Communications to the Editor

[Chem. Pharm. Bull. 31(11)4195—4197(1983)]

CHIRAL PHENYLSULFENYLMETHANEPHOSPHONIC ESTERS, THEIR PREPARATIONS AND ABSOLUTE CONFIGURATIONS[1)]

Toru Koizumi*, Masanori Iwata, Nobuyuki Tanaka, Kazuhiko Hirutani, and Eiichi Yoshii

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani 2630, Toyama 930-01, Japan

Optically active phenylsulfenylmethanephosphonic acid derivatives 2, 3, 4 were prepared and their absolute configurations were determined based on the established absolute configuration of chiral ethyl methyl methanephosphonate 7.

KEYWORDS—chiral phenylsulfenylmethanephosphonate; absolute configuration; chiral methanephosphonate; ethyl L-prolinate

Aryl- or alkylsulfenylmethanephosphonates are known as versatile synthetic intermediates for the preparation of various organophosphorus[2)] and organosulfur[3)] compounds. As a typical example, we have recently introduced a convenient method of preparing diethyl 1-alkenephosphonates[4)] from diethyl phenylsulfenylmethanephosphonate. There have been, however, no reports on synthesizing in optically active form those kinds of phosphonates which could be converted into a wide variety of chiral organophosphorus and organosulfur compounds. Here we should like to present the first method for the preparation of optically active arylsulfenylmethanephosphonates, whose absolute configurations were established by chemical correlation.

As illustrated in Chart 1, a diastereomeric mixture of the phosphonamidates 2 and 3 was prepared by the reaction of ethyl L-prolinate[5)] with ethyl phenylsulfenyl-

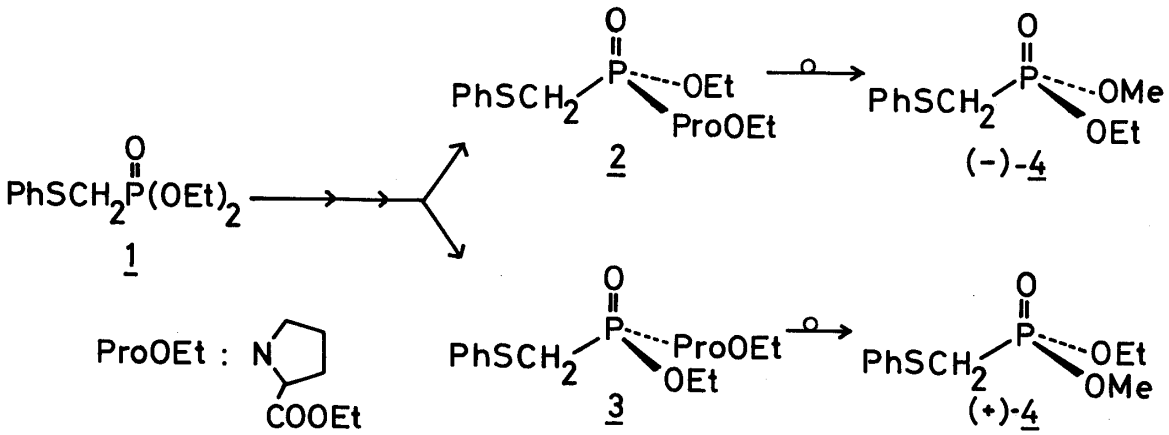
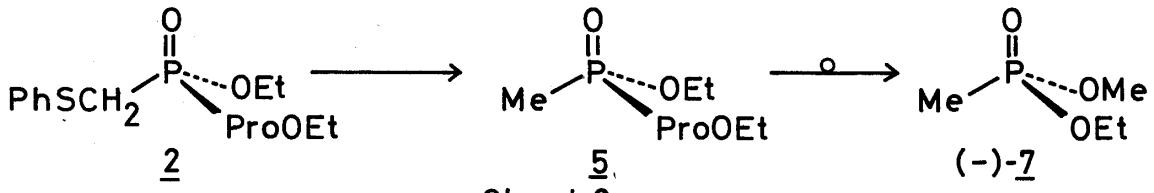


