Tetrahedron Letters,Vol.25,No.23,pp 2493-2496,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

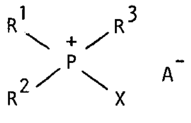
A GENERAL SYNTHESIS OF OPTICALLY ACTIVE PHOSPHINES,PHOSPHINITES AND THIOPHOSPHINITES FROM ALKYLTHIO(ALKYLSELENO)PHOSPHONIUM SALTS AND TRIS(DIMETHYLAMINO)PHOSPHINE AS A THIOPHILIC AGENT

J.Omelańczuk and M.Mikołajczyk*

Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Organic Sulfur Compounds,90-362 Łódź,
Boczna 5, Poland

Abstract: *Tris(dimethylamino)phosphine was found to be a suitable thiophilic reagent which converts optically active alkylthio(alkylseleno)phosphonium salts into chiral tertiary phosphines and phosphinites with a high stereoselectivity. The first synthesis of optically active thiophosphinites from bis(alkylthio)phosphonium salts and tris(dimethylamino)phosphine is also reported.*

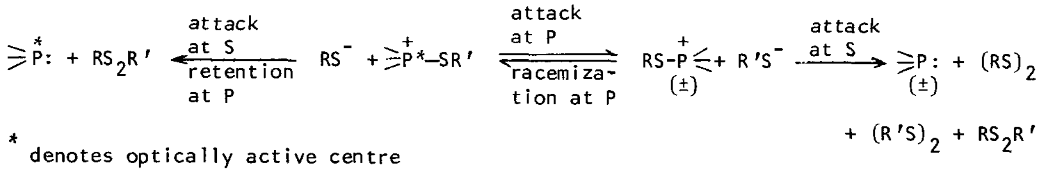
There has been a continuing interest in optically active tertiary phosphines and trivalent phosphorus acids derivatives as model compounds in the study of the mechanism and stereochemistry of reactions taking place at phosphorus[1] and also as potential ligands in asymmetric catalysis[2]. Recently, new methods have been developed for the stereoselective synthesis of optically active trivalent phosphorus compounds in which optically active heterophosphonium salts (1) are used as convenient starting materials.



1

R^1,R^2= Alk,Ar
R^3= All,Bz,H
X = OR,SR,SeR,NR_2

These methods include electroreduction of 1[3a,b,c], cyanolysis of the P-C or P-S bond in 1[3c,e], reaction of alkanethiolate anions with alkylthio(alkylseleno)phosphonium salts[4] and deprotonation of alkoxyphosphonium salts containing the P-H bond[5]. Although these methods allowed to prepare for the first time optically active phosphinous acid esters and amides, all of them, however, are not general and have some serious limitations. For instance, in spite of many attempts[3d,f], Horner and Jordan were not able to synthesize optically active thiophosphinites. The disadvantage of the method developed in our Laboratory[4] is that it requires the use of sterically hindered substituents at phosphorus in alkylthio(alkylseleno)phosphonium salts or bulky mercapto-anions (like t-BuS$^-$) in order to get optically active P^{III} compounds. This is connected with the fact that alkanethiolate anions tend to react primarily at phosphorus and then at sulfur in alkylthiophosphonium salts which causes racemization due to the fast alkylthio-alkylthio exchanges at phosphorus. The two possible reaction pathways and their relationship with the stereochemistry at phosphorus are shown below.



* denotes optically active centre

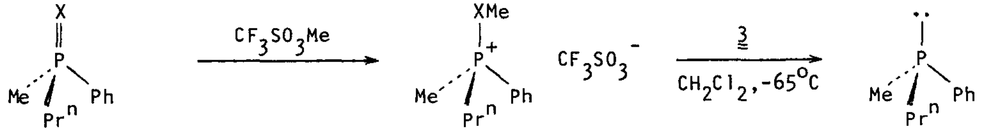
In the hope of overcoming the difficulties discussed above we investigated the behaviour of alkylthio(alkylseleno)phosphonium salts towards other thiophilic reagents. Among the thiophiles tested [NCS^-, $NCSe^-$, CN^-, $P(NMe_2)_3$] *tris(dimethylamino)phosphine* (3) - *known as excellent* desulfurizing agent[6] - was found to be the reagent of choice. The results obtained with 3 are reported here.

