PREPARATION OF OPTICALLY ACTIVE 1,3,2-OXATHIAPHOSPHORINANES USING (-)-10-MERCAPTOISOBORNEOL AS A CHIRAL SOURCE†

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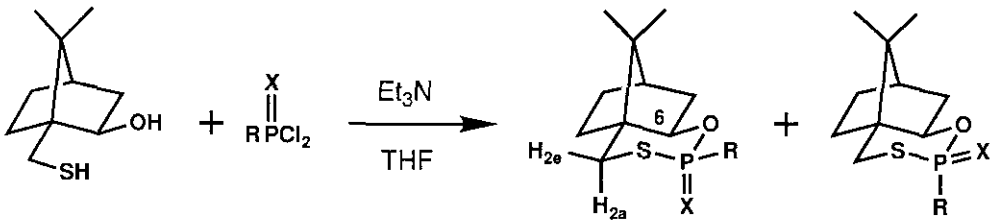
Abstract——Optically active 1,3,2-oxathiaphosphorinanes (3) and (4) were prepared from (-)-10-mercaptoisoborneol (1) and phosphorus dichlorides [$RP(X)Cl_2$] (2). The configuration at phosphorus in these derivatives was assigned on the basis of their ^1H nmr spectral data and X-ray diffraction analysis of 4f.

For the preparation of chiral phosphorus compounds, simple and practical methods have so far been established using optically active amines, such as (-)-ephedrine,[1] L-proline ethyl ester,[2] and L-prolinol,[3] as chiral sources. The diastereomeric phosphorus amides [N-P(X)<], thus obtained from these amines, were separated and subjected to stereoselective P-N bond fission to give simple chiral phosphorus esters. However, there has been little information available concerning the use of other chiral sources, such as diols and hydroxy-thiols, for the practical synthesis. For hydroxy-thiols, there has been only one report with D-glucopyranoside derivatives giving 1,3,2-oxathiaphosphorinanes.[4] The method requires four steps to get the starting chiral thiols from methyl 2,3-di-O-methyl-α-D-glucopyranoside and does not seem to be a practical method to obtain optically active phosphorus compounds in general. Recently, Modena et al.[5] and we[6] have indicated that (-)-10-mercaptoisoborneol (1) is a valuable chiral source for the preparation of optically active sulfoxides. The hydroxy-thiol (1) is obtained quite easily in two steps from commercially available (+)-10-camphorsulfonic acid. We thus planned to prove that 1 is useful for obtaining chiral phosphorus compounds. In the present studies, we found that the reaction of 1 with phosphorus dichlorides [$RP(X)Cl_2$] (2) gave 1,3,2-oxathiaphosphorinanes as a mixture of diastereomers in fair yield and that the optically active oxathiaphosphorinanes (3) and (4) were separated readily by column and/or thin layer chromatography (silica gel). In addition, we determined the absolute configuration at phosphorus of 3 and 4.

A mixture of (-)-10-mercaptoisoborneol (1) and phosphorus dichlorides [$RP(X)Cl_2$] (2) (1 equivalent) was stirred in anhydrous tetrahydrofuran (THF) in the presence of triethylamine (2 equivalents) (Scheme 1). The diastereomeric 1,3,2-oxathiaphosphorinanes (3) and (4) were obtained and separated readily.[7] Yield, melting

† This paper is dedicated to the memory of the late Professor Tetsuji Kametani.



(-)-1 2a-h 3a-h 4a-h

Scheme 1

Table 1. Yield, mp, and optical rotations of 1,3,2-oxathiaphosphorinanes (3) and (4)

