(1)

Stereochemistry of Tetra- and Pentacoordinate Organic Compounds of Phosphorus and Antimony

(4配位および5配位有機リンおよびアンチモン化合物の立体化学)

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General Introduction

General Introduction

Phosphorus partakes a vital role in biological processes in the form of phosphates. Its most spectacular role is as the central building block in nucleic acids which make up the polymeric deoxyribonucleic acid (DNA). Phosphates are also involved in adenosine triphosphates (ATP) which serve to store chemical energy by the transformation to and from adenosine diphosphates (ADP). Further, phosphate residues which are attached to several coenzymes combine with the hydroxyl groups of the serine, threonine, and tyrosine residues of enzymes to control the actions of these biocatalysts.[1] Although the number is small naturally occurring phosphorus compounds bearing P-C bonds such as $NH_2CH_2CH_2P(O)(OH)_2$ and P-N bonds such as $HO_2CCH_2N(Me)C(=NH)NHP(O)(OH)_2$ are also known.[2]

Particularly from the early mid-twentieth century artificial phosphorus compounds have seen application as pesticides and research aiming at the development of effective phosphorus based chemicals exhibiting physiological activity became popular. In some instances it has been found that with optically active phosphoryl based agrochemicals the acetylcorrin inhibition activity was quite different between the compounds of R and S chiralities, implying the need for obtaining optically active compounds with phosphoryl groups. Phosphorus based medicines have also been developed.[3]

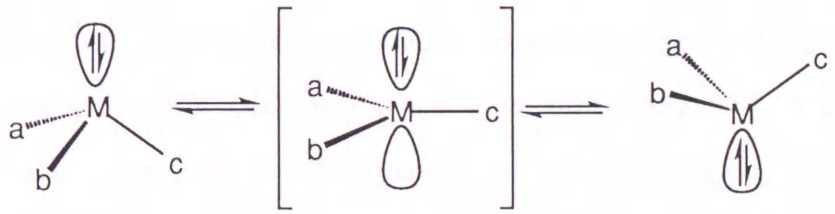
Because of the importance of phosphorus compounds the mechanism of reactions involving phosphorus compounds, particularly those having a P=O segment, has been a topic of interest for quite some time. Through the pioneering work of Westheimer and others it is now widely accepted that nucleophilic substitution reactions involve pentavalent phosphorus intermediates (or transition states) formed by nucleophilic attack of anionic species upon the tetracoordinate phosphorus atom, and that the stability and stereochemistry (both steric and electronic effects combined) of the transient species (or transition state) greatly influence the outcome of reaction

processes.[4] Therefore in order to deduce a basic understanding of the processes much work has been devoted to its stereochemical aspects. To this end various simplified model compounds including optically active phosphate derivatives have been designed and utilized. For instance, isotope labeled optically active (R)-phenyl [^{16}O, ^{17}O, ^{18}O]phosphate prepared by a method developed by Inch et al.[5] has been used in the stereochemical analysis of the reactants and products in enzyme catalyzed transphosphorylation by Knowles et al.[6] and hydrolysis by Gerlt et al.[7]

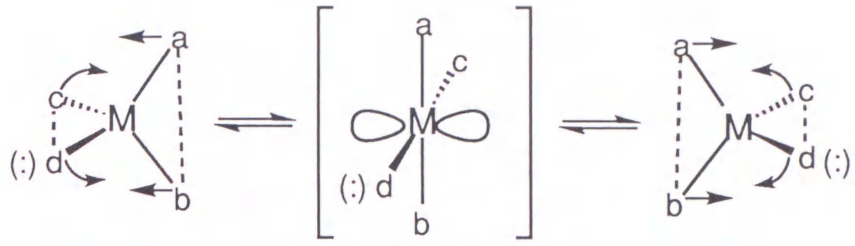
A recent and important application of phosphorus is in the form of tricoordinate phosphine derivatives as ligands in metal complex catalyzed synthesis. The milestone in this field of chemistry was the industrial utilization of the Wilkinson catalyst [$Rh(PPh_3)_3Cl$] in the stereoselective cis hydrogenation of olefins.[8] The preparation of enantiomerically pure cyclohexyl-o-anisylmethylphosphine (CAMP) by Mislow et al.[9] and diphenyl-o-anisylmethylphosphine (diPAMP) by Knowles et al.[10] coupled with the use of these phosphines as ligands in the Wilkinson catalyst led to asymmetric hydrogenation of prochiral olefins to efficiency levels comparable with enzymes of which efficiency is usually keenly dependent on the substrate, thus paving the road for metal complex catalyzed asymmetric synthesis on the industrial level. However, the difficulty of readily obtaining enantiomerically pure phosphines with asymmetric phosphorus has lead to the development of optically active phosphines with asymmetric carbon centers in the backbone, which are free of the occurrence of epimerization. The breakthrough was the preparation and utilization of (+) and (-)-2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (DIOP) by Kagan et al.[11] and the development of (+) and (-)-2,2'-bis(diphenylphosphine)-1,1'-binaphthyl (BINAP) by Noyori et al.[12] has raised the potential of these backbone chiral compounds. Although the chiral center is situated away from the metal center in these compounds, the chiral center serves to control the orientation of the phenyl groups upon phosphorus thus creating a chiral environment. The limitation in obtaining enantiomerically pure phosphines with asymmetric phosphorus comes from the fact that it is difficult to carry

