Heteroatom Chemistry
Volume 2, Number 1, 1991

The Synthesis of *P*-Chiral Optically Pure Phosphorothioates, Phosphorotrithioates, Phosphoroselenothioates, Methanephosphonothioates, and Methylphenylphosphinothioates

Bożenna Krzyżanowska and Wojciech J. Stec*

Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Department of Bioorganic Chemistry, Sienkiewicza 112, 90-363 Łódź, Poland

Received 27 June 1990.

ABSTRACT

Enantiomers of representative alkyl esters of phosphorothioic (**7**), *phosphorodithioic* (**6**), *phosphorotrithioic* (**11**), *phosphoroselenothioic* (**9**), *methanephosphonothioic* (**28**), *methanephosphonodithioic* (**25**), *and methylphenylphosphinothioic* (**31**) *acids were prepared from corresponding pure diastereoisomers of* N-[R(+)- *or* S(−)-*α-methylbenzyl*] *phosphamidochalcogenates* (*e.g.* **2**, **3**, **12**, **17**, **23**, **26**, *and* **30**) via *PN* → *PX conversion, which has been proved to proceed with full retention of configuration at phosphorus.*

INTRODUCTION

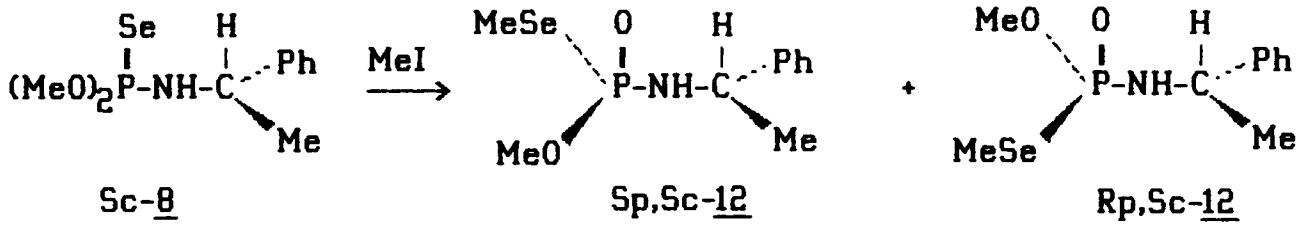
In an earlier paper [1] we presented our results on the rearrangement of *P*-prochiral *O,O*-dimethyl-*N*-(α-methylbenzyl)phosphoramidothioates (**1**), derivatives of optically active *R*(+)- or *S*(−)-(α-methylbenzyl)amine, into *O,S*-dimethyl-*N*-(α-methylbenzyl)phosphoramidothioates (**2**), which can easily be separated into diastereoisomeric species via fractional crystallization. Interestingly, the epimeric pairs Rp,Rc- and Sp,Sc-**2** are obtainable in pure diastereoisomeric forms without necessity of chromatographic purification. Ethanolysis of individual diastereoisomers of **2** performed in the presence of $AgNO_3$ leads to *O*-ethyl-*O*-methyl-*N*-(α-methylbenzyl)phosphoramidates (**3**). Each diastereoisomer of **2** or **3** under treatment with NaH/CS_2 (or KH/CS_2) gives *O,S*-dimethyl phosphorodithioate (**4**) or *O*-ethyl-*O*-methyl phosphorothioate (**5**), respectively, which, after alkylation, provide neutral enantiomers of *O,S*-dimethyl-*S*-alkyl phosphorodithioate (**6**) or *O*-ethyl-*O*-methyl-*S*-alkyl phosphorothioate (**7**). We have also demonstrated [2] that similar transformations of *O,O*-dimethyl-*N*-(α-methylbenzyl)phosphoramidoselenoate (**8**) allow us to prepare enantiomers of *O,S*,Se-trimethyl phosphoroselenothioate (**9**), while N^1,N^2-diphenyl-N^3-(α-methylbenzyl)phosphortriamidates (**10**) under stepwise treatment with NaH/CS_2, followed by alkylation and separation of diastereoisomers, give the enantiomers of *S*-ethyl-*S*-methyl-*S*-propyl phosphorotrithioate (**11**). In this report we wish to present experimental details for preparation of the above compounds as well as some new results on preparation of enantiomers of *P*-chiral methanephosphonothioates and methylphenylphosphinothioates.

RESULTS

Condensation of *O,O*-dimethyl phosphorochloridite with enantiomeric *N*-α-methylbenzylamine, followed by addition of elemental selenium, gives Rc- and Sc-**8**. Heating a methylene chloride solution of **8** with MeI effects a Pistchimuka Rearrangement and leads to an equimolar mixture of diastereo-

*To whom correspondence should be addressed.

1042-7163/91/$3.50 + .25



Sc-8 Sp,Sc-12 Rp,Sc-12

SCHEME 1

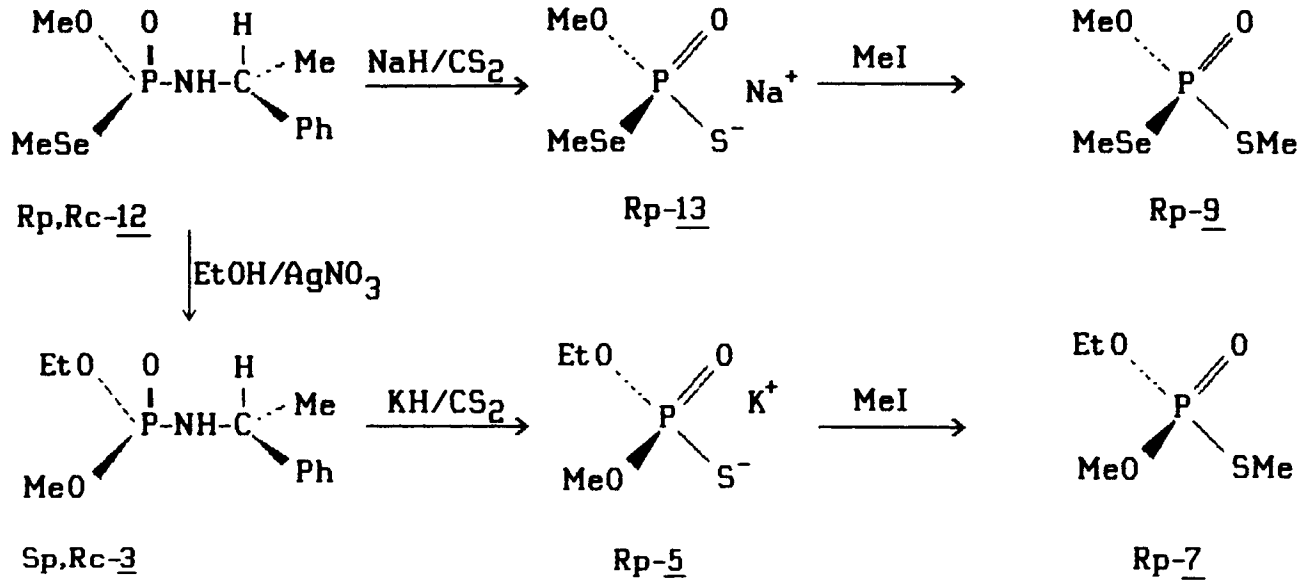
isomers of *O*,Se-dimethyl-*N*-(α-methylbenzyl)phosphoramidoselenoate (**12**) (Scheme 1). Solvolysis of each separated diastereoisomer **12** by means of EtOH in the presence of $AgNO_3$ gives the corresponding *O*-ethyl-*O*-methyl-*N*-(α-methylbenzyl)phosphoramidates (**3**).

Independently, each diastereoisomer of **12**, under treatment with NaH/CS_2 in DMF solution, gives the corresponding enantiomer of *O*-methyl-Se-methyl phosphoroselenothioate (**13**), while under similar conditions compounds **3** are converted into *O*-ethyl-*O*-methyl phosphorothioates (**5**). Methylation of **13** and **5** gives enantiomers of *O*,*S*,Se-trimethyl phosphoroselenothioate (**9**) and enantiomers of *O*,*S*-dimethyl-*O*-ethyl phosphorothioate (**7**), respectively (Scheme 2). The optical purity of each of the enantiomers **13** has been confirmed following its conversion into the corresponding α-methylbenzylammonium salt [3] (Figure 1). The optical purity of **7** has been confirmed on the basis of its optical rotation in comparison with the literature value [4].

A route to *P*-chiral phosphorotrithioates was opened through the preparation of **10**, available from condensation of *N*,*N*-diphenyl phosphordiamidochloridate [5] with enantiomers of α-methylbenzylamine. Reaction of **10** with NaH/CS_2 is fully chemoselective and leads to an equimolar mixture of diastereoisomers of *N*-phenyl-*N'*-(α-methylbenzyl)phosphorodiamidothioate (**14**), which, after alkylation with MeI, give diastereoisomers of *S*-methyl-*N*-phenyl-*N'*-(α-methylbenzyl)phosphordiamidothioates (**15**) (Scheme 3). When the separated diastereoisomers of **15** are treated with NaH/CS_2 and the resulting *S*-methyl-*N*-(α-methylbenzyl)phosphoramidodithioates (**16**) are alkylated with ethyl iodide, diastereoisomers of *S*-ethyl-*S*-methyl-*N*-(α-methylbenzyl)phosphoramidodithioate (**17**) are obtained. Under similar conditions to those used in the case of **3** and **12**, we have obtained enantiomeric compounds derived from **17**, namely *S*-ethyl-*S*-methyl phosphorotrithioates (**18**) and *S*-ethyl-*S*-methyl-*S*-propyl phosphorotrithioates (**11**) (Scheme 4).

The optical purity of **18** has been checked analogously to that of **13**.

Methanolysis of **15** in the presence of $AgNO_3$ leads to *O*-methyl-*N*-phenyl-*N'*-(α-methylbenzyl)-phosphordiamidate (**19**). Each diastereoisomer of **19**, when treated with NaH/CS_2, undergoes chemoselective PN → PS conversion to give *O*-methyl-



