reagents, attacked the phosphorus atom of **1B** to produce triphenylphosphine oxide (80% yield) together with geraniol (92%) and phenol (86%). The reaction of **1B** with sodium ethoxide, a representative of hard bases, in ethanol at room temperature gave a complex product mixture.

It has been shown that the reaction of **1** with soft

Table 1. Reaction of allyl diphenyl phosphates (**1A**—**1C**) with soft nucleophiles

Entry	Phosphate (**1**)	Nucleophile (B⁻)[a)]	Products (**2**)[b)]	Isolated yield/%
a	**1A**	I^-	Allyl-I (**2a**)	47
b	**1A**	PhS^-	Allyl-SPh (**2b**)	78
c	**1B**	$N{\equiv}C^-$	Geranyl-C≡N (**2c**)	85
d	**1B**	PhS^-	Geranyl-SPh (**2d**)	83
e	**1B**	S^{2-}	$(Geranyl)_2S$ (**2e**)	74
f	**1B**	$(H_2N)_2C{=}S$	$Geranyl\text{-}SC^+(NH_2)_2\cdot O^-P(O)(OPh)_2$ (**2f**)	56
g	**1B**	$N{\equiv}CS^-$	Linalyl–N=C=S ⇆ Geranyl-SC≡N (**2g**)	82
h	**1C**	$N{\equiv}C^-$	Neryl-C≡N (**2h**)	84
i	**1C**	PhS^-	Neryl-SPh (**2i**)	94
j	**1C**	$(H_2N)_2C{=}S$	$Neryl\text{-}SC^+(NH_2)_2\cdot O^-P(O)(OPh)_2$ (**2j**)	63

a) Counter cation: Na^+. b) Allyl:  Geranyl:  Neryl:  Linalyl: 

bases proceeds with complete preservation of the double bond geometry as evidenced by the fact that geranyl diphenyl phosphate **1B** gave geranyl derivatives (**2c**—**2f**) and the corresponding *cis*-isomer **1C** yielded neryl ones (**2h**—**2j**). All the reactions (except entry g) are regiospecific, exclusively leading to the α-substituted products. No evidence for the allylic rearrangement (γ-substitution) was detected.

Experimental

Melting points are uncorrected. The elemental analyses were performed at the Elemental Analysis Center of Kyoto University. IR spectra were measured with a JASCO IRA-1 spectrometer. ^{1}H- and ^{13}C-NMR were obtained on a Hitachi R-24A spectrometer and a JEOL JNM-FX100 spectrometer, respectively, in deuteriochloroform using tetramethylsilane as an internal standard. Phosphates **1A**—**1C** were prepared according to the method of Miller and Wood.[2] The following preparation of **2f** is representative of the reactions between **1** and soft nucleophiles.

Reaction of Geranyl Diphenyl Phosphate (1B) with Thiourea. A mixture of **1B** (386 mg, 1 mmol) and thiourea (76 mg, 1 mmol) in 2 ml of *N,N*-dimethylformamide was stirred at room temperature for 3 h. The reaction mixture was poured into water and the resulting white precipitate was collected by filtration, and washed with water. The crude product was recrystallized from ethanol to afford colorless needles of *S*-geranylisothiuronium diphenyl phosphate (**2f**) (253 mg, 56% yield), mp 134.5—135.5 °C. IR (KBr): 3280, 3068, 1676, 1500, 1240, 1218, 1094, and 922 cm^{-1}. ^{1}H-NMR: δ 9.81 (2H, br, NH), 8.03 (2H, br, NH), 7.04 (10H, m, Ph), 4.90 (2H, m, olefin), 3.37 (2H, d, J=7 Hz, SCH_2), 1.91 (4H, m, CH_2), 1.61, 1.52, 1.46 (each 3H, s, CH_3). ^{13}C-NMR: 171.7 ($SC^+(NH_2)_2$), 153.3 (P–O–C), 144.9 (=C–), 132.7 (=C–), 129.9 (=CH–), 124.2 (=CH–), 121.1 (=CH–), 120.9 (=CH–), 115.5 (=CH–), 40.1 (CH_2), 30.1 (CH_2), 26.9 (CH_2), 26.4 (CH_3), 18.4 (CH_3), 17.0 (CH_3). Found: C, 59.75; H, 6.87%. Calcd for $C_{23}H_{31}N_2O_4PS$: C, 59.73; H, 6.76%.

In a similar way, *S*-nerylisothiuronium diphenyl phosphate (**2j**) was obtained in 63% yield, mp 128.5—130.0 °C. IR (KBr): 3250, 3000, 1678, 1500, 1240, 1218, 1096, and 926 cm^{-1}. ^{1}H-NMR: δ 9.90 (2H, br, NH), 8.00 (2H, br, NH), 7.10 (10H, m, Ph), 4.96 (2H, m, olefin), 3.42 (2H, d, J=7 Hz, SCH_2), 1.92 (4H, m, CH_2), 1.62 (6H, m, CH_3), 1.50 (3H, s, CH_3). ^{13}C-NMR: 171.4 ($SC^+(NH_2)_2$), 153.3 (P–O–C), 144.5 (=C–), 132.8 (=C–), 129.8 (=CH–), 124.1 (=CH–), 121.0 (=CH–), 120.8 (=CH–), 116.5 (=CH–), 32.5 (CH_2), 29.8 (CH_2), 27.0 (CH_2), 26.3 (CH_3), 24.0 (CH_3), 18.3 (CH_3). Found: C, 59.21; H, 6.72%. Calcd for $C_{23}H_{31}N_2O_4PS$: C, 59.73; H, 6.76%.

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References

1) D. C. Harper and R. F. Hudson, *J. Chem. Soc.*, **1958**, 1356.

2) J. A. Miller and H. C. S. Wood, *J. Chem. Soc., C*, **1968**, 1837.

3) J. Carnduff, J. A. Miller, B. R. Stockdale, J. Larkin, D. C. Nonhebel, and H. C. S. Wood, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 692.

4) Y. Kitagawa, S. Hashimoto, S. Iemura, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **98**, 5030 (1976), see also S. Ozawa, A. Itoh, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, **1979**, 2909.

5) **2b**: C. D. Hurd and H. Greengard, *J. Am. Chem. Soc.*, **52**, 3356, (1930); **2c**: M. Matsui and G. Yabuta, *Agric. Biol. Chem.*, **32**, 1044 (1968); **2d** and **2i**: J. F. Biellmann and J. B. Ducep, *Tetrahedron*, **27**, 5861 (1971); **2e**: J. E. Baldwin and D. P. Kelly, *J. Chem. Soc., Chem. Commun.*, **1968**, 899; **2g**: see Ref. 6.

6) G. Pala, A. Antonio, and G. Coppi, *J. Med. Chem.*, **12**, 725 (1969).

7) Alkylation of **1B** and **1C** with trialkylaluminum, see Ref. 4.

8) R. C. Haley, J. A. Miller, and H. C. S. Wood, *J. Chem. Soc., C*, **1969**, 264.