out substitution at phosphorus with complete stereoselectivity due to the fact that although the initial attack of a nucleophilic reactant could be completely stereoselective, the substitution is not a straightforward S_N2 reaction as in carbon reactions because phosphorus is capable of forming pentacoordinate phosphorus intermediates and these reaction intermediates are often susceptible to permutation (by Berry pseudorotation, vide infra) resulting in the partial or complete epimerization of the phosphorus center.

Although the inversion barrier is generally high, tricoordinate phosphines themselves are susceptible to positional isomerization. The mechanism for this process had conventionally been thought to involve vertex (pyramidal) inversion at phosphorus such as that invoked in tricoordinate nitrogen compounds in which the barrier is generally too low to allow even the observation of topological isomers. Hybridization (and thus rehybridization) of s and p orbitals for elements situated lower than the first row on the periodic table is known to be an energetically unfavored process. Therefore, since vertex inversion involves a transition state in which the sp^3-like orbital (or an orbital of more s character) of the lone pair rehybridizes to a p type orbital in the transition state on to a new sp^3-like orbital, the barrier for phosphorus is generally considered to be high.

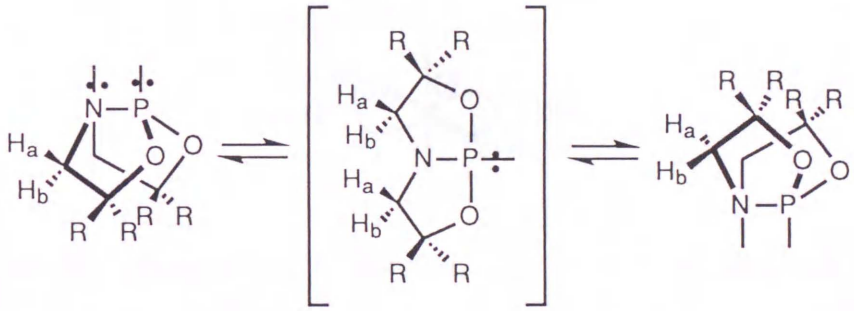


vertex inversion process

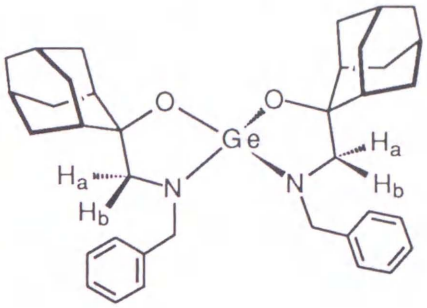


edge inversion process

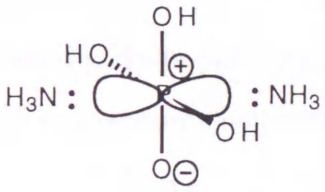
However Arduengo et al. have put forward an alternative mechanism for inversion, i. e., edge inversion.[13] According to this mechanism the transition state involves a species in which the central atom and all the atoms attached to it (including the lone pair) are essentially coplanar. They have designed a system bearing a tridentate ligand that would lower the barrier for inversion and experimental determination ($\Delta H^{\neq}$=23.4 kcal/mol in o-dichlorobenzene-d_4) was found to be in good agreement with theoretical predictions ($\Delta H^{\neq}$=28.1 kcal/mol), thus verifying this concept.[14]



This theory was applied to tetracoordinate compounds of group XIV, in which the lone pair in group XV compounds has been substituted with a covalent substituent,[15] and using a spiro germanium compound it was again found to be reasonable to assume an edge inversion process.[16]