SCHEME 2

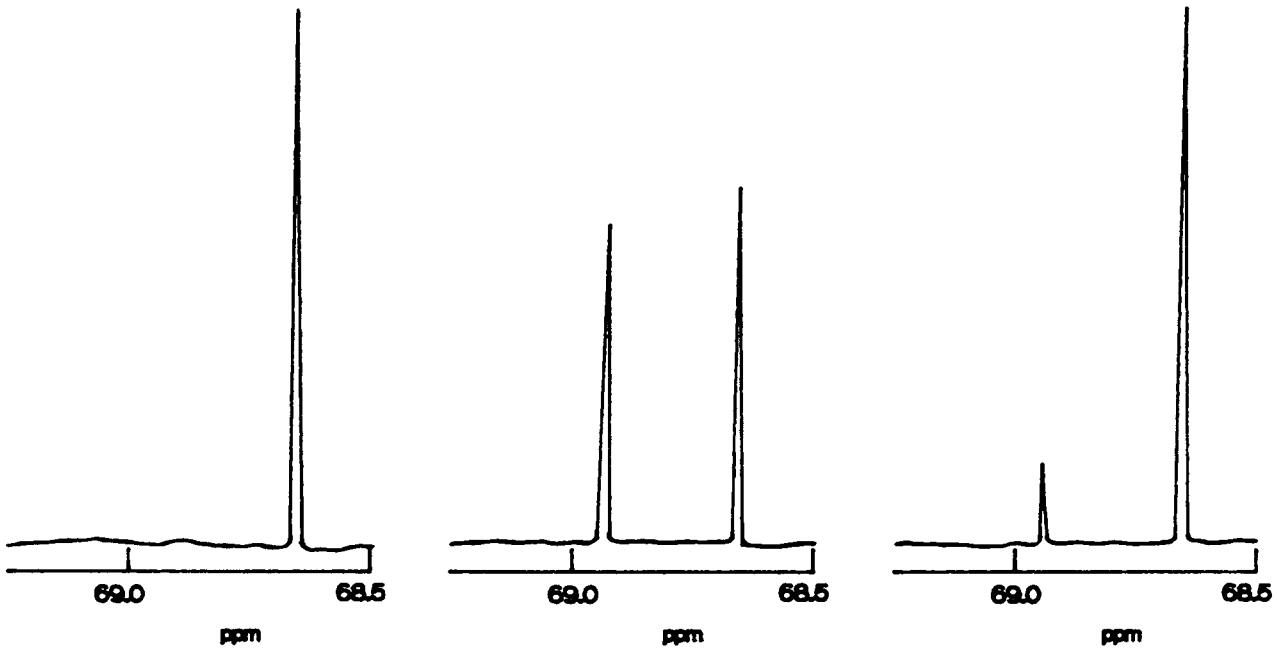
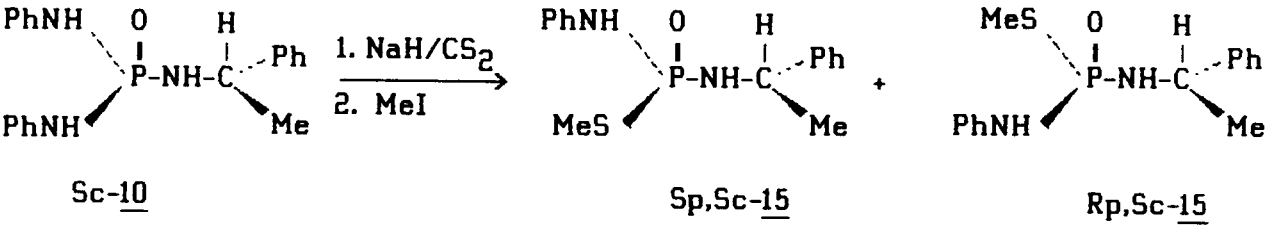
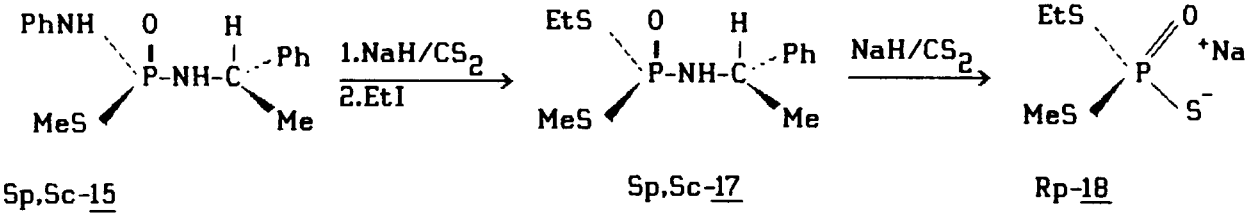


FIGURE 1 ^{31}P NMR spectra (benzene d-6, 5%) of S(−)-(α)-methylbenzylammonium salts of: a) Sp-**13**; b) racemic **13**, J = 28.0 Hz; c) Sp-**13** and ca 25% racemic **13**, J = 28.0 Hz.

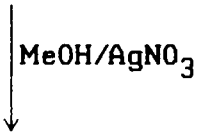


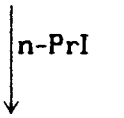
Sc-10 Sp,Sc-15 Rp,Sc-15

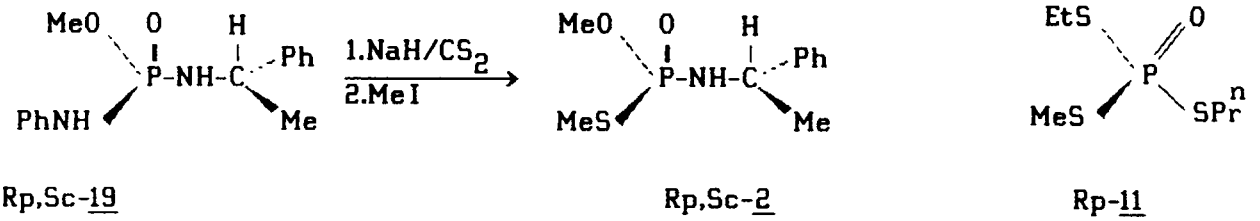
SCHEME 3



Sp,Sc-15 Sp,Sc-17 Rp-18







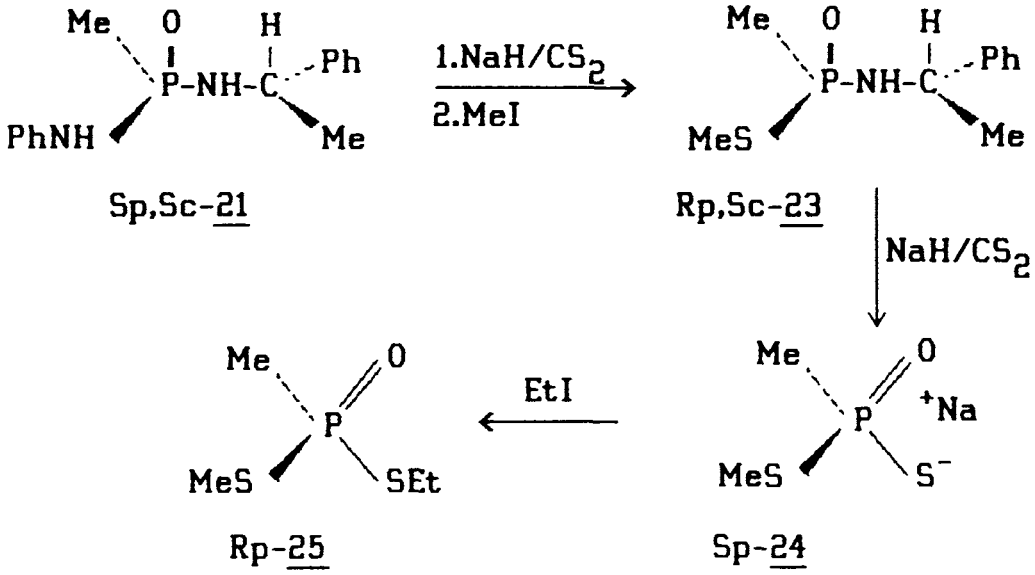
Rp,Sc-19 Rp,Sc-2 Rp-11

SCHEME 4

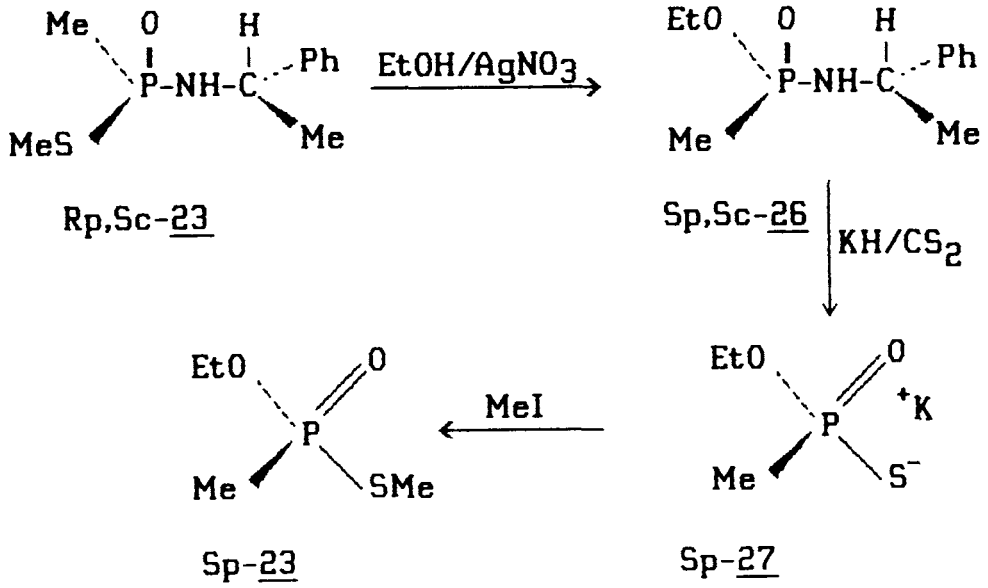
N-(α-methylbenzyl)phosphoramidothioate (**20**). Methylation of **20** leads to *O*,*S*-dimethyl-*N*-(α-methylbenzyl)phosphoramidothioate (**2**) [1]—a precursor of phosphorodithioic acid derivatives **4** and **6** (Scheme 4, Tables 2 and 3).

Successful preparation of enantiomeric forms of phosphorothioic, phosphorodithioic, phosphoroselenothioic, and phosphorotrithioic acids, demonstrated by examples such as **4**, **5**, **13**, and **18**, has prompted us to extend our methodology to the preparation of enantiomeric forms of methanephosphonothioic and methanephosphonodithioic acids. Thus, condensation of methanephosphonodichloridate [6] with aniline and α-methylbenzylamine, gives *N*-phenyl-*N'*-(α-methylbenzyl) methanephosphonodiamidates (**21**).

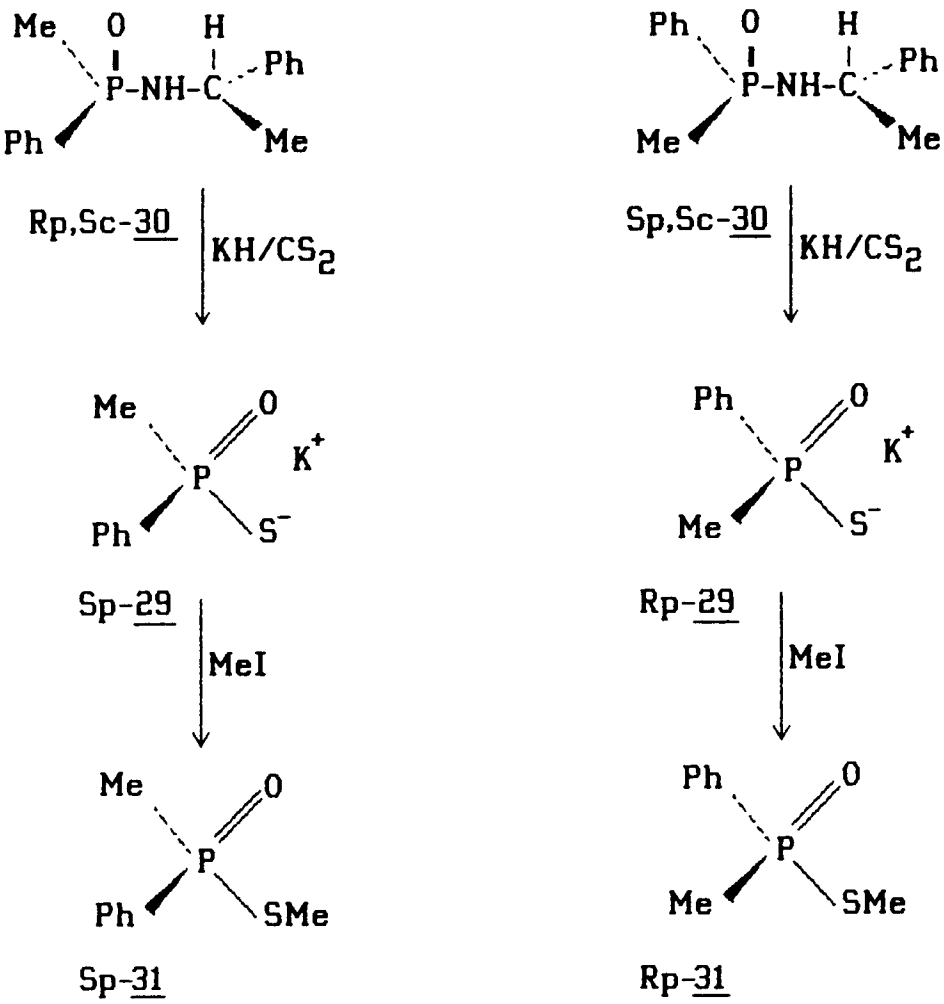
As in the case of **15**, chemoselective reaction of **21** with NaH/CS_2, followed by methylation, leads to *S*-methyl-*N*-(α-methylbenzyl)methanephosphonamidothioate (**23**). Treatment of compound **23** with NaH/CS_2, followed by ethylation, leads to *S*-methyl methanephosphonodithionate (**24**) and *S*-methyl-*S*-ethyl methanephosphonodithioate (**25**), respectively (Scheme 5). Solvolysis of **23** with $EtOH/AgNO_3$ gives *O*-ethyl-*N*-(α-methylbenzyl)methanephosphonamidate (**26**). Conversion PN → PS performed with **26** gives *O*-ethyl methanephosphonothionate (**27**), which, after methyla-



