Communications to the Editor

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PREPARATION OPTICALLY ACTIVE α,β-UNSATURATED PHOSPHONATES AND SULFOXIDES FROM PHENYLSULFENYLMETHANEPHOSPHONATES[1)]

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The first preparation of optically active α,β-unsaturated phosphonyl compounds from chiral phenylsulfenylmethanephosphonates 1 and 2 has been described. The optically active α,β-unsaturated sulfoxides have also been prepared by the Emmons-Horner reaction of phenylsulfinylmethanephosphonamidate 4 with several aldehydes.

KEYWORDS —: chiral α,β-unsaturated phosphonate; chiral α,β-unsaturated sulfoxide; absolute configuration; chirality transfer reaction

In the preceding paper,[2)] we reported the preparation of the optically active phenylsulfenylmethanephosphonate 1 and phosphonamidate 2 whose absolute configurations were determined by chemical correlation. Here we describe the first synthesis of optically active α,β-unsaturated phosphonates from 1 and 2 (Chart 1). Furthermore, the transformation of the phosphonamidate 2 to optically active α,β-unsaturated sulfoxides by the chirality-transfer reaction is described (Chart 2).

Optically active ethyl methyl styrenephosphonate was prepared according to our recently developed method.[3)] Thus, optically active ethyl methyl phenylsulfenylmethanephosphonate (-)-$(S)_P$-1 in anhydrous THF was treated with 1.3 eq of n-BuLi

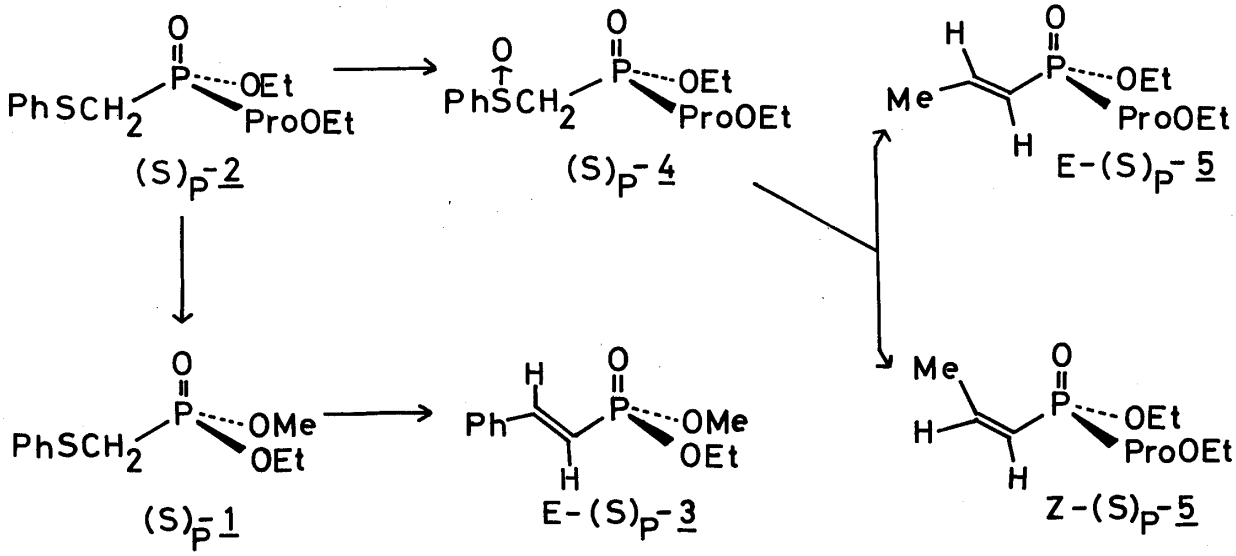

Chart 1

followed by the addition of benzyl bromide(2.5 eq) to afford the corresponding monobenzylated product which, without further purification, was treated with 1.3 eq of m-chloroperbenzoic acid(MCPBA) to afford the corresponding sulfoxide. The crude sulfoxide was heated under reflux in toluene and the product was purified by silica gel column chromatography to give the optically active styrenephosphonate (-)-$(S)_P$-3 in 61% yield.[4] Similarly, (+)-$(R)_P$-1 afforded (+)-$(R)_P$-3 in 52% yiled.[5] The optical purities of the both enantiomers were determined to be no less than 93% by the NMR method using chiral shift reagent Eu(hfc)$_3$.