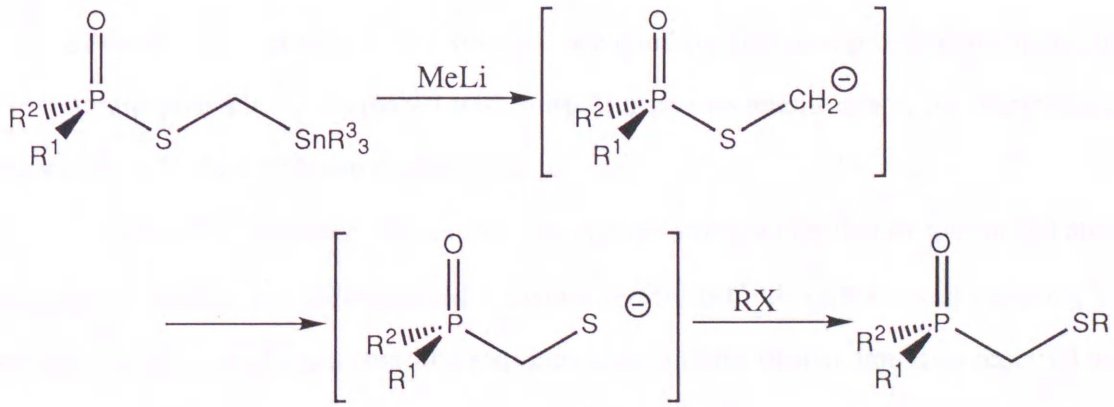
Furthermore theoretical calculations showed that nucleophilic assistance by interaction of electron donating species with the unoccupied p orbital appearing in the transition state could substantially lower the inversion barrier thus giving the possibility for even tetracoordinate phosphates to cause edge inversion ($\Delta H^{\neq}$=24.1 kcal/mol),[17] thus giving an alternative to the conventional perception of attack of a nucleophilic species upon phosphorus to form a pentacoordinate species, followed by pseudorotation and extrusion of the nucleophilic species.

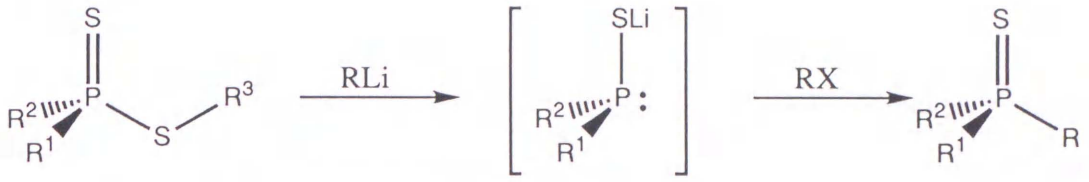


In this way phosphorus can undertake many profiles and thus there are quite a few possible ways in which stereochemical integrity can break down, a feature not seen in trivial carbon atoms. Therefore the main stream in the field of catalytic asymmetric synthesis has become the development of enantiomerically pure phosphines with backbone carbon asymmetry. However, in order to widen the scope of catalytic asymmetric synthesis using optically active phosphine derivatives, the preparation of enantiomerically pure phosphine (III) derivatives with asymmetry upon phosphorus still remains an attractive and challenging target, and general methodology for this purpose is awaited.[18] It would also be desirable to have many chiral phosphorus compounds in hand for the development of pharmaceuticals and for thorough stereochemical investigations of phosphorus related reactions. Conventional methods of preparing

scalemic P-chiral phosphines mostly consisted of the direct resolution of the desired species by forming diastereomeric salts or complexes with optically active resolving agents, or via resolution of covalent diastereomers with chiral auxiliaries in one of the substituents which do not involve the direct substitution of the phosphorus center in the removal of the auxiliary. The use of commercially available chiral columns has also been found to be satisfactory in some cases although on a small scale basis. A more flexible and more general method of preparing a series of scalemic phosphines and their derivatives would be the direct stereoselective displacement of resolvable diastereomeric derivatives at the phosphorus center. A major recent advancement in this field can be said to be the transformation of resolvable optically active phosphine-borane complexes $Ph(R)P(BH_3)O$-(-)-Men by Imamoto et al.[19]

In chapter one novel methods of preparing optically active phosphine derivatives possessing new P-C bonds from optically active phosphinothioic acids via [1,2] rearrangement of phosphinothioic S-esters and via selective P-S cleavage of phosphinodithioic esters followed by electrophilic alkylation are described. Among phosphorus compounds optically active phosphinothioic acids are known to be the most accessible by conventional optical resolution methods, namely fractional crystallization. Thus the method developed by us can be considered of wide applicability.