SCHEME 5



SCHEME 6



SCHEME 7

tion, gives *O*-ethyl-*S*-methyl methanephosphonothionate (**28**) [4] (Scheme 6). Finally, enantiomers of methylphenylphosphinothioic acid (**29**) were obtained by means of transformation of diastereoisomers of *N*-(α-methylbenzyl) methylphenylphosphinamidates (**30**) (originally described and configurationally characterized by Cram and Nudelman [7]) through treatment with KH/CS_2 (Scheme 7). Physicochemical characteristics and yields of all compounds presented vide supra are included in Tables 1 and 2. Additional spectroscopic data (^1H and $^{13}CNMR$) are collected in Tables 3 and 4. Table 5 contains the values of chemical shift differences $\Delta\delta$ recorded for *C*-chiral ammonium salts of enantiomeric acids **13**, **18**, **24**, **27**, and **29**.

DISCUSSION

Although the regio- and stereochemistry of reactions of organophosphorus compounds are relatively well understood and synthesis of *P*-chiral substances provide high enantiomeric excess [8], the synthetic convenience of their preparations for applications in organic synthesis, biology, and medicine still remains a challenging problem. Due to high reactivity of phosphylamidates this class of organophosphates is of special interest because *P*-chiral phosphylamidates, derivatives of optically active amines, are relatively cheap and easily available compounds. Their separation into diastereoisomeric species is achievable, and their acid-catalyzed solvolysis leads to enantiomeric phosphates [9], phosphonates [10], and phosphinates [11]. In this laboratory we have elaborated methodology for stereospecific conversion of phosphylamidates as derivatives of primary amines, into phosphylthioates, phosphylselenoates, and isotopomeric phosphates [12].

Intrinsic interest in preparation of *P*-chiral systems and in the study of many stereoselective transformations of *P*-chiral organophosphates is a continuous goal of this laboratory, and since the elucidation of the stereoretentive mode of conversion of tetracoordinated *P*-chiral phosphorami-

TABLE 1 Characteristics of Diastereoisomeric Compounds $R^1R^2R^3PX$

No.	R^1	R^2	R^3	X	Abs. Config.	$[\alpha]_D$ (c, solv.)	mp (b.p.) [°C]	Yield %	$\delta^{31}P$	MS (70 ev, m/z)
1.	MeO	MeO	NHR*	S	Rc	+37.8 (c5.0, A)	128/0.05Tr	74	74	245 (M^+, 27%) 230 (8%) 120 (46%) 93 (100%)
					Sc	−37.8 (c5.0, A)		90	74	245 (M^+, 27%) 230 (8%) 120 (46%) 93 (100%)
2.	MeO	MeS	NHR*	O	Rp,Rc	+84.8 (c5.0, A)	129–130	36	35.7	245 (M^+, 2%) 230 (100%) 120 (66%)
					Sp,Rc[a]	+22.4 (c1.3, A)	82–83	57	35.6	245 (M^+, 2%) 230 (100%) 120 (85%)
					lit.	+22.0 (A) [4]	82–83 [4]			
					Rp,Sc[a]	−23.5 (c1.5, A)	82–83	57	35.6	245 (M^+, 2%) 230 (100%) 120 (85%)
					lit.	−22.0 (A) [4]	82–83 [4]			
					Sp,Sc	−85.0 (c5.0, A)	129–130	34	35.7	245 (M^+, 2%) 230 (100%) 120 (67%)
3.	MeO	EtO	NHR*	O	Rp,Rc[b]	+51.8 (c1.2, B)	70–71	57	9.42	243 (M^+, 28%) 228 (100%) 200 (86%) 120 (73%)
					[b]	+64.5 (c0.8, C)				
					Sp,Rc[b]	+50.9 (c1.5, B)	87–89	62	9.33	243 (M^+, 18%) 228 (82%) 200 (100%) 120 (67%)
					[b]	+60.5 (c1.3, C)				
					[c]	+47.7 (c1.3, B)	87–89	82.5	9.33	
					[c]	+61.3 (c1.4, C)				
					Rp,Sc[b]	−47.3 (c1.3, B)	87–89	57	9.38	243 (M^+, 27%) 228 (100%) 200 (89%) 120 (42%)
					[b]	−64.2 (c1.2, C)				
					[c]	−47.4 (c1.1, B)	87–89	76	9.38	
					[c]	−62.3 (c1.2, C)				
					Sp,Sc[b]	−51.2 (c3.4, B)	70–71	65	9.38	243 (M^+, 27%) 228 (100%) 200 (88%) 120 (69%)
					[b]	−64.5 (c1.1, C)				
8.	MeO	MeO	NHR*	Se	Rc	+31.8 (c3.1, B)		60	75.8 [d]	293 (M^+, Se = 80; 5%) 120 (5%) 105 (30%) 93 (100%)
					Sc	−31.7 (c2.9, B)		60	75.8 [d]	293 (M^+, Se = 80; 7%) 120 (6%) 105 (28%) 93 (100%)
10.	PhNH	PhNH	NHR*	O	Rc	+35.7 (c1.2, B)	150–152	62	0.97	352 (M^+ + 1, 47%) 93 (100%)
					Sc	−35.8 (c1.5, B)	150–152	62	0.97	351 (M^+, 41%) 93 (100%)
12.	MeO	MeSe	NHR*	O	Rp,Rc	+67.2 (c1.4, B)	124–126	35	27.9 [e]	293 (M^+, Se = 80, 3%) 278 (12%) 183 (2%) 120 (17%) 105 (100%)
					Sp,Sc	−67.5 (c1.3, B)	124–126	35	28.0 [e]	293 (M^+, Se = 80, 2%) 278 (9%) 183 (1%) 120 (18%) 106 (100%)
15.	PhNH	NHR*	SMe	O	Rp,Rc	+41.1 (c1.2, B)	170–172	61	24.9	306 (M^+, 20%) 291 (12%) 120 (65%) 105 (100%)
					Sp,Rc	+47.8 (c1.8, B)	131–133	20	25.8	306 (M^+, 31%) 291 (12%) 120 (68%) 105 (100%)
					Rp,Sc	−48.2 (c1.6, B)	131–133	20	25.7	306 (M^+, 27%) 291 (17%) 120 (81%) 105 (100%)
					Sp,Sc	−42.5 (c1.6, B)	170–172	61	24.8	306 (M^+, 45%) 291 (17%) 120 (82%) 105 (100%)
17.	MeS	NHR*	SEt	O	Rp,Rc	+44.3 (c1.5, B)	69–71	73	49.25	276 (M^+, 0.5%) 260 (9%) 120 (24%) 105 (100%)
					Sp,Rc	+55.0 (c0.9, B)	96–97	33	49.32	276 (M^+, 0.7%) 260 (9%) 120 (23%) 105 (100%)
					Rp,Sc	−60.0 (c1.0, B)	96–97	33	49.32	276 (M^+, 0.4%) 260 (9%) 120 (25%) 105 (100%)

(continued)

TABLE 1 (*continued*)

No.	R^1	R^2	R^3	*X*	*Abs. Config.*	$[\alpha]_D$ (*c, solv.*)	*mp (b.p.)* [°C]	*Yield* %	$\delta\ ^{31}P$	*MS (70 ev,* m/z)
					Sp,Sc	−45.6 (c1.4, B)	69–71	73	49.25	276 (M^+, 1.3%) 260 (8%) 120 (24%) 105 (100%)
19.	PhNH	NHR*	MeO	O	Rp,Rc	+77.2 (c1.1, B)	101–103	62.5	8.8	290 (M^+, 52%) 275 (8%) 120 (100%) 105 (26%)
					Sp,Rc	+31.8 (c1.1, B)	88–89	69	8.6	290 (M^+, 45%) 275 (71%) 120 (100%) 105 (46%)
					Rp,Sc	−32.4 (c1.1, B)	88–89	69	8.6	290 (M^+, 48%) 275 (73%) 120 (100%) 105 (36%)
					Sp,Sc	−80.3 (c0.9, B)	101–103	71	8.8	290 (M^+, 45%) 275 (79%) 120 (100%) 105 (35%)
21.	Me	PhNH	NHR*	O	Rp,Rc	+53.1 (c1.5, B)	161–163	34	23.2	274 (M^+, 38%) 259 (31%) 120 (100%)
					Sp,Sc	−54.6 (c1.2, B)	161–163	44	23.2	274 (M^+, 31%) 259 (23%) 120 (100%)
23.	Me	Mes	NHR*	O	Sp,Rc	+96.1 (c1.2, B)	117–119	55	44.7	229 (M^+, <1%) 214 (28%) 120 (75%)
					Rp,Sc	−97.6 (c1.3, B)	119–120	57	44.3	229 (M^+, <1%) 214 (22%) 120 (61%)
26.	Me	EtO	NHR*	O	Rp,Rc	+85.4 (c1.4, B)	82–83	61	31.3	227 (M^+, 17%) 212 (49%) 120 (100%)
					Sp,Sc	−90.0 (c1.3, B)	82–83	66	31.5	227 (M^+, 13%) 212 (51%) 120 (100%)
30.	Me	Ph	NHR*	O	Rp,Sc	−17.3 (c1.4, A)	119–121	20	30.1	259 (M^+, 4%) 244 (42%) 120 (100%)
					lit.	−16.1 (c1.6, A) [7]	117–119 [7]			
					Sp,Sc	−61.8 (c1.4, A)	133–136	29	30.7	259 (M^+, 4%) 244 (45%) 120 (100%)
					lit.	−64.6 (c2.0, A) [7]	133–134 [7]			

[a] Obtained from **19**.
[b] Obtained from **2**.
[c] Obtained from **12**.
[d] $^1J_{P-Se}$ = 891 Hz (measured in methylene chloride-d_2).
[e] $^1J_{P-Se}$ = 435 Hz.
R* = $CH(CH_3)Ph$.
A = chloroform.
B = methanol.
C = benzene.