Next the conversion of phenylsulfenylmethanephosphonamidate $(S)_P$-2 to the α,β-unsaturated phosphonamidate 5 was undertaken. The alkylation of 2 using n-BuLi was not successful, probably due to the undesired n-butylation of the ester site of ethyl L-prolinate. So we attempted an alternative route which involved MCPBA oxidation of the sulfide followed by alkylation and a subsequent desulfenylation reaction. The MCPBA oxidation of the phosphonamidate $(S)_P$-2 at room temperature provided almost quantitatively a diastereomeric mixture of the sulfoxide $(S)_P$-4 which, without separation, was treated with 1.5 eq NaH and ethyl iodide in HMPA-THF to give the corresponding monoethylated product. The reaction mixture was heated in toluene under reflux for 3-4 hr and the product was purified by silica gel column chromatography to give the 1-propenephosphonamidate $(S)_P$-5 in overall yield of 50% as a 1:5 mixture of Z and E isomers. The separation of the Z and E isomers was effected again by silica gel column chromatography (AcOEt as an eluent) to give Z-$(S)_P$-5 and E-$(S)_P$-5 in 9 and 39% yields respectively.[6] Similarly, $(R)_P$-2 afforded Z-$(R)_P$-5 and E-$(R)_P$-5 in 8 and 25% yields respectively.[7] Since the synthetic utility of α,β-unsaturated phosphonyl compounds has recently received much attention,[8] their first preparation in optically active form could be important in terms of asymmetric organic syntheses.[9]

We next turned our attention to the newly formed chiral ceter at sulfur of the above-mentioned phosphonamidate 4. If one could separate these diastereomers, they should become good precursors for the preparation of chiral sulfoxides such as phenyl α,β-unsaturated sulfoxides. Fortunately, the diastereomeric mixture $(S)_P$-4 showed two distinct spots on TLC and the diastereomers were quite easily[10]

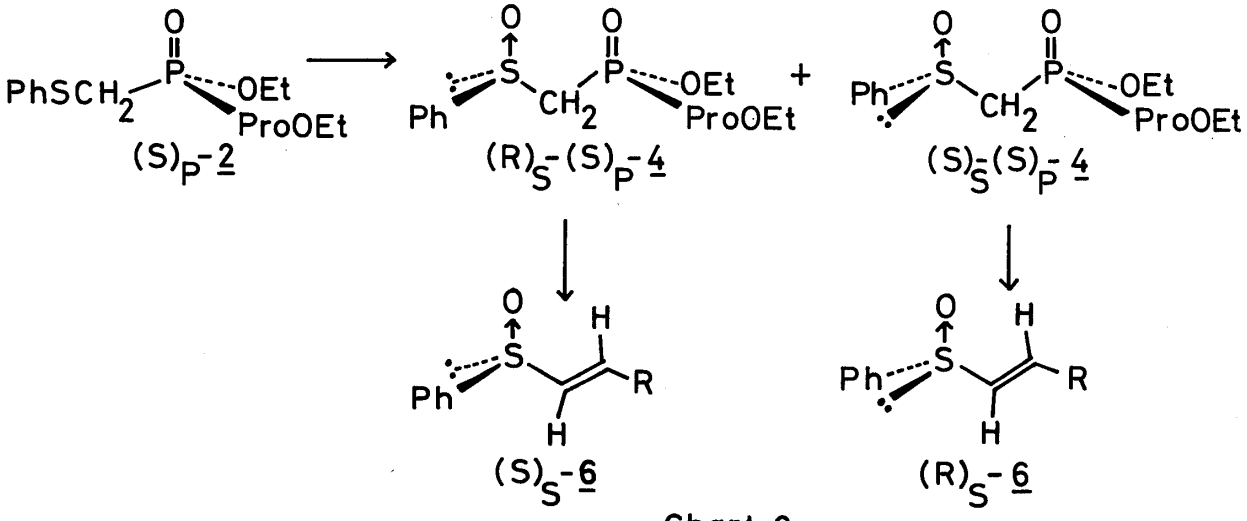

Chart 2

separated by silica gel chromatography to give $(R)_S$-$(S)_P$-4 and $(S)_S$-$(S)_P$-4[11] in 48 and 20% yields respectively.[12] The sulfoxide $(R)_S$-$(S)_P$-4 was then subjected to the Emmons-Horner reaction with formaldehyde using NaH as a base to afford the phenyl vinyl sulfoxide, (-)-$(S)_S$-6(R=H) in 47% yield.[13] The same reaction of $(S)_S$-$(S)_P$-4 gave (+)-$(R)_S$-6(R=H) in 46% yield.[14] The absolute configurations of both enantiomers were determined by comparing the CD spectra with that of (+)-$(R)_S$-p-tolyl vinyl sulfoxide.[15] Similarly, the reactions of $(R)_S$- and $(S)_S$-$(S)_P$-4 with benzaldehyde and p-chlorobenzaldehyde afforded optically active phenyl styryl sulfoxides, (-)-$(S)_S$-6(R=Ph) and (+)-$(R)_S$-6(R=Ph), in 74 and 63% yields, and the phenyl p-chlorostyryl sulfoxides, (-)-$(S)_S$-6(R=p-Cl-Ph) and (+)-$(R)_S$-6(R=p-Cl-Ph), in 86 and 75% yields respectively.[16] The optical purities of these α,β-unsaturated sulfoxides should be very high because little racemization occurs during the Emmons-Horner reaction. The α,β-unsaturated sulfoxides have been successfully employed as the effective chirality inducing agents(or substrates).[17] However, their preparation method is quite limited, mostly starting from optically active sulfinic esters.[17b, 18] Our present investigation may provide another useful method of preparing these compounds and research along this line is now in progress in this laboratory.