Chart 1

NII-Electronic Library Service

methanephosphonic chloridate, which was obtained from diethyl phenylsulfenylmethanephosphonate 1 by alkaline hydrolysis followed by chlorination with thionyl chloride.[6] The diastereomers were easily separated by column chromatography on silica gel to give the phosphonamidates 2 and 3 in 30 and 32% overall yields respectively.[7] Treatment of the each diastereomer with methanolic sulfuric acid gave the corresponding optically active ethyl methyl phenylsulfenylmethanephosphonates 4 in 70-75% yield.[8] The optical purities of (+)-4 and (-)-4 were determined to be no less than 93% by the NMR method using shift reagent $Eu(hfc)_3$.[9] The absolute configurations of 2 and 3 were then chemically correlated with (-)-$(S)_P$- or (+)-$(R)_P$-ethyl methyl methanephosphonate 7[10] as shown in Chart 2. The phosphonamidates 2 and 3 were



2 5 (-)-7

Chart 2

treated with Raney Ni(W4) in EtOH to afford the methylphosphonamidate 5 and 6 in 89 and 84% yields respectively.[11] Acid-catalyzed methanolysis(1M H_2SO_4-MeOH) of 5 and 6 provided the optically active ethyl methyl methanephosphonates (-)-$(S)_P$-7 and (+)-$(R)_P$-7 in 60 and 62% yields respectively.[10, 12] From these results the absolute configurations of 2, 3, 4, 5, and 6 were determined as depicted in Chart 1 and 2.

Although the present study is concerned only with optically active ethyl phenylsulfenylmethanephosphonyl derivatives, the method can be applied to other alkyl phenylsulfenylmethanephosphonates.[13] Our method has advantages in that the acid-catalyzed alcoholysis of 2 (or 3) and 5 (or 6) may provide, as shown in our previous reports[5], various phosphonates of known absolute configurations with high optical purities. Furthermore, the phenylsulfenylmethanephosphonates could be converted by known methods[2, 4] into various chiral phosphonyl derivatives. The research along this line is now in progress in this laboratory and the results in part are described in the succeeding paper.

ACKNOWLEDGEMENT This work was partially supported by grants to T. K., for Developmental Scientific Research (No 57570755) from the Ministry of Education, Sciences, and Culture of Japan and for Scientific Research 1982 from the Naito foundation.

REFERENCES AND NOTES

1) All new compounds were fully characterized spectroscopically(IR, ^1H NMR, MS spectra) and by combustion and/or high resolution mass spectral analyses.
2) J. Drabowitz and M. Mikołajczyk, Synthesis, 1978, 758.
3) a) E. J. Corey and J. I. Shulman, J. Org. Chem., 35, 777(1970);
b) E. J. Corey and J. I. Shulman, J. Am. Chem. Soc., 92, 5522(1970);

NII-Electronic Library Service

c) M. Mikołajczyk, S. Grzejszczak, and A. Zatorski, J. Org. Chem., 40, 1979(1975);
d) M. Mikołajczyk, G. Grzejszczak, and P. Łyżwa, Tetrahedron Letters, 23, 2237 (1982).

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

5) a) T. Koizumi, Y. Kobayashi, and E. Yoshii, J. Org. Chem., 42, 3459(1977);
b) T. Koizumi, H. Amitani, and E. Yoshii, Tetrahedron Letters, 1978, 3741;
c) T. Koizumi, H. Amitani, and E. Yoshii, Synthesis, 1979, 110;
d) T. Koizumi, H. Takagi, and E. Yoshii, Chemistry Letters, 1980, 1403;
e) T. Koizumi, Y. Kobayashi, E. Yoshii, M. Takamoto, K. Kamiya, and H. Asakawa, Tetrahedron Letters, 21, 3995(1980).