TABLE 2 Characteristics of Enantiomeric Compounds $R^1R^2P(O)Y$

No.	R^1	R^2	*Y*	*Abs. Config.*	$[\alpha]_D$ (*c, solv.*)	*Yield* %	$\delta\ ^{31}P$	*MS (70 ev,* m/z)
6.	MeO	MeS	SEt	Sp	−14.1 (c5.6, B)	68	56	186 (M^+, 43%) 106 (100%)
				Rp	+13.0 (c7.6, B)	72	56	186 (M^+, 43%) 106 (100%)
7.	MeO	EtO	SMe	Sp from **3**	−0.95 (c1.4, A)	60	30.1	170 (M^+, 60%) 155 (6%) 126 (80%) 95 (100%)
				from **9**	−1.00 (c3.3, A)	53		
				lit.	−1.00 (A) [4]			
				Rp from **3**	+1.00 (c2.1, A)	59	30.1	170 (M^+, 21%) 155 (2%) 126 (30%) 95 (100%)
				from **9**	+0.91 (c0.9, A)	50		
				lit.	+0.90 (A) [4]			
9.	MeO	MeS	MeSe	Sp	+3.8 (c3.4, C)	73	51.3	220 (M^+, ^{80}Se, 15%) 125 (100%)
							$^1J_{P-Se}$ 486 Hz	
				Rp	−3.8 (c3.3, C)	73	51.3	220 (M^+, ^{80}Se, 19%) 125 (100%)
							$^1J_{P-Se}$ 486 Hz	

(*continued*)

TABLE 2 Characteristics of Enantiomeric Compounds $R^1R^2P(O)Y$ (*continued*)

No.	R^1	R^2	Y	Abs. Config.	$[\alpha]_D$ (c, solv.)	Yield %	$\delta^{31}P$	MS (70 ev, m/z)
11.	MeS	EtS	PrS	Rp	−1.49 (c6.1, C)	70	65.4	230 (M^+, 22%) 127 (100%)
				Sp	+1.45 (c3.2, C)	63	65.4	230 (M^+, 36%) 127 (100%)
25.	Me	MeS	EtS	Rp	−20.0 (c1.75, A)	70	62.3	170 (M^+, 31%) 95 (100%)
				Sp	+20.6 (c3.0, A)	63	62.3	170 (M^+, 35%) 95 (100%)
28.	Me	MeS	EtO	Rp	+82.8 (c0.4, A)	65	54.4	154 (M^+, 13%) 139 (1%) 107 (6%) 79 (100%)
				lit.	+85.5 (A) [4]			
				Sp	−81.2 (c1.9, A)	65	54.4	154 (M^+, 16%) 139 (1%) 107 (8%) 79 (100%)
				lit.	−87.5 (A) [4]			
31.	Me	Ph	MeS	Sp	−123.2 (c4.4, A)	54	48	186 (M^+, 24%) 171 (5%) 139 (100%) 77 (31%)
				Rp	+124.2 (c5.7, A)	75	48	186 (M^+, 27%) 171 (5%) 139 (100%) 77 (33%)

A = chloroform
B = methanol
C = benzene

TABLE 3 ^1H and ^{13}C Chemical Shifts of Diastereoisomeric Compounds $R^1R^2R^3PO$

No.	R^1	R^2	R^3	Abs. Config.	^1H NMR [ppm]	^{13}C NMR [ppm]
2.	MeO	MeS	NHR*	Sp,Sc (Rp,Rc)	1.53 (d, 3H, $^3J_{H-H}$ = 6.8 Hz, CH_3CH) 2.15 (d, 3H, $^3J_{P-H}$ = 14.8 Hz, CH_3S) 3.90 (m, 1H, NH) 3.60 (d, 3H, $^3J_{P-H}$ = 12.5 Hz, CH_3O) 4.45 (m, 1H, CH—CH_3) 7.23–7.39 (m, $5H_{arom}$)	12.0 (d, $^2J_{P-C}$ = 3.5 Hz, CH_3S) 25.14 (d, $^3J_{P-C}$ = 5.3 Hz, CH_3—CH) 51.37 (s, CH_3—CH) 52.46 (d, $^2J_{P-C}$ = 6.0 Hz, CH_3O) 125.88 (s, C—2) 127.23 (s, C—4) 128.54 (s, C—3), 144.59 (d, $^3J_{P-C}$ = 4.5 Hz; s, C—1).
				Rp,Sc (Sp,Rc)	1.53 (d, 3H, $^3J_{H-H}$ = 6.8 Hz, CH_3CH) 2.13 (d, 3H, $^3J_{P-H}$ = 14.7 Hz, CH_3S) 3.44 (m, 1H, NH) 3.75 (d, 3H, $^3J_{P-H}$ = 12.5 Hz, CH_3O) 4.50 (m, 1H, CH—CH_3) 7.23–7.39 (m, $5H_{arom}$)	12.0 (d, $^2J_{P-C}$ = 3.5 Hz, CH_3S) 24.81 (d, $^3J_{P-C}$ = 5.3 Hz, CH_3—CH) 51.37 (s, CH_3—CH) 52.68 (d, $^2J_{P-C}$ = 6.0 Hz, CH_3O) 125.88 (s, C—2) 127.23 (s, C—4) 128.54 (s, C—3), 144.59 (d, $^3J_{P-C}$ = 4.5 Hz; s, C—1).
3.	MeO	EtO	NHR*	Sp,Sc (Rp,Rc)	1.32 (t, 3H, $^3J_{H-H}$ = 7.1 Hz; CH_3CH_2O) 1.49 (d, 3H, ^3J = 6.8 Hz; CH_3CH) 3.22 (m, 1H, NH) 3.48 (d, 3H, $^3J_{P-H}$ = 11.2 Hz; CH_3O) 4.0–4.1 (m, 2H, $^3J_{H-H}$ = 7.1 Hz; CH_3CH_2O) 4.3 (m, 1H, CH_3CH) 7.2–7.4 ($5H_{arom}$)	16.11 (d, $^3J_{P-C}$ = 7 Hz; CH_3CH_2O) 25.0 (d, $^3J_{P-C}$ = 6.0 Hz; CH_3CH) 51.37 (s, CH_3CH) 52.65 (d, $^2J_{P-C}$ = 5.5 Hz; CH_3O) 62.38 (d, $^2J_{P-C}$ = 5.3 Hz; CH_3CH_2O) 125.7; 127.1; 128.4; 145.0—C_{arom}.
				Rp,Sc (Sp,Rc)	1.13 (t, 3H, $^3J_{H-H}$ = 7.1 Hz; CH_3CH_2O) 1.48; 1.49 (2d, 3H, $^3J_{H-H}$ = 6.8 Hz; CH_3CH)	15.84 (d, $^3J_{P-C}$ = 7.0 Hz; CH_3CH_2O) 25.12 (d, $^3J_{P-C}$ = 6.0 Hz; CH_3CH) 51.37 (s, CH_3CH) 52.80 (d, $^2J_{P-C}$ = 5.5 Hz; CH_3O)

(*continued*)

TABLE 3 (*continued*)

No.	R^1	R^2	R^3	Abs. Config.	^1H NMR [ppm]	^{13}C NMR [ppm]
					3.11 (m, 1H, NH) 3.69 (d, 3H, $^3J_{P-H}$ = 11.2 Hz; CH_3O) 3.83–3.95 (m, 2H, CH_3CH_2O) 4.33 (m, 1H, CH_3CH) 7.2–7.35 (m, $5H_{arom}$)	62.23 (d, $^2J_{P-C}$ = 5.3 Hz; CH_3CH_2O) 125.7; 127.1; 128.4; 145.0—$C_{arom.}$
12.	MeO	MeSe	NHR*	Sp,Sc	1.54 (d, 3H, $^3J_{H-H}$ = 6.8 Hz; CH_3—CH)	4.33 (d, $^3J_{P-C}$ = 4.3 Hz; CH_3—Se) 25.18 (d, $^2J_{P-C}$ = 5.8 Hz, CH_3—CH)
				(Rp,Rc)	2.00 (d, 3H, $^3J_{P-H}$ = 13.2 Hz; $^2J_{H-Se}$ = 10.35 Hz, CH_3Se) 3.61 (d, $^3J_{P-H}$ = 13.0 Hz; CH_3O) 4.47 (m, 1H, $^3J_{H-H}$ = 6.8 Hz; CH—NH) 7.24–7.41 (m, $5H_{arom}$)	51.51 (s, CH) 52.40 (d, $^2J_{P-C}$ = 6.3 Hz, CH_3O) 126.02 (s, C—2), 127.28 (s, C—4) 128.59 (s, C—3) 144.70 (d, $^3J_{P-C}$ = 4.9 Hz, C—1)
				Rp,Sc	1.54 (d, 3H, $^3J_{H-H}$ = 6.8 Hz; CH_3—CH)	4.36 (d, $^3J_{P-C}$ = 4.3 Hz; CH_3—Se) 24.68 (d, $^2J_{P-C}$ = 5.8 Hz, CH_3—CH)
				(Sp,Rc)	2.03 (d, 3H, $^3J_{P-H}$ = 13.2 Hz; $^2J_{H-Se}$ = 10.4 Hz, CH_3Se) 3.74 (d, $^3J_{P-H}$ = 13.0 Hz; CH_3O) 4.47 (m, 1H, $^3J_{H-H}$ = 6.8 Hz; CH—NH) 7.24–7.41 (m, $5H_{arom}$)	51.33 (s, CH) 52.53 (d, $^2J_{P-C}$ = 6.3 Hz, CH_3O) 125.94 (s, C—2), 127.29 (s, C—4) 128.57 (s, C—3) 144.41 (d, $^3J_{P-C}$ = 4.9 Hz, C—1)
15.	MeS	NHPh	NHR*	Sp,Sc	1.52 (d, 3H, $^3J_{H-H}$ = 6.8 Hz, CH_3—CH)	12.72 (s, CH_3S) 25.11 (d, $^3J_{P-C}$ = 5.5 Hz, CH_3CH)
				(Rp,Rc)	2.25 (d, 3H, $^3J_{P-H}$ = 14.4 Hz, CH_3—S) 3.59 (m, 1H, NH—CH—CH_3) 4.56 (m, 1H, CH—CH_3) 5.63 (d, 1H, $^2J_{P-H}$ = 9.1 Hz, NH—Ph) 6.9–7.4 (m, $10H_{arom}$)	51.45 (s, CH), 118.62 (d, $^3J_{P-C}$ = 7 Hz, C—2) 122.04 (s, C—4), 129.09 (s, C—3) 139.81 (s, C—1), 126.01 (s, C—2) 127.31 (s, C—4), 128.61 (s, C—3) 144.5 (d, $^3J_{P-C}$ = 5 Hz, C—1)
				Rp,Sc	1.52 (d, 3H, $^3J_{H-H}$ = 6.8 Hz, CH_3—CH)	12.42 (s, CH_3S) 25.11 (d, $^3J_{P-C}$ = 5.5 Hz, CH_3CH)
				(Sp,Rc)	2.20 (d, 3H, $^3J_{P-H}$ = 14.4 Hz, CH_3—S) 3.76 (m, 1H, NH—CH—CH_3) 4.56 (m, 1H, CH—CH_3) 5.45 (d, 1H, $^2J_{P-H}$ = 9.1 Hz, NH—Ph) 6.86–7.36 (m, $10H_{arom}$)	51.45 (s, CH), 118.62 (d, $^3J_{P-C}$ = 7 Hz, C—2) 122.04 (s, C—4), 129.09 (s, C—3) 139.70 (s, C—1), 126.10 (s, C—2) 127.43 (s, C—4), 128.73 (s, C—3) 144.5 (d, $^3J_{P-C}$ = 5 Hz, C—1)
17.	MeS	EtS	NHR*	Sp,Sc	1.37 (t, 3H, $^3J_{H-H}$ = 7.5 Hz, CH_3—CH_2—S)	13.57 (d, $^3J_{P-C}$ = 4 Hz, CH_3—CH—NH)
				(Rp,Rc)	1.58 (d, 3H, $^3J_{H-H}$ = 6.8 Hz; CH_3—CH—Ph) 2.28 (d, 3H, $^3J_{P-H}$ = 15.0 Hz; CH_3—S) 2.85 (m, 2H, CH_3CH_2S) 3.31 (m, 1H, NH—CH—CH_3) 4.60 (m, 1H, CH) 7.2–7.45 (m, $5H_{arom}$)	16.32 (d, $^3J_{P-C}$ = 5.5 Hz, CH_3CH_2S) 25.03 (d, $^2J_{P-C}$ = 5.0 Hz, CH_3S) 26.26 (s, CH_3CH_2S) 51.74 (s, CH) 126.17 (s, C—2) 127.34 (s, C—4) 128.64 (s, C—3) 144.64 (d, $^3J_{P-C}$ = 5.9 Hz, C—1)
				Sp,Rc	1.35 (t, 3H, $^3J_{H-H}$ = 7.5 Hz, CH_3—CH_2—S)	13.64 (d, $^3J_{P-C}$ = 4 Hz, CH_3—CH—NH)
				(Rp,Sc)	1.58 (d, 3H, $^3J_{H-H}$ = 6.8 Hz; CH_3—CH—Ph) 2.27 (d, 3H, $^3J_{P-H}$ = 15.0 Hz; CH_3—S) 2.89 (m, 2H, CH_3CH_2S) 3.44 (m, 1H, NH—CH—CH_3) 4.65 (m, 1H, CH) 7.2–7.45 (m, $5H_{arom}$)	16.11 (d, $^3J_{P-C}$ = 5.5 Hz, CH_3CH_2S) 25.14 (d, $^2J_{P-C}$ = 5.0 Hz, CH_3S) 26.25 (d, CH_3CH_2S) 51.73 (s, CH) 126.00 (s, C—2) 127.30 (s, C—4) 128.60 (s, C—3) 144.4 (d, $^3J_{P-C}$ = 5.9 Hz, C—1)
19.	MeO	NHPh	NHR*	Sp,Sc	1.44 (2d, 3H, $^3J_{H-H}$ = 6.8 Hz; CH_3—CH)	25.28 (d, $^3J_{P-C}$ = 6.3 Hz, CH_3—CH) 51.76 (s, CH) 52.58 (d, $^2J_{P-C}$ = 5.2 Hz, CH_3O)
				(Rp,Rc)	3.23 (dd = t, 1H, $^3J_{H-H}$ = $^2J_{H-H}$ = 9.5 Hz; NH—CH)	118.17 (d, $^3J_{P-C}$ = 6.9 Hz, C—2)