Compound	R	X	Yield(%)	mp(°C)	$[\alpha]_D$ deg.
3a	Ph	O	21	135-136	+98.0
4a	Ph	O	29	160-161	-40.9
3b	PhO	O	27	130-131	-205.7
4b	PhO	O	24	81-82	+152.7
3c	$PhCH_2$	O	17	192-193	+104.8
4c	$PhCH_2$	O	15	163-164	-26.3
3d	CH_2=$CHCH_2$	O	24	syrup	+67.4
4d	CH_2=$CHCH_2$	O	15	76-78	-1.6
3e	CH_2=C=CH	O	22	69-70	+113.6
4e	CH_2=C=CH	O	13	97-99	-106.5
3f	EtOC(O)CH_2	O	17	syrup	+54.6
4f	EtOC(O)CH_2	O	13	91-92	-8.2
3g	$PhSCH_2$	O	49	80-81	+80.5
4g	$PhSCH_2$	O	12	94-97	-8.9
3h	Ph	S	29	syrup	+50.2
4h	Ph	S	20	133-135	-45.8

points, and optical rotations of 3 and 4 are shown in Table 1. Ir, ^{1}H nmr, and ^{31}P nmr spectral data are summarized in Table 2. The configuration at phosphorus was assigned from the chemical shifts of H-6 signals in the ^{1}H nmr spectra. H-6 signal of 3 appeared at lower field than that of 4. In other words, the P=X (X=O, S) group must be oriented cis to H-6 in 3.[1] This assignment was confirmed by a single-crystal X-ray diffraction study of 4f (Figure 1).[8] The configurational assignment to the 2-sulfides (3h) and (4h) was evidenced by chemical correlations with the corresponding 1,3,2-oxathiaphosphorinane 2-oxides; oxidation with m-chloroperbenzoic acid converted 3h and 4h into 3a and 4a, respectively, under the conditions known to give configurationally retained products.[9]

Table 2. Ir, ^{1}H nmr, and ^{31}P nmr spectral data of 1,3,2-oxathiaphosphorinanes (3) and (4)

Compound	Ir $\nu_{P=O}(cm^{-1})$	^{1}H nmr[c] (δ) H_{2e}	H_{2a}	H_6	Coupling constants (Hz) P,H_{2e}	P,H_{2a}	P,H_6	^{31}P nmr[c,d] (δ)
3a	1235[a]	2.74	2.88	4.72	22.2	8.1	8.4	-41.61
4a	1235[a]	2.84	3.28	4.21	14.2	14.2	3.7	-41.47
3b	1270[a]	2.88	3.21	4.71	23.7	6.4	0	-13.51
4b	1255[a]	2.58	2.87	4.54	28.3	10.0	6.4	-24.04
3c	1220[a]	2.40	2.26	4.50	23.0	5.7	8.9	-48.79
4c	1220[a]	2.72	3.20	3.79	15.6	12.0	4.0	-52.27
3d	1240[b]	2.60	2.88	4.51	23.6	5.5	8.7	-52.82
4d	1230[a]	2.82	3.21	4.17	14.5	12.9	3.9	-48.51
3e	1260[b]	2.64	2.86	4.54	25.4	7.8	8.6	-37.82
4e	1225[a]	3.16	2.92	4.31	15.9	13.4	4.2	-34.07
3f	1245[b]	2.65	3.00	4.53	26.1	6.4	8.8	-44.68
4f	1255[b]	2.90	3.24	4.32	14.5	14.5	3.9	-39.21
3g	1240[a]	2.64	3.15	4.52	24.4	5.4	8.8	-48.77
4g	1240[a]	2.84	3.21	4.13	15.4	12.7	3.8	-45.34
3h	1260[b]	2.92	2.96	4.76	14.2	0	8.8	33.03
4h	1260[a]	3.11	2.95	4.15	17.0	11.0	3.2	37.02

a: KBr, b: neat, c: measured in $CDCl_3$, d: from 85% H_3PO_4 (low field negative)