In the first part of this study we have demonstrated that achiral phosphonium trifluoromethanesulfonates (2a-c)[4a] react with 3 very cleanly affording alkylthio- or alkylseleno tris-(dimethylamino)phosphonium salt (4) and the corresponding phosphines 5a and 5b in a high yield. Moreover, this reaction was found by means of ^{31}P NMR spectra to be irreversible.

$$\underset{2}{R^1R^2R^3\overset{+}{P}XMe}\quad CF_3SO_3^- \xrightarrow[CH_2Cl_2]{(Me_2N)_3P,\,3} \underset{5}{R^1R^2R^3P:} \quad + \quad \underset{4}{MeX\overset{+}{P}(NMe_2)_3}\quad CF_3SO_3^-$$

2	5	yield(%)
a, $R^1=R^2=R^3=Ph$, X=S	a,	79
b, $R^1=R^2=R^3=Ph$, X=Se	a,	76
c, $R^1=R^2=R^3=Bu$, X=S	b,	80

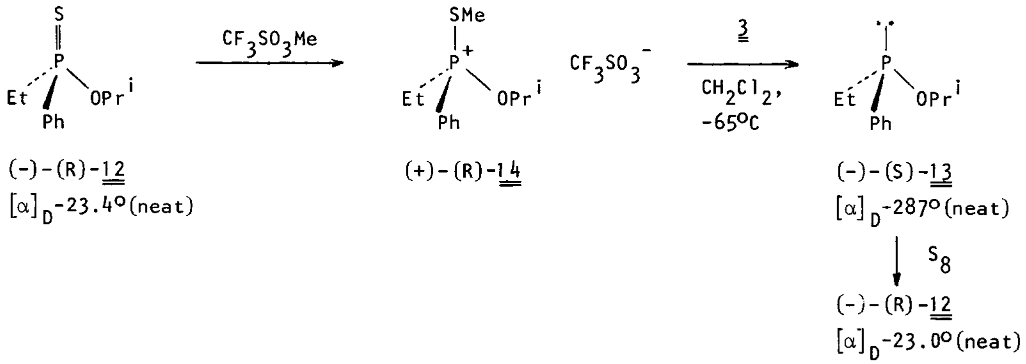
To check the stereochemistry of the above reaction the experiments with optically active methylthio-methyl-*n*-propylphenylphosphonium trifluoromethanesulfonate (7)[4a,7] and its selenium analogue 8 were carried out. Thus, treatment of 7 with 3 at low temperature gave optically active methyl-*n*-propylphenylphosphine (9) in 30% yield[8]. Similarly, optically active 9 was obtained from 8 and 3 in 56% yield.



(+)-(R)-10, X=S $[\alpha]_D$+21.7°(MeOH)(97.5% op)	(+)-(R)-7	(+)-(S)-9 $[\alpha]_D$+15.5°(PhH)(79% op)
(+)-(R)-11, X=Se $[\alpha]_D$+20.4°(MeOH)(100% op)	(+)-(R)-8	(+)-(S)-9 $[\alpha]_D$+16.1°(PhH)(82% op)

A comparison of the optical purity values of and chirality at phosphorus in the phosphine 9 obtained with those of the phosphine sulfide 10 and selenide 11 used for the preparation of the salts 7 and 8 indicates that both conversions 7→9 and 8→9 occured with a high stereoselectivity and retention of configuration at phosphorus. It is worthy of note that, in contrast to *thiolate anions, the use of 3 as a thiophilic reagent in these reactions* permits the synthesis of chiral, sterically unhindered tertiary phosphines.

Tris(dimethylamino)phosphine (3) was also found to be a suitable reagent for the synthesis of simple, optically active phosphinous acid esters. The almost fully stereoselective conversion of (-)-(R)-O-isopropyl ethylphenylphosphinothionate (12) into (-)-(S)-O-isopropyl ethylphenylphosphinite (13) *via* the corresponding phosphonium salt 14 is the best exemplification.



(-)-(R)-12 $[\alpha]_D$ -23.4°(neat)

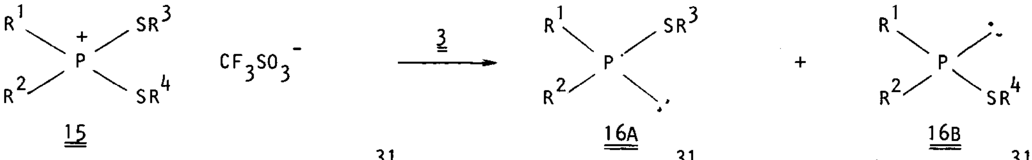
(+)-(R)-14

(-)-(S)-13 $[\alpha]_D$ -287°(neat)

(-)-(R)-12 $[\alpha]_D$ -23.0°(neat)

The reaction of 3 with the salt 14 prepared as described earlier gave, after the usual work-up and distillation, the ester (-)-13 in 78% yield. Its reaction with elemental sulfur taking place with retention of configuration at phosphorus[9] afforded the starting phosphinothionate 12 with almost full optical activity (98.3%) and the same (-)-(R) configuration at phosphorus.

Finally, it should be emphasized that we succeeded in accomplishing the first stereoselective synthesis of optically active thiophosphinites. In this case, chiral bis(alkylthio)phosphonium salts 15 were used as substrates. Generally, the reaction of 3 with the salts 15 bearing two different alkylthio groups at phosphorus may result in the formation of two different thiophosphinites 16A and 16B. This was found, indeed, for the salts 15a-c (^{31}P NMR assay). However, in the case of the salts 15d and 15e containing methylthio and isopropylthio groups we observed exclusive formation of the one product 16B derived from a regioselective attack of 3 at the sterically better accessible sulfur atom of the methylthio group. The results obtained are summarized below.