(*continued*)

TABLE 3 ^{1}H and ^{13}C Chemical Shifts of Diastereoisomeric Compounds $R^1R^2R^3PO$ (*continued*)

No.	R^1	R^2	R^3	Abs. Config.	^{1}H NMR [ppm]	^{13}C NMR [ppm]
					3.59 (d, 3H, $^{3}J_{P-H}$ = 11.5 Hz; CH_3—O) 4.35 (m, 1H, C*H*—NH) 5.28 (d, 1H, $^{2}J_{P-H}$ = 8.0 Hz; N*H*—Ph) 7.00–7.30 ($10H_{arom}$)	122.00 (s, C—4) 129.69 (C—3) 140.48 (s, C—1), 126.41 (s, C—2) 127.73 (s, C—4), 129.05 (s, C—3) 145.47 (d, $^{3}J_{P-C}$ = 4.7 Hz, C—1)
				Rp,Sc	1.43 (2d, 3H, $^{3}J_{H-H}$ = 6.8 Hz; CH_3—CH)	25.53 (d, $^{3}J_{P-C}$ = 6.2 Hz, CH_3—CH) 51.98 (s, CH) 52.78 (d, $^{2}J_{P-C}$ = 5.2 Hz, CH_3O)
				(Sp,Rc)	3.19 (m, 1H, N*H*—CH) 3.71 (d, 3H, $^{3}J_{P-H}$ = 11.5 Hz; CH_3—O) 4.41 (m, 1H, C*H*—NH) 5.18 (d, 1H, $^{2}J_{P-H}$ = 8.0 Hz; N*H*—Ph) 6.88–7.34 ($10H_{arom}$)	118.48 (d, $^{3}J_{P-C}$ = 6.9 Hz, C—2) 122.16 (s, C—4) 129.83 (C—3) 140.85 (s, C—1), 126.68 (s, C—2) 127.93 (s, C—4), 129.27 (s, C—3) 145.49 (d, $^{3}J_{P-C}$ = 4.7 Hz, C—1)
21.	Me	NHPh	NHR*	Sp,Sc (Rp,Rc)	1.47 (d, 3H, $^{3}J_{H-H}$ = 6.8 Hz; CH_3CH) 1.54 (d, 3H, $^{2}J_{P-H}$ = 15.4 Hz; CH_3—P) 3.04 (m, 1H, N*H*CHCH$_3$) 4.48 (m, 1H, CH$_3$C*H*) 5.00 (d, 1H, $^{2}J_{P-H}$ = 7.6 Hz; NHPh) 6.84–7.34 (m, $10H_{arom}$)	14.62 (d, $^{1}J_{P-C}$ = 115.9 Hz; CH_3—P) 25.27 (d, $^{3}J_{P-C}$ = 6.3 Hz; CH_3CH) 50.80 (s, CH_3CH) 118.10 (s, C—2), 121.29 (s, C—4) 129.22 (s, C—3), 140.88 (s, C—1) 126.07 (s, C—2), 127.26 (s, C—4) 128.67 (s, C—3), 145.2 (d, $^{3}J_{P-C}$ = 3.0 Hz; C—1)
23.	Me	MeS	NHR*	Rp,Sc (Sp,Rc)	1.48 (d, 3H, $^{3}J_{H-H}$ = 6.8 Hz; CH_3CH) 1.64 (d, 3H, $^{2}J_{P-H}$ = 14.5 Hz; CH_3—P) 2.13 (d, 3H, $^{3}J_{P-H}$ = 12.6 Hz; CH_3S) 3.02 (m, 1H, NH) 4.46 (m, 1H, C*H*CH$_3$) 7.15–7.33 (m, $5H_{arom}$)	11.4 (d, $^{2}J_{P-C}$ = 3.2 Hz; CH_3S) 19.76 (d, $^{1}J_{P-C}$ = 97.4 Hz; CH_3—P) 25.18 (d, $^{3}J_{P-C}$ = 5.2 Hz; CH_3CH) 50.79 (s, CH) 125.97 (s, C—2), 127.26 (s, C—4) 128.59 (s, C—3), 144.67 (d, $^{3}J_{P-C}$ = 4.0 Hz; C—1)
26.	Me	EtO	NHR*	Sp,Sc (Rp,Rc)	1.14 (d, 3H, $^{1}J_{P-H}$ = 16.6 Hz; CH_3—P) 1.25 (t, 3H, $^{3}J_{H-H}$ = 7.1 Hz; CH_3CH$_2$) 1.41 (d, 3H, $^{3}J_{H-H}$ = 6.8 Hz; CH_3CHPh) 3.84–3.96 (m, 1H, NH) 3.98–4.10 (m, 2H, CH_2O) 4.20–4.27 (m, 1H, CH) 7.16–7.33 (m, $5H_{arom}$)	14.33 (d, $^{1}J_{P-C}$ = 132.1 Hz; CH_3—P) 17.06 (d, $^{3}J_{P-C}$ = 6.3 Hz; CH_3CH_2O) 26.67 (d, J_{P-C} = 6.3 Hz; CH_3CH) 51.74 (CH_3CH) 60.09 (d, $^{2}J_{P-C}$ = 6.2 Hz, CH_3CH_2O) 126.43 (s, C—2) 127.86 (s, C—4) 129.29 (s, C—3) 145.97 (s, C—1)
30.	Me	Ph	NHR*	Sp,Sc	1.45 (d, 3H, $^{3}J_{H-H}$ = 6.7 Hz; CH_3CH) 1.54 (d, 3H, $^{2}J_{P-H}$ = 14.0 Hz; CH_3—P) 2.95 (m, 1H, NH) 4.56 (m, 1H, CH) 7.2–7.9 ($10H_{arom}$)	16.98 (d, $^{1}J_{P-C}$ = 92.3 Hz; CH_3—P) 25.97 (d, $^{3}J_{P-C}$ = 3.5 Hz; CH_3CH) 50.99 (s, CH) 126.05 (s, C—2), 127.15 (s, C—4) 128.54 (s, C—3), 145.02 (d, $^{3}J_{P-C}$ = 4.1 Hz, C—1) 128.41 (d, $^{2}J_{P-C}$ = 12.6 Hz, C—2) 131.67 (s, C—4) 131.75 (d, $^{3}J_{P-C}$ = 7.4 Hz, C—3); 133.06 (d, $^{1}J_{P-C}$ = 125.3 Hz, C—1)
				Rp,Sc	1.56 (d, 3H, $^{3}J_{H-H}$ = 6.7 Hz, CH_3CH) 1.64 (d, 3H, $^{2}J_{H-H}$ = 14.0 Hz, CH_3P) 3.07 (m, 1H, NH) 4.23 (m, 1H, CH) 7.2–7.8 (m, $10H_{arom}$)	16.49 (d, $^{1}J_{P-C}$ = 93.9 Hz, CH_3P) 25.81 (d, $^{3}J_{P-C}$ = 5.2 Hz, CH_3CH) 50.54 (s, CH) 126.13 (s, C—2), 127.29 (s, C—4) 128.72 (s, C—3), 145.47 (d, $^{3}J_{P-C}$ = 4.1 Hz, C—1) 128.56 (d, $^{2}J_{P-C}$ = 12.3 Hz, C—2) 131.44 (d, $^{4}J_{P-C}$ = 9.7 Hz, C—4) 131.90 (d, $^{3}J_{P-C}$ = 2.2 Hz, C—3); 133.92 (d, $^{1}J_{P-C}$ = 125.3 Hz, C—1)

R* = CH(CH_3)Ph.