6) To a solution of diethyl phenylsulfenylmethanephosphonate 1(3.5 g) in EtOH(10 ml) was added 2*N* aq. NaOH solution(13 ml) and the mixture was heated under reflux for 1-2 h. The alkaline solution was acidified with dil H_2SO_4 to pH 1 and was extracted with ether(10 mlx4). The ether extracts was washed with brine(10 ml x2) and dried over magnesium sulfate. The solvent was evaporated to give an oily product(3.3 g), which was heated with thionyl chloride(8.2 g) at 70-80°C for 1 h. Excess thionyl chloride was evaporated to give crude phosphonic chloridate, to which was added a mixture of triethylamine(5 ml) and freshly prepared ethyl L-prolinate(1.8 g) in THF(5 ml) with stirring. The reaction mixture was kept overnight at r. t. and worked up as usual. The crude phosphonamidate was separated by silica gel column chromatography eluting with ethyl acetate.

7) 2: bp(Torr) 165-175(0.1); $[\alpha]_D^{26}$ -86.2°(c 1.4, MeOH); TLC R_f 0.47(AcOEt).

3: bp(Torr) 165-175(0.1); $[\alpha]_D^{26}$ -8.7°(c 1.2, MeOH); TLC R_f 0.37(ACOEt).

All distillations were carried out by use of Kugelrohr apparatus, and the bath temperatures are described.

8) The methanolysis was conducted by using 1*M* H_2SO_4-MeOH solution. (see ref.5).

(-)-4 from 2: bp(Torr) 95-105(0.1); $[\alpha]_D^{24}$ -1.4°(c 1.8, MeOH).

(+)-4 from 3: bp(Torr) 95-105(0.1), $[\alpha]_D^{24}$ +1.7°(c 1.9, MeOH).

9) The same degree of optical purities was obtained by HPLC using JASCO chiral PAK (+)-T.

10) a) C. R. Hall, T. D. Inch, C. J. Lewis, and R. A. Chittenden, J. Chem. Soc., Chem. Commun., 1975, 720;
b) D. B. Cooper, C. R. Hall, J. M. Harrison, and T. D. Inch, J. Chem. Soc., Perkin Trans. 1, 1977, 1969.

11) 5: bp(Torr) 100-105(0.1); $[\alpha]_D^{24}$ -88.6°(c 1.3, MeOH).

6: bp(Torr) 100-105(0.1); $[\alpha]_D^{24}$ -10.8°(c 1.2, MeOH).

12) (-)-7: bp(Torr) 80-90(15); $[\alpha]_D^{24}$ -1.9°(c 1.1, $CHCl_3$).

(+)-7: bp(Torr) 80-90(15); $[\alpha]_D^{24}$ +1.7°(c 1.2, $CHCl_3$).

13) When starting with di-n-butyl phenylsulfenylmethanephosphonate, the corresponding diastereomeric n-butyl phenylsulfenylmethanephosphonamidate 8 and 9 were obtained in 25 and 22% yields respectively.

8: bp(Torr) 170-180(0.15); TLC R_f 0.60(AcOEt:PhH=2:1); $[\alpha]_D^{26}$-70.6°(c 1.1, MeOH).

9: bp(Torr) 175-185(0.15); TLC R_f 0.51(ACOEt:PhH=2:1); $[\alpha]_D^{26}$-28.2°(c 1.2, MeOH).

The methanolysis (1*M* H_2SO_4-MeOH) of 8 and 9 afforded optically active n-butyl methyl phenylsulfenylmethanephosphonate 10 in 40-50% yield.

(-)-10 from 8: bp(Torr) 130-140(0.05-0.1); $[\alpha]_D^{24}$ -2.9°(c 1.8, MeOH).

(+)-10 from 9: bp(Torr) 130-140(0.05-0.1); $[\alpha]_D^{24}$ +2.8°(c 1.8, MeOH).

(Received September 16, 1983)

NII-Electronic Library Service