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REFERENCES AND NOTES

1) All new compounds were fully characterized spectoscopically(IR, ^{1}H NMR, MS spectra) and by combustion and/or high resolution mass spectral analyses.

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3) T. Koizumi, N. Tanaka, M. Iwata, and E. Yoshii, Synthesis, 1982, 917.

4) (-)-$(S)_P$-3: bp(Torr) 115-120(0.04); $[\alpha]_D^{22}$ -3.3°(c 0.96, MeOH). All distillations were carried out by use of Kugelrohr apparatus, and the bath temperatures are described.

5) (+)-$(R)_P$-3: bp(Torr) 115-120(0.04); $[\alpha]_D^{22}$ +2.9°(c 1.1, MeOH).

6) E-$(S)_P$-5: bp(Torr) 105-110(0.2); $[\alpha]_D^{24}$ -71.6°(c 1.66, MeOH); TLC R_f 0.22(AcOEt).
Z-$(S)_P$-5: bp(Torr) 105-110(0.2); $[\alpha]_D^{24}$ -55.9°(c 1.43, MeOH); TLC R_f 0.29(AcOEt).

7) E-$(R)_P$-5: bp(Torr) 105-110(0.2); $[\alpha]_D^{23}$ +2.1°(c 1.54, MeOH); TLC R_f 0.22(AcOEt).
Z-$(R)_P$-5: bp(Torr) 105-110(0.2); $[\alpha]_D^{24}$ -15.8°(c 0.33, MeOH); TLC R_f 0.27(AcOEt).

8) a) G. Märkl, and B. Merkl, Tetrahedron Letters, 22, 4459, 4463(1981);
b) T. Minami, K. Nishimura, I. Hirao, H. Suganuma, and T. Agawa, J. Org. Chem., 47, 2360(1982);
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d) R. J. Linderman, and A. I. Meyers, Tetrahedron Letters, 24, 3043(1983).

9) The electrophilic addition of phenylselenenyl chloride to E- and Z-$(S)_P$-5 proceeded highly diastereoselectively. A part of the results has been presented at the Ninth International Congress of Heterocyclic Chemistry(Tokyo, 1983). The absolute stereochemistry of the products is now being investigated.

10) Chromatographic separation of the corresponding diastereomeric mixture of sulfoxides, $(S)_S$-$(R)_P$- and $(R)_S$-$(R)_P$-4, was difficult. Effective separation is now being investigated using medium pressure silica gel column chromatography.

11) Both compounds are oily materials and decomposed on attempted distillation. $(R)_S$-$(S)_P$-4: $[\alpha]_D^{25}$ -74.6°(c 0.07, MeOH), TLC R_f 0.26(AcOEt).
$(S)_S$-$(S)_P$-4: $[\alpha]_D^{25}$ -2.7°(c 2.23, MeOH), TLC R_f 0.17(AcOEt).
The absolute configurations at sulfur were established, based on the absolute stereochemistry of (-)-$(S)_S$- and (+)-$(R)_S$-6(R=H).

12) Although the observed chiral inductivity is not high enough at present, investigations to optimize the selectivity is now being underway in this laboratory.

13) (-)-$(S)_S$-6(R=H): bp(Torr) 70-80(0.25); $[\alpha]_D^{26}$ -385°(c 0.46, MeOH).

14) (+)-$(R)_S$-6(R=H): bp(Torr) 90-95(0.5); $[\alpha]_D^{22}$ +375°(c 0.54, MeOH).

15) $(R)_S$-p-tolyl vinyl sulfoxide was prepared according to the method of D. J. Abbott, S. Colonna, and C. J. M. Stirling, J. Chem. Soc., Perkin Trans. 1., 1976, 492 and its CD spectrum was compared with those of (-)-6 and (+)-6(R=H).

16) (-)-$(S)_S$-6(R=Ph): bp(Torr) 140-150(0.15); $[\alpha]_D^{24}$ -106°(c 1.12, MeOH).
(+)-$(R)_S$-6(R=Ph): bp(Torr) 140-150(0.15); $[\alpha]_D^{24}$ +99°(c 1.10, MeOH).
(-)-$(S)_S$-6(R=p-Cl-Ph): mp 114°C; $[\alpha]_D^{24}$ -109°(c 0.91, MeOH).
(+)-$(R)_S$-6(R=p-Cl-Ph): mp 114°C; $[\alpha]_D^{24}$ +107°(c 0.91, MeOH).

17) a) T. Koizumi, H. Hirai, and E. Yoshii, J. Org. Chem., 47, 4004(1982).
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