TABLE 4 ^1H and ^{13}C Chemical Shifts of Enantiomeric $R^1R^2R^3PO$

No.	R^1	R^2	R^3	*^1H NMR*	*^{13}C NMR*
7.	MeO	EtO	MeS	1.38 (t, 3H, $^3J_{H-H}$ = 7.1 Hz; CH_3CH_2); 2.29 (d, 3H, $^3J_{P-H}$ = 14.9 Hz; CH_3S); 3.81 (d, 3H, $^3J_{P-H}$ = 12.6 Hz; CH_3O); 4.20 (m, 2H, $^3J_{H-H}$ = 7.1 Hz; CH_3CH_2)	12.34 (d, $^2J_{P-C}$ = 4.7 Hz; CH_3S); 16.08 (d, $^3J_{P-C}$ = 7.3 Hz; CH_3CH_2); 53.64 (d, $^2J_{P-C}$ = 5.7 Hz; CH_3O); 63.69 (d, $^2J_{P-C}$ = 5.9 Hz; CH_3CH_2)
9.	MeO	MeSe	MeS	2.25 (d, 3H, $^3J_{P-H}$ = 14.4 Hz; $^2J_{H-Se}$ = 10.7 Hz; CH_3Se); 2.35 (d, 3H, $^3J_{P-H}$ = 16.7 Hz; CH_3S); 3.84 (d, 3H, $^3J_{P-H}$ = 13.8 Hz; CH_3O);	6.56 (d, $^2J_{P-C}$ = 4.4 Hz; CH_3Se); 13.70 (d, $^2J_{P-C}$ = 3.4 Hz; CH_3S); 53.55 (d, $^2J_{P-C}$ = 8.2 Hz; CH_3O)
11.	MeS	EtS	n-PrS	1.03 (t, 3H, $^3J_{H-H}$ = 7.4 Hz; $SCH_2CH_2CH_3$); 1.43 (t, 3H, $^3J_{H-H}$ = 7.4 Hz; SCH_2CH_3); 1.79 (m, 2H, $SCH_2CH_2CH_3$) 2.43 (d, 3H, $^3J_{P-H}$ = 15.9 Hz; CH_3S); 2.97 (m, 2H, $SCH_2CH_2CH_3$); 3.01 (m, 2H, SCH_2CH_3)	13.88 (s, $SCH_2CH_2CH_3$); 15.19 (d, $^3J_{P-C}$ = 3.9 Hz; $SCH_2CH_2CH_3$); 16.81 (d, $^3J_{P-C}$ = 5.3 Hz; SCH_2CH_3); 24.70 (d, $^2J_{P-C}$ = 4.9 Hz; SCH_3); 28.00 (d, $^2J_{P-C}$ = 3.4 Hz; SCH_2CH_3); 35.36 (d, $^2J_{P-C}$ = 3.4 Hz; $SCH_2CH_2CH_3$)
25.	Me	MeS	EtS	1.36 (t, 3H, $^3J_{H-H}$ = 7.4 Hz; CH_3CH_2); 1.99 (d, 3H, $^2J_{P-H}$ = 13.5 Hz; CH_3—P); 2.34 (d, 3H, $^3J_{P-H}$ = 13.7 Hz; SCH_3); 2.4–3.0 (m, 2H, SCH_2CH_3)	12.46 (d, $^3J_{P-C}$ = 3.6 Hz; SCH_2CH_3); 16.45 (d, $^2J_{P-C}$ = 5.0 Hz; SCH_3); 24.56 (d, $^1J_{P-C}$ = 76.7 Hz; CH_3—P); 25.4 (d, $^2J_{P-C}$ = 3.4 Hz; SCH_2CH_3)
28.	Me	MeS	EtO	1.36 (t, 3H, $^3J_{H-H}$ = 7.1 Hz; CH_3CH_2); 1.79 (d, 3H, $^2J_{P-H}$ = 15.6 Hz; CH_3—P); 2.30 (d, 3H, $^3J_{P-H}$ = 12.9 Hz; CH_3S); 4.06–4.25 (m, 2H, CH_2)	12.17 (d, J_{P-C} = 3.6 Hz, CH_3CH_2O); 16.20 (d, J_{P-C} = 7.1 Hz; CH_3—S); 18.70 (d, $^1J_{P-C}$ = 110.8 Hz; CH_3—P) 61.28 (d, $^2J_{P-C}$ = 7.0 Hz, CH_2O)
31.	Me	MeS	Ph	1.98 (d, 3H, $^2J_{P-H}$ = 13.3 Hz; CH_3—P); 2.19 (d, 3H, $^3J_{P-H}$ = 12.0 Hz; CH_3—S); 7.5–7.9 (m, 5H_{arom})	10.67 (d, $^2J_{P-C}$ = 2.7 Hz; CH_3S); 20.86 (d, $^1J_{P-C}$ = 75.2 Hz; CH_3—P); 129.41 ($^1J_{P-C}$ = 12.9 Hz; C—2); 131.52 (d, $^4J_{P-C}$ = 10.4 Hz; C—4) 132.88 (s, C—3); 133.56 ($^1J_{P-C}$ = 103.5 Hz; C—1)

TABLE 5 Phosphorus Chemical Shift Differences $\Delta\delta$(Hz) at 121.49 MHz and Sense of Magnetic Nonequivalence for Diastereoisomeric Salts of Chiral Phosphorus Thioacids $R^1R^2POS^-$ $R^3NH_3^+$

No.	R^1	R^2	R^{3a}	$\delta(C_6D_6)$	$\Delta\delta$ *Hz*	*Sense of Nonequivalence*
5	MeO	EtO	—$CH(CH_3)$Ph	59.50	0	
5	MeO	EtO	—$CH(CH_3)$Ar[b]	59.50	0	
13	MeO	MeSe	—$CH(CH_3)$Ph	68.90	28	downfield for Rp
18	MeS	EtS	—$CH(CH_3)$Ph	87.75	6	downfield for Rp
24	Me	MeS	—$CH(CH_3)$Ph	79.50	38	downfield for Sp
27	Me	EtO	—$CH(CH_3)$Ph	76.50	21.5	downfield for Sp
29	Me	Ph	—$CH(CH_3)$Ar[b]	60.50[c]	37	downfield for Sp

[a] S(−) amines were used.
[b] Ar = α-naphthyl.
[c] $CDCl_3$ used as a solvent.

dates (amidothioates) into phosphorothioates (isotopomeric phosphates), our efforts are focused on the broadening of the scope of this reaction (PN → PX conversion).

Although diastereoisomeric *P*-chiral phosphylamidates have been used in numerous studies on acid-catalyzed solvolysis, resulting in the preparation of neutral *P*-chiral phosphates [9] and phosphonates [10], the approach of PN → PX conversion [12] still seems to be underexploited. Since this approach leads to phosphorothioate and other anions, which may undergo many transformations with high stereoselectivity under similar conditions, both phosphylamidates and phosphylthioates are synthetically useful and provide the basis for chemical correlations of absolute configuration of products with that of starting materials.

Synthesis

The results presented above indicate that diastereoisomeric phosphylamidates, as derivatives of cheap and easily available enantiomers of α-methylben-

zylamine [13], can be prepared and isolated as pure diastereoisomeric species in satisfactory yields.

For example, condensation of *O,O*-dimethyl phosphorochloridite with *R*(+)-α-methylbenzylamine in the presence of triethylamine and elemental selenium gives *P*-prochiral **8**, which undergoes a facile Pistchimuka Rearrangement to *P*-chiral **12**, separable into diastereoisomeric species by fractional crystallization. The related condensation of methanephosphonodichloridate with aniline, and subsequently α-methylbenzylamine, gives directly the pair of diastereoisomers **21**. Condensation of racemic methylphenylphosphinochloridate with α-methylbenzylamine gives the pair of diastereoisomers of **30**, as described originally by Cram and Nudelmann [7], while *N,N*-diphenylphosphordiamidochloridate, condensed with the same amine and aniline, provides *P*-prochiral **10**.

The key step for the preparation of *P*-chiral diastereoisomers of **2**, **3**, **14**, **15**, **16**, **17**, **19**, **20**, **22**, **23**, and **26** and enantiomers of **4**, **5**, **6**, **7**, **9**, **11**, **13**, **18**, **24**, **25**, **27**, **28**, **29**, and **31** relies upon reaction of *N*-metallated phosphoramidates with carbon disulfide. This process, earlier described as PN → PS conversion, is fully stereoretentive [12]. Moreover, high chemoselectivity is emphasized when the substrate contains both *N*-phenyl and *N*-α-methylbenzyl residues. In such cases as **10**, **15**, **19**, and **21** exclusive involvement of *N*-phenylamido-function in PN → PS conversion is observed. Yields for PN → PS conversion are specified in Table 1 and Table 2 and vary from 53–75%.

It is also worth emphasizing that neutral diastereoisomers bearing only one *S*-alkyl group or Se-alkyl group such as **2**, **12**, **15**, or **23** can undergo alcoholysis under conditions reported formerly from this laboratory [14]. Silver ion-assisted solvolysis occurs stereospecifically and with inversion of configuration, as has been proved by NMR analysis (vide infra). In the case of enantiomeric **9**, bearing both an *S*-alkyl and an Se-alkyl group it is possible to substitute only the Se-alkyl group during ethanolysis to give enantiomerically pure **7**. Chemoselective and stereoinvertive silver ion-assisted alcoholysis broadens the scope of these preparatively useful transformations.

As has been demonstrated in the above Schemes we have dealt with several diastereoisomeric systems and we have found that their diastereoisomeric purity (d.p.) can be effectively monitored by ^{31}P NMR as a result of measurable differences in chemical shift values for pure specimens (Table 1). Moreover, the d.p. of these synthesized compounds has been also been confirmed on the basis of ^{1}H NMR and ^{13}C NMR (Table 3).

Stereochemistry

Although several enantiomeric compounds reported in this paper have been described as available from other synthetic routes, simplicity of the approach designed in this laboratory is of overriding importance. The basic reaction is a fully stereoselective PN → PS conversion. In our earlier work [2] we were unable, because of instrumental limitations, to prove that PN → PS conversion is fully stereospecific. This led us to speculations about stereomutation at a stereogenic phosphorus atom involved in pentacoordinated intermediates. Careful reinvestigation of the reaction of **12** with NaH/CS_2 and assignment of optical purity of the *S*(−)-α-phenylethylammonium salt of **13** has proved that **13** as well as the product of its methylation, *O,S*,Se-trimethylphosphoroselenothioate (**9**), have been prepared as enantiomerically pure specimens. Similarly, the product of reaction of **17** with NaH/CS_2, namely (MeS)(EtS)$POS^- Na^+$ (**18**), and the product of its methylation **11** have proved to be optically pure compounds.

As shown in Figure 1 and Table 5, the methodology developed by Mikołajczyk et al. [3] and based on the NMR studies of diastereoisomeric salts forming "dynamic diastereoisomeric systems" has been very useful for the assignment of optical purity of enantiomeric phosphorothioates and phosphoroselenothioates.

An absolute configuration at the P atom in Sp,Sc-**15** has been assigned by X-ray crystallography techniques [15], which will be reported separately. It has provided us with the stereochemical relay-compound and has strengthened our conclusions concerning the assignment of absolute configuration on the basis of chemical correlations.

Methanolysis of Sp,Sc-**15** in the presence of $AgNO_3$, which occurs with inversion of configuration at phosphorus, leads to Rp,Sc-**19**. Chemoselective and stereoretentive PN → PS conversion of **19** gives Rp-**20**. Methylation of **20** leads to pure diastereoisomeric *O,S*-dimethyl-*N*-(α-methylbenzyl)phosphoramidothioate, Rp,Sc-**2**. A comparison of physical characteristics of **2** with those given by Inch [16], together with the known stereochemical course of each step, constitutes the chemical correlation for the assignment of absolute configuration of **11**, **15**, **17**, and **19** (Scheme 4).

Assignment of the absolute configuration of each of the diastereoisomers of **21** is proposed on the basis of retroanalysis: since laevorotary **28** (Scheme 6) has the Sp configuration, its precursor **26** (mp 82–83°C, δ 31.5/$CDCl_3$, $[\alpha]_D$ −90 (c1.3, MeOH)), has to possess the Sp,Sc configuration because of the stereoretentive mode of PN → PS conversion. Since Sp,Sc-**26** was achieved from **23** (mp 119–120°C, δ 44.3/$CDCl_3$, $[\alpha]_D$ −97.6 (c1.3, MeOH)) as the result of silver-ion promoted ethanolysis, which is known to proceed with inversion of configuration at the P atom, we could assign the absolute configuration of **23** as Rp,Sc. Since Rp,Sc-**23** was obtained in a stereoretentive reaction from **21** (mp 161–163°C, δ 23.2/$CDCL_3$, $[\alpha]_D$ −54.6 (c1.2, MeOH)), we could

assign its absolute configuration as Sp,Sc-**21**. It is obvious from earlier correlations that conversion of Rp,Sc-**23** to **25** is a stereoretentive process, and thus this last compound has to possess the absolute configuration Rp-**25** (Schemes 5 and 6).

Assignment of absolute configuration in compounds **12**, **13**, **3**, **5**, and **9** has been proposed on the basis of analogous retroanalysis, starting from the configurationally characterized Rp-**7** (Scheme 2). Moreover, the absolute configuration of **3** has been correlated with that of **2**, since **3** can be obtained as a result of silver ion-assisted ethanolysis of **2** occurring with inversion of configuration at phosphorus.