15

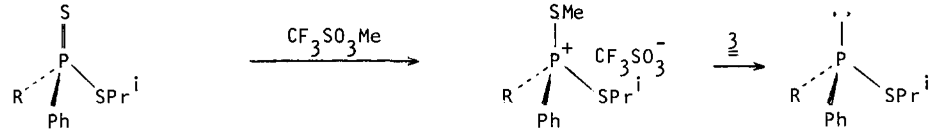
16A

16B

15	δ^{31}P	16A (%)	δ^{31}P	16B (%)	δ^{31}P
a, R^1=Ph,R^2=Et,R^3=Me,R^4=Et	85.2	21	31.3	79	28.0
b, R^1=Ph,R^2=Bu^t,R^3=Me,R^4=Et	99.7	5	59.6	95	50.7
c, R^1=Ph,R^2=Et,R^3=Me,R^4=Pr^n	-	16.5	31.3	83.5	29.2
d, R^1=Ph,R^2=Et,R^3=Me,R^4=Pr^i	83.6	0		100	22.3
e, R^1=Ph,R^2=Bu^t,R^3=Me,R^4=Pr^i	97.6	0		100	44.9

Starting from optically active phosphonium salts 15d and 15e obtained from (-)-(S)-phosphinodithioates 17d and 17e we were able to obtain optically active (-)-(S)-thiophosphinites 16B-d and 16B-e. Their sulfurization gave back (-)-(S)-17d, $[\alpha]_D$ -45.3 and (-)-(S)-

-17e, $[\alpha]_D$-30.8, with 43.5 and 65% of the initial optical activity, respectively. The experiments carried out are summarized below.



(-)-(S)-17d, $[\alpha]_D$-104.1°(neat),R=Et
(-)-(S)-17e, $[\alpha]_D$-47.3°(PhH),R=Bu^t

(-)-(S)-15d
(-)-(S)-15e

(-)-(S)-16B-d, $[\alpha]_D$-156.6°(neat)
(-)-(S)-16B-e, $[\alpha]_D$-153.8°(neat)

$\downarrow S_8$

(-)-(S)-17d, $|\alpha|_D$-45.3(neat)
(-)-(S)-17e, $|\alpha|_D$-30.8(PhH)

The successful synthesis of optically active thiophosphinites indicates that the energy for pyramidal inversion at phosphorus in this class of chiral compounds is comparable with that of other phosphinous acid derivatives. The slow decrease of optical rotation of 16B-d and 16B-e observed on standing at room temperature may be due to chemically induced racemization and not to pyramidal inversion. This point as well as the application of 3 to the synthesis of other chiral trivalent phosphorus compounds are under current study.

References and Notes

1. M.Mikołajczyk, *Pure and Appl.Chem.*, 52, 959 (1980).
2. L.Horner, *Pure and Appl.Chem.*, 52, 843 (1980).
3. (a) L.Horner and M.Jordan, *Phosphorus and Sulfur*, 6, 491 (1979); (b) L.Horner and M.Jordan, *ibid.*, 8, 209 (1980); (c) L.Horner and M.Jordan, *ibid.*, 8, 215(1980); (d) L.Horner and M.Jordan, *ibid.*, 8, 221 (1980); (e) L.Horner and M.Jordan, *ibid.*, 8, 225 (1980); (f) L.Horner and M.Jordan, *ibid.*, 8, 235 (1980).
4. (a) J.Omelańczuk and M.Mikołajczyk, *J.Am.Chem.Soc.*, 101, 7292 (1979); (b) J.Omelańczuk, W.Perlikowska and M.Mikołajczyk, *J.C.S.Chem.Commun.*, 1980, 24; (c) J.Omelańczuk and M.Mikołajczyk, *Phosphorus and Sulfur*, 15, 321 (1983).
5. L.J.Szafraniec, L.L.Szafraniec and H.S.Aaron, *J.Org.Chem.*, 47, 1936 (1982).
6. D.H.Harpp, J.Gleason and D.Ash, *J.Org.Chem.*, 36, 322 (1971).
7. All optically active phosphonium trifluoromethanesulfonates were obtained from the appropriate thio-or selenophosphoryl compounds and methyl trifluoromethanesulfonate in CH$_2$Cl$_2$ solution at room temperature and used in the crude state for further transformations.
8. The lower yields of 2 are due to a small scale of the experiments with optically active compounds.
9. D.P.Young, W.E.McEven, D.C.Velez, J.W.Johnson and G.A.Van der Werf, *Tetrahedron Lett.*, 359 (1964); L.Horner, *Pure Appl.Chem.*, 225 (1964).

(Received in UK 26 March 1984)