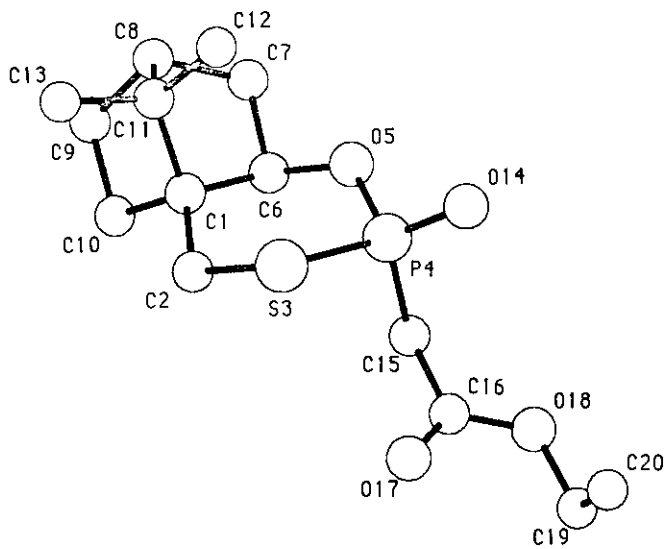
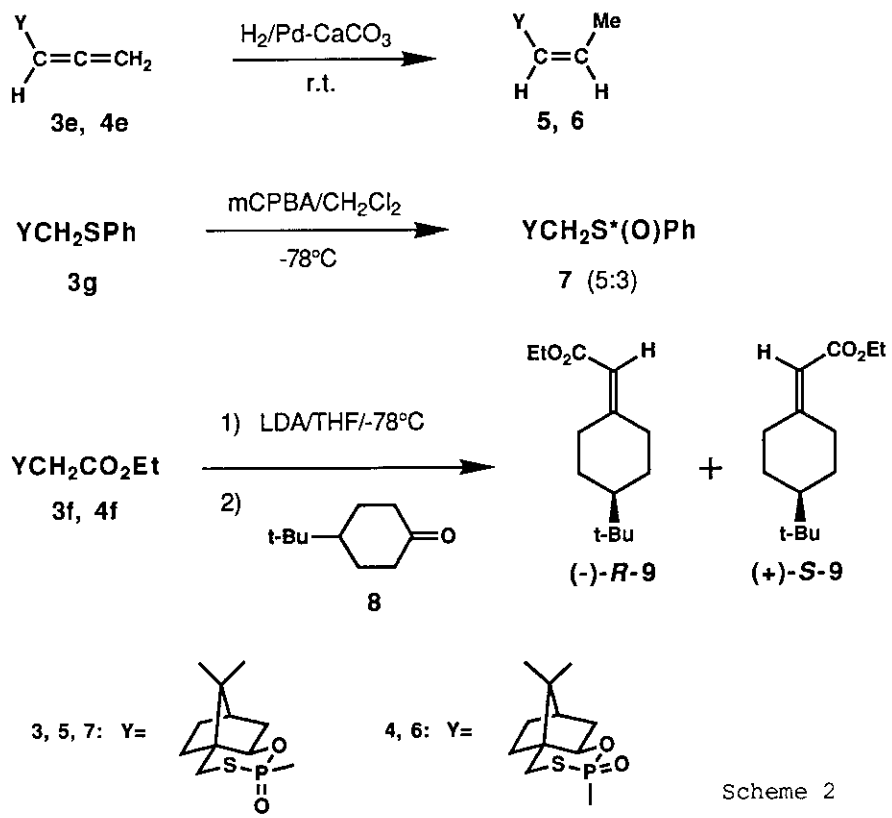


Figure 1. Perspective Structure of 4f

The optically active oxathiaphosphorinanes thus obtained may be applied to the synthesis of other chiral compounds in two ways: (i) a transformation to simple chiral phosphorus compounds by the known P-O and P-S bond fission[4] and (ii) an application to diastereoselective reactions[10] without cleavage of the phosphorinane ring. We investigated along the latter line and obtained several results in the preliminary experiments (Scheme 2). Hydrogenation of the allene phosphonates (3e) and (4e)[11] proceeded stereoselectively in the presence of Lindlar catalyst to give cis-1-propene phosphonates (5) and (6), respectively.[12] cis-Olefins (5) and (6) would be desirable for a chiral synthesis of fosfomycin.[13] Oxidation of the sulfenylmethanephosphonate (3g) with m-chloroperbenzoic acid gave the sulfinylmethanephosphonate (7)[14] as a mixture of diastereomers (5:3). Moreover, an attempt to apply the chiral phosphorinanes to an asymmetric Emmons-Horner reaction was performed with the anion of 3f and 4-tert-butylcyclohexanone (8) in THF. A mixture of R and S olefins (9) was obtained in 59% yield corresponding to an optical purity of 16% e.e.[15] in favor of the (-)-R isomer.[16] The ratio was reversed with the diastereomer 4f. We are currently studying the reactions with 3 and 4.