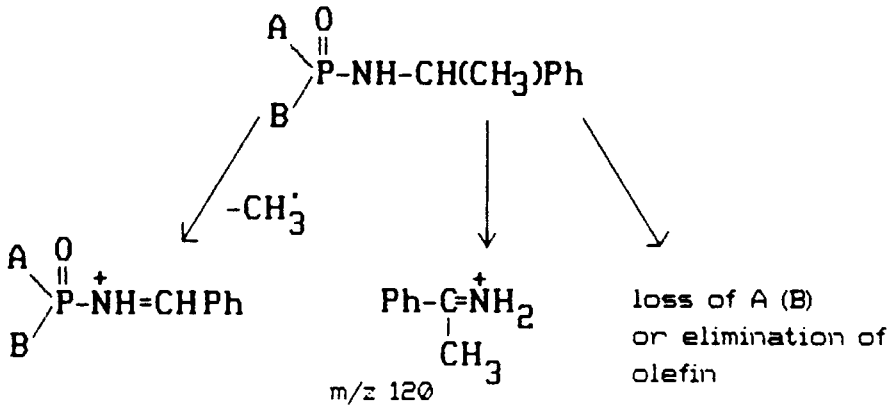
The most straightforward method for the assignment of absolute configuration was stereochemical analysis of a reaction sequence as depicted in Scheme 7. The absolute configuration at phosphorus in the diastereoisomers of **30** has been assigned by the stereoretentive reaction of methylphenylbenzylphosphine oxide with BuLi/PhCH=NCH(CH_3)Ph. Since both diastereoisomeric pair **30** and enantiomeric pair **29** have well defined stereochemistry [7], we could prove that conversion **30** → **29** occurs, as in all other cases, with retention of configuration.

Among the colligative data collected in Tables 1–4 the patterns of electron impact induced fragmentation of all diastereoisomers, derivatives of *S*(−)-(α)-methylbenzylamine, seem to be the most interesting. Beside the fact that the mass spectra do contain rather abundant molecular ions (intensities 2–45%), the common feature is the loss of methyl radical and appearance of M-15+ ions of abundance 8–100% (Scheme 8). This observation is of great importance since enantioisotopomeric compounds of general formula APB(O)●H (● means ^{18}O) can be converted (data not included) into diastereoisotopomeric *N*-(α-methylbenzyl)phosphylamidates ABP(O)NHR and ABP(●)NHR with inversion of configuration at phosphorus. Since ^{31}P NMR allows us to distinguish between Rp and Sp diastereoisomers, their separation and mass spectral analyses formulate the basis for assignment of absolute configuration at phosphorus in enantioisotopomeric compounds [17]. Representative examples will be published elsewhere.

An inspection of Table 1 indicates that, starting from all four diastereoisomers of **2**, we have obtained four pure diastereoisomers of **3** (Table 3). It should be noticed, however, that specific rotation values for all of these compounds are very similar and could not readily be used for differentiation between values that have proved to be comparable to the errors of measurement. However, careful analysis of ^1H NMR and ^{13}C NMR spectra enabled us to confirm the diastereoisomeric purity of particular compounds **3**.

EXPERIMENTAL

All melting and boiling points are uncorrected. Solvents and commercial reagents were purified by conventional methods before use. Column chromatography and TLC were performed on silica gel 70–230 mesh and on silica gel F_{254} plates, respectively (both from E. Merck). Nuclear magnetic resonance spectra were recorded in $CDCl_3$ solution with a Bruker MSL-300 spectrometer operating at 300.13 MHz (^1H), 75.47 MHz (^{13}C), and 121.47 MHz (^{31}P). Positive chemical shift values are assigned for compounds absorbing at lower field than standards (internal TMS for ^1H and ^{13}C and external H_3PO_4 for ^{31}P). Mass spectra were measured on a LKB 2091 spectrometer at 70 eV ionizing energy. Optical activity measurements were performed with a Perkin–Elmer 241MC photopolarimeter. Relevant analytical data for diastereoisomeric and enantiomeric compounds presented in this paper are collected in Tables 1–4 and are not repeated within the Experimental section.



SCHEME 8

S(−)-N^1,N^2-*Diphenyl*-N^3-α-*methylbenzylphosphortriamidate* (**10**)

Into a stirred solution of *S*(−)-α-methylbenzylamine {$[\alpha]^{20} = -39.3 \pm 0.2$ (neat), 6.1 g, 0.05 mol} in pyridine (20 mL) a solution of *N*,*N*′-diphenylphosphordiamidochloridate [5] (13,4 g, 0.05 mol) in pyridine (120 mL) was added dropwise at room temperature. Stirring was continued for 16 h. Pyridine was evaporated and the oily residue was concentrated twice with toluene (2 × 20 mL). Then it was dissolved in chloroform (100 mL), washed with water (3 × 20 mL), and dried over $MgSO_4$. Chloroform was evaporated and the oily residue solidified when treated with a small amount of ether. Its recrystallization from benzene/petroleum ether (20:1) gave 11 g (62%) of *S*(−)-**10** (mp 150–152°C). $R_F = 0.58$ (chloroform–acetone 1:1).

^{1}H NMR ($CDCl_3$):
δ = 1.42 (d, $^3J_{HH}$ = 6.8 Hz, 3H, CH_3—CH)
3.83 (m, 1H, N*H*—CH—CH_3)
4.48 (m, 1H, C*H*—(Ph)CH_3)
5.45 (m, 2H, N*H*Ph)
6.85–7.40 (m, 15$H_{arom.}$)

^{13}C NMR ($CDCl_3$):
δ = 25.13 (d, $^3J_{P—C}$ = 7.4 Hz, CH_3) 51.68 (s, *C*H)
118.34 (d, $^3J_{P—C}$ = 7.4 Hz, C—2)
121.62 (s, C—4)
129.23 (s, C—3)
140.47 (s, C—1)
126.11 (s, C—2)
127.34 (s, C—4)
128.77 (s, C—3)
144.15 (d, $^3J_{P—C}$ = 3 Hz, C—1)

In the same way *R*(+)-**10** was obtained.

S(−)-O,O-*Dimethyl*-N-(α)-*methylbenzylphosphoramidoselenoate* (**8**)

Into a solution of α-methylbenzylamine ($[\alpha]_D = -39.3 \pm 0.2$ (neat), 6.1 g, 0.05 mol) in pyridine (25 mL), selenium (4.0 g, 0.05 mol) was added in one portion and into the resulting slurry, *O*,*O*-dimethylphosphorochloridite (6.4 g, 0.05 mol) was added dropwise with external cooling at a temperature not exceeding 50°C. The reaction mixture was left to stand at room temperature for 16 h. Pyridine was evaporated, the oily residue was dissolved in 120 mL chloroform, washed with 5% aqueous HCl (60 mL) and water (2 × 30 mL) and dried over $MgSO_4$. Then chloroform was evaporated and the crude product was purified chromatographically with chloroform as eluent giving 8.5 g (60%) of pale yellow oil characterized as *S*(−)-**8**. $R_F = 0.74$ (chloroform).

^{1}H NMR ($CDCl_3$):
δ = 1.49 (d, 3H, $^3J_{H—H}$ = 6.8 Hz, CH_3—CH)
3.43, 3.69 (2d, 6H, $^3J_{P—H}$ = 14.5 Hz, CH_3O)
3.60 (m, 1H, NH), 4.46 (m, 1H, C*H*—CH_3)
7.2–7.4 (m, 5$H_{arom.}$)

^{13}C NMR ($CDCl_3$):
δ = 24.91 (d, $^3J_{P—C}$ = 5.7 Hz; CH_3—CH);
52.09 (d, $^2J_{P—C}$ = 3.9 Hz, CH—CH_3);
53.83, 54.06 (2d, $^2J_{P—C}$ = 3.9 Hz, CH_3O)
125.93 (s, C—2)
127.39 (s, C—4)
128.64 (s, C—3)
144.4 (d, $^3J_{P—C}$ = 4.2 Hz, C—1)

In the same way *R*(+)-**8** was obtained.

Sp,Sc-(−)-S-*Methyl*-N-*phenyl*-N′-(α-*methylbenzyl*)*phosphordiamidothioate* (**15**)

Into a stirred solution of *S*(−)-**10** (10.5 g, 0.03 mol) in dry dioxane (120 mL) sodium hydride (1.7 g, 50% suspension in oil; 0.036 mol) was added portionwise. Stirring was continued until hydrogen evolution ceased (ca. 0.5 h). Then an excess of carbon disulfide (3 mL) was added in one portion and the stirred mixture was warmed to 50–60°C for 5 h [18]. The mixture was then cooled to room temperature and an excess of methyl iodide (2 mL) was added in one portion. Alkylation was performed at 60–70°C for 2 h. Reaction mixture was filtered through celite, the filtrate was concentrated under reduced pressure, and the residue was dissolved in chloroform (100 mL), washed with water (2 × 50 mL), and dried over $MgSO_4$. Evaporation of the chloroform left 13.5 g of an oil that crystallized under treatment with diethyl ether (50 mL), giving 3 g (61%) Sp,Sc(−)-**15** (mp 170–172°C).

Evaporation of the mother liquor left an oily residue that was purified chromatographically (chloroform–acetone 10:1) and the second diastereoisomer Rp,Sc(−)-**15** was isolated by fractional crystallization from methanol/H_2O (90:10), mp 131–133°C, yield: 1 g (20%). $R_F = 0.29$ (chloroform–acetone 10:3).

In the same way, but starting from *R*(+)-**10**, the opposite diastereoisomers Rp,Rc(+) and Sp,Rc(+) were prepared.

Sp,Sc-(−)-S-*Ethyl*-S-*methyl*-N-(α-*methylbenzyl*)*phosphoramidodithioate* (**17**)

Sp,Sc-(−)-**17** was obtained by the above procedure from Sp,Sc-**15**, except for ethyl iodide (2 mL) being used in the alkylation step. The product was crystallized from acetone at 0°C, mp 69–71°C. Yield 73%, $R_F = 0.61$ (chloroform–acetone 1:3).

Analogously, other diastereomers of **17**: Rp,Sc-, Rp,Rc-, and Sp,Rc- were obtained starting from Rp,Sc-, Rp,Rc-, and Sp,Rc-**15**, respectively.

Rp-(−)-S-*Ethyl*-S-*methyl*-S-n-*propyl phosphorotrithioate* (**11**)

Into a stirred solution of Sp,Sc(−)-**17** (0.28 g; 1 mmol) in dry dimethoxyethane (4 mL) sodium hydride (0.06 g; 50% suspension in oil, 1.2 mmol) was added in one portion. When hydrogen evolution ceased (ca 30 min) an excess of carbon disulfide (0.5 mL) was added in one portion and the stirred mixture was kept at 40°C for 1 h. Then *n*-propyl iodide (0.5 mL) was added and stirring was continued at 30–45°C for 1–1.5 h. After the alkylation was over the reaction mixture was concentrated to dryness and the oily residue was chromatographed (chloroform–acetone 10:1) giving 0.16 g (70%) of Rp(−)-**11**. R_F = 0.8 (chloroform:acetone 10:3).

In the same way Sp(+)-**11** was obtained starting from Rp,Rc(+)-**17**.

Sp,Sc(−)-O,*Se-Dimethyl*-N-(*α-methylbenzyl*)-*phosphoramidoselenoate* (**12**)

Into a stirred solution of *S*(−)-**8** (14.7 g, 0.05 mol) in methylene chloride (20 mL), methyl iodide (21.3 g; 0.15 mol) was added in one portion and the mixture was left at ambient temperature for 72 h. A small amount of trimethylselenonium iodide was filtered off, and the filtrate was washed with water (10 mL) and dried over $MgSO_4$. Methylene chloride was evaporated leaving an oily residue. Its dilution with diethyl ether (20 mL) caused the crystallization of one diastereoisomer Sp,Sc(−)-**12**. The crude product was recrystallized from acetone (mp 124–126°C). Yield: 2.6 g (35%) R_F = 0.47 (chloroform–acetone 10:3).

In the same way Rp,Rc(+)-**12** was obtained from *R*(+)-**8**.

Rp,Sc(−)-O-*Methyl*-N-*phenyl*-N′-(*α-methylbenzyl*)*phosphordiamidate* (**19**)

Into a stirred suspension of powdered silver nitrate (0.68 g, 4 mmoles) in anhydrous MeOH (5 mL) a solution of Sp,Sc(−)-**15** (0.61 g, 2 mmoles) in anhydrous MeOH (10 mL) was added in one portion. Stirring was continued at room temperature for 48 h. After this time only a trace of substrate was observed on TLC. Triethylamine (0.56 mL, 4 mmoles) was then added and the mixture was stirred for an additional 15 min. Then the precipitate was filtered off and the filtrate was evaporated to dryness. The oily residue was chromatographed (chloroform–acetone 10:1) and the crude product was crystallized from diethyl ether (mp 88–89°C). Yield: 0.4 g (69%) of Rp,Sc(−)-**19**. R_F = 0.31 (chloroform–acetone 10:3).