Scheme 2

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REFERENCES AND NOTES

1. C. R. Hall and T. D. Inch, J. Chem. Soc., Perkin Trans. 1, 1979, 1104; D. B. Cooper, J. M. Harrison, and T. D. Inch, Tetrahedron Lett., 1974, 2697.
2. T. Koizumi, Y. Kobayashi, H. Amitani, and E. Yoshii, J. Org. Chem., 1977, 42, 3459.
3. T. Koizumi, R. Yanada, H. Takagi, H. Hirai, and E. Yoshii, Tetrahedron Lett., 1981, 22, 477.
4. D. B. Cooper, J. M. Harrison, T. D. Inch, and G. J. Lewis, J. Chem. Soc., Perkin Trans. 1, 1974, 1049, 1058.
5. O. De Lucchi, C. Marchioro, G. Valle, and G. Modena, J. Chem. Soc., Chem. Commun., 1985, 878; O. De Lucchi, V. Lucchini, C. Marchioro, G. Valle, and G. Modena, J. Org. Chem., 1986, 51, 1457.
6. Y. Arai, K. Hayashi, T. Koizumi, M. Shiro, and K. Kuriyama, Tetrahedron Lett., 1988, 29, 6143.
7. All new compounds gave satisfactory spectroscopic and analytical data. Optical rotations were taken in $CHCl_3$ (c 0.67-1.24).
8. Crystal data are: $C_{14}H_{23}O_4PS$, M=318.3, orthorhombic, space group $P2_12_12_1$, a=10.763(1), b=15.406(1), c=9.478(1) Å, V=1571.6(2) $Å^3$, D_c=1.346 g cm^{-3}, z=4, R=0.044 for 1487 reflections. Atomic coordinates, bond lengths, and bond angles have been deposited at the Cambridge Crystallographic Data Centre.
9. A. W. Herriott, J. Am. Chem. Soc., 1971, 93, 3304.
10. (a) D. H. Hua, R. Chan-Yu-King, J. A. McKie, and L. Myer, J. Am. Chem. Soc., 1987, 109, 5026; (b) S. Hanessian, D. Delorme, S. Beaudoin, and Y. Leblanc, ibid., 1984, 106, 5754; (c) S. E. Denmark and J. E. Marlin, J. Org. Chem., 1987, 52, 5742; (d) S. E. Denmark, G. Rajendra, and J. E. Marlin, Tetrahedron Lett., 1989, 30, 2469.
11. For the synthesis of allene phosphonates, there has so far been only one report by Denmark and Marlin. They have applied the cyclic allene phosphonates to an asymmetric Claisen rearrangement, see ref. 10c.
12. The geometry about C=C double bonds of 5 and 6 was assigned by comparing their ^1H nmr data with those of cis- and trans-1-butene phosphonates; A. A. Petrov, B. I. Ionin, and V. M. Ignatyev, Tetrahedron Lett., 1968, 15.
13. C. Giordano and G. Castaldi, J. Org. Chem., 1989, 54, 1470, and references cited therein.
14. Optically active sulfinylmethanephosphonates have been converted to chiral sulfinylethenes; T. Koizumi, M. Iwata, N. Tanaka, and E. Yoshii, Chem. Pharm. Bull., 1983, 31, 4198.
15. The optical purity was checked by the 270 MHz ^1H nmr spectroscopy with a chiral shift reagent, $Eu(hfc)_3$.
16. The absolute configuration of the favored enantiomer was determined by conversion of the mixture to the corresponding carboxylic acids; M. Duraisamy and H. M. Walborsky, J. Am. Chem. Soc., 1983, 105, 3252.

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