In the same way Sp,Rc(+)-, Sp,Sc(−), and Rp,Rc(+)-**19** were obtained starting from Rp,Rc(+)-, Rp,Sc(−), and Sp,Rc(+)-**15**, respectively.

Sp,Rc(+)-O,S-*Dimethyl*-N-(*α-methylbenzyl*)-*phosphoramidothioate* (**2**)

Sp,Rc(+)-**2** was obtained from Sp,Rc(+)-**19** according to the procedure described for **15** except that only a stoichiometric amount of methyl iodide should be used in the alkylation step. Yield: 0.28 g (57%) of Sp,Rc(+)-**2**, mp 82–83°C (from benzene). R_F = 0.47 (chloroform:acetone 1:3).

In the same way Rp,Sc(−)-, Rp,Rc(+)-, and Sp,Sc(−)-**2** were obtained from Rp,Sc(−)-, Rp,Rc(+)-, and Sp,Sc(−)-**19**, respectively.

Sp,Rc(+)-O-*Ethyl*-O-*methyl*-N-(*α-methylbenzyl*)*phosphoramidate* (**3**)

Sp,Rc(+)-**3** was obtained from Rp,Rc(+)-**2** according to the procedure described for **19** using ethanol instead of methanol in the alcoholysis step, which was prolonged to 72 h. Yield 62%. R_F = 0.38 (chloroform–acetone 10:3), mp 87–89°C (from benzene/petroleum ether 2:1).

Analogously, starting from Sp,Rc(+)-, Sp,Sc(−)- and Rp,Sc(−)-**2** corresponding diastereisomeric Rp,Rc-, Rp,Sc-, and Sp,Sc-**3** were obtained.

The diastereisomers Rp,Sc-**3** and Sp,Rc-**3** were also obtained from Sp,Sc-**12** and Rp,Rc-**12**, respectively, by the same procedure (reaction time 1 h).

Sp(−)-O,S-*Dimethyl*-O-*ethyl Phosphorothioate* (**7**)

A. To a stirred solution of Rp,Sc(−)-**3** (0.24 g, 1 mmol) in anhydrous tetrahydrofuran (4 mL), carbon disulfide (0.5 mL) was added and subsequently potassium hydride (0.24 g, 20% suspension in oil, 1.2 mmol) was added in one portion. Stirring was continued at room temperature for 1 h. Then methyl iodide (0.1 mL) was added in one portion and stirring was continued for 1.5 h. After the alkylation had been completed the reaction mixture was concentrated to dryness. The oily residue was dissolved in chloroform (5 mL), washed with water (3 × 2 mL) and dried over $MgSO_4$. Chloroform was evaporated and the crude mixture was chromatographed (chloroform–acetone 10:3) to give 0.1 g (60%) of Sp-**7**. R_F = 0.48 (benzene–chloroform–dioxane 6:2:1).

In the same way Rp(+)-**7** was obtained starting from Sp,Rc(+)-**3**.

B. Sp(−)-**7** and Rp(+)-**7** were also obtained from Sp(+)-**9** and Rp(−)-**9**, respectively, according to the procedure described for **19**, with ethanol being used instead of methanol in the alcoholysis step (reaction time 5 h).

Sp(+)-O,S,*Se-Trimethyl phosphoroselenothioate* (**9**)

To a stirred solution of Sp,Sc(−)-**12** (0.3 g, 1 mmol) in anhydrous, freshly distilled *N,N*-dimethyl-

formamide (4 mL) carbon disulfide (0.5 mL) was added and, subsequently, sodium hydride (0.060 g, 50% suspension in oil, 1.2 mmol) was added in one portion. The stirred mixture was kept at room temperature for 1 h. Then methyl iodide (0.1 mL) was added in one portion and stirring was continued for 1 h. The reaction mixture was diluted with benzene (10 mL), washed with water (3 × 5 mL), and dried over $MgSO_4$. Solvents were evaporated and the oily residue was chromatographed (chloroform–acetone 10:1) giving 0.16 g (73.5%) of Sp(+)-**9**. R_F = 0.55 (benzene–chloroform–dioxane 6:2:1).

In the same way Rp(−)-**9** was obtained starting from Rp,Rc(+)-**12**.

Sp,Sc(−)-N-*Phenyl*-N′-(α-*methylbenzyl*)-*methanephosphondiamidate* (**21**)

Into a stirred solution of methanephosphonodichloridate (6.6 g; 0.05 mol) in dichloromethane (100 mL) a solution of aniline (4.7 g; 0.05 mol) and triethylamine (5.1 g; 0.05 mol) in dichloromethane (10 mL) was added dropwise with external cooling at a temperature not exceeding 40°C. Stirring was continued for 1 h at room temperature. Then a solution of α-methylbenzylamine ($[\alpha]_D$ = −39.3; ±0.2(neat); 6.1 g; 0.05 mol) and triethylamine (5.1 g, 0.05 mol) in dichloromethane (10 mL) was added dropwise with cooling at a temperature not exceeding 40°C. Stirring was continued for an additional 1 h. Then the reaction mixture was washed with water (3 × 20 mL) and dried over $MgSO_4$. Dichloromethane was evaporated to give an oily residue. Its treatment with a mixture of ethyl ether and acetone (10 mL 1:1 v/v) caused the crystallization of diastereoisomeric Sp,Sc-**21**. Its recrystallization from acetone gave 3 g (44%) of pure compound (mp 161–163°C). R_F = 0.5 (chloroform–ethanol 9:1).

In the same way Rp,Rc(+)-**21** was obtained.

Rp,Sc(−)-S-*Methyl*-N-(α-*methylbenzyl*)-*methanephosphonamidothioate* (**23**)

The Rp,Sc(−)-**23** and Sp,Rc(+)-**23** were obtained from Sp,Sc(−)- and Rp,Rc(+)-**21**, respectively, according to the procedure described for **15** except that tetrahydrofuran was used as a solvent and chloroform–ethanol (9:1) was used as an elution system during chromatography purification. The crude product was crystallized from benzene/petroleum ether (2:1), mp 119–120°C. Yield 57%, R_F = 0.57 (chloroform–ethanol 9:1).

Sp,Sc(−)-O-*Ethyl*-N-(α-*methylbenzyl*)-*methanephosphonamidate* (**26**)

The Sp,Sc(−)-**26** and Rp,Rc(+)-**26** were obtained from Rp,Sc(−)- and Sp,Rc(+)-**23**, respectively, according to the procedure described for **19**. The oily residue was chromatographed (chloroform–ethanol 25:1) and the crude product was crystallized from ethyl ether, mp 82–83°C. Yield: 61–66%, R_F = 0.54 (chloroform–ethanol 9:1).

Sp(−)-O-*Ethyl*-S-*methylmethanephosphonothioate* (**28**)

Sp(−)- and Rp(+)-**28** were obtained from Sp,Sc(−)- and Rp,Rc(+)-**26**, respectively, according to the procedure A described for compound **7**. The oily product was chromatographed with chloroform–ethanol (25:1) as an elution system. Yield: 65%, R_F = 0.66 (chloroform–ethanol 9:1).

Rp(−)-S-*Methyl*-S-*ethylmethanephosphonodithioate* (**25**)

Rp(−)- and Sp(+)-**25** were obtained from Rp,Sc(−)- and Sp,Rc(+)-**21**, respectively, according to the procedure described for compound **21** except that ethyl iodide was used in the alkylation step. Yield 63–70%, R_F = 0.62 (chloroform–acetone 10:3).

Sp(−)-S-*Methyl methylphenylphosphinothioate* (**31**)

Sp(−)- and Rp(+)-**31** were obtained from Rp,Sc(−)- and Sp,Sc(+)-**30** [7], respectively, according to the procedure A described for compound **7**. Yield 54%, R_F = 0.47 (chloroform–acetone 10:3).

General Procedure for Sample Preparation for Optical Purity Measurement by Means of ^{31}P NMR Analysis

A crude reaction mixture containing the alkaline salt of a corresponding thioacid (**5**, **13**, **18**, **24**, **27**, or **29**) was concentrated, dissolved in water, and washed twice with chloroform. The upper layer was then applied onto an ion exchange column (Dowex 50W, H^+ form) and the eluant was neutralized with *S*(−)-α-methylbenzylamine (or *S*(−)-α-methylnaphthylamine) giving the corresponding ammonium salt. The resulting solution was then evaporated to dryness, dried under high vacuum, and dissolved in an appropriate solvent (benzene-d_6 or $CDCL_3$). ^{31}P NMR spectra of such prepared salts were compared with those obtained for racemic compounds (Figure 1, Table 5).

ACKNOWLEDGMENTS

Studies reported in this paper were financially assisted by the Polish Academy of Sciences and CPBR 3.13.4. Authors are indebted to Mr. M. Sochacki for recording and interpretation of mass spectra and to Mr. P. Guga for critical evaluation and technical preparation of the manuscript.

REFERENCES

[1] A. Kotyński, K. Lesiak, W. J. Stec, *Pol. J. Chem., 53,* 1979, 2403.

[2] B. Krzyżanowska, W. J. Stec, *Phosphorus and Sulfur, 30,* 1987, 287.

[3] M. Mikołajczyk, J. Omelańczuk, M. Leitloff, J. Drabowicz, A. Ejchart, J. Jurczak, *J. Am. Chem. Soc., 100,* 1978, 7003.

[4] C. R. Hall, T. D. Inch, *Phosphorus and Sulfur, 7,* 1979, 171.

[5] D. E. Gibbs, *Nucl. Acid Chem., 1978,* 801.

[6] K. L. Agarwal, F. Riftina, *Nucl. Acid Res., 6,* 1979, 3009.

[7] A. Nudelman, D. J. Cram, *J. Org. Chem., 36,* 1971, 335.

[8] D. Valentine, Jr.: in *Asymmetric Synthesis,* vol. 4, Academic Press, New York, pp. 263–311 (1984).

[9] T. Koizumi, Y. Kobayashi, H. Amitani, E. Yoshii, *J. Org. Chem., 42,* 1977, 3459.

[10] T. Koizumi, H. Amitani, E. Yoshii, *Tetrahedron Lett., 1978,* 3741.

[11] T. Koizumi, H. Amitani, E. Yoshii, *Synthesis, 1979,* 110.

[12] W. J. Stec, *Acc. Chem. Res., 16,* 1983, 411.

[13] H. E. Baumgarten (ed): *Organic Syntheses,* vol. 5, Wiley, New York, p. 932 (1973).

[14] W. J. Stec, *Bull. Acad. Polon. Sci., Ser. Sci. Chim., 21,* 1973, 709.

[15] J. V. Silverton, unpublished results.

[16] C. R. Hall, T. D. Inch, *Tetrahedron Lett., 1977,* 3761.

[17] S. Trippet, C. L. White, *J. Chem. Soc., Chem. Commun., 1984,* 287.

[18] ^{31}P NMR data for diastereoisomeric salts: Sp,Sc-**14** δ^{31}P = 46.7 (dioxane), Rp,Sc-**14** δ^{31}P = 47.1 (dioxane), Rp,Sc-**16** δ^{31}P = 70.9 (tetrahydrofuran), Sp,Sc-**16** δ^{31}P = 71.2 (tetrahydrofuran), Rp,Sc-**20** δ^{31}P = 60.7 (dioxane) and Rp,Sc-**22** δ^{31}P = 61.5 (tetrahydrofuran).