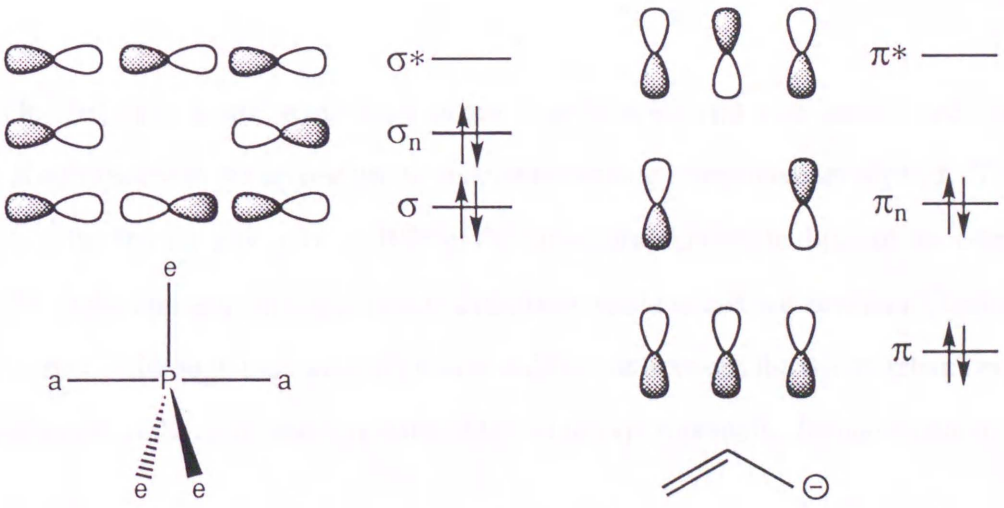
The implication that pentacoordinate species are involved in biological processes as either the transition state or intermediate has triggered a new field of research concerning the fundamental nature of pentacoordinate compounds. In order to gain insight many thermodynamically stable pentacoordinate compounds have been prepared and examined.[20]

The basic structure of pentacoordinate compounds is unique in that there is no way to fit five points on a sphere so that they are all equivalent other than to place all five points in a planar pentagon, which is not realistic in considering the structure of existing molecules. Thus, the arrangement that would best fit the axioms of VSEPR theory is to place the five points in a trigonal bipyramid which has two sets of inequivalent sites, the two apical sites and the three equatorial sites.[21] In an ideal arrangement the three equatorial points would form a regular triangle meaning that the angle comprising an arbitrary equatorial site, the center, and another arbitrary equatorial site is 120°, while the two apical sites are positioned linearly with the center which intersects perpendicularly with the equatorial plane. This inequivalency causes an abrupt increase in the possible number of isomers. When all five sites are occupied by different substituents up to 20 isomers are possible as compared with only 2, a pair of enantiomers, for tetrahedral molecules with four different substituents.

As for the electronic structure of the central atom, while that of pyramidal and tetrahedral species can be explained based on hybrid orbitals of the s and the three p orbitals, in the case of pentacoordinate species an additional orbital would be required to accommodate 10 electrons coming from the five covalent bonds. The conventional explanation proposed by Pauling[22] was that the lowest lying d orbital would participate in the hybridization of orbitals to form a dsp^3 type combination to account for the

violation of the Octet rule and has found support particularly in the field of inorganic chemistry.

However an alternative explanation was proposed by Pimental[23] and by Rundle[24] in 1951, which utilized the concept of three-center four-electron (3c-4e) bonds, in which the electrons are delocalized into the apical substituents to relieve the electron density upon the central atom. Musher gave a simplified bonding scheme to describe the electronic structure and extended it to a wide range of molecules including compounds of even higher coordination number.[25] For the pentacoordinate species he proposed an sp^2 hybridization to account for the six electrons in the equatorial plane while three-center four-electron bonds could be comprised of the σ and σ_n bond formed by the linear combination of the remaining p orbital on the central atom and one valence atomic orbital each of the two apical atoms. This concept is very similar to the concept of π electron conjugation as seen in the allylic anion. The difference between the two is the use of σ bonding for the 3c-4e bond and π bonding for the allylic bond. In order to obtain a stable compound it would be natural to have electron accepting substituents in these apical positions, leading to the concept of apicophilicity.

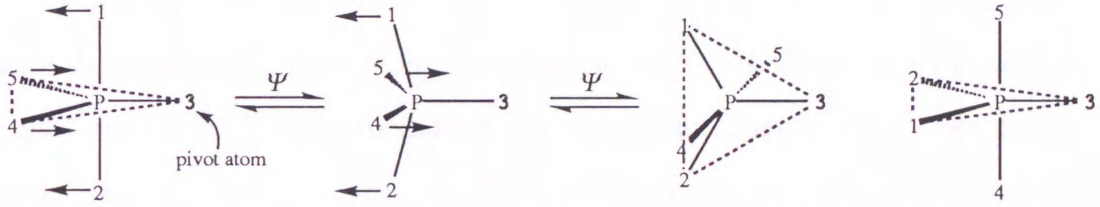


All recent theoretical calculations favor the 3c-4e bond, i. e., hypervalent bonding. Calculations including d functions upon the central atom show that the

contribution of the d orbital in forming the hypervalent bond is less than 10 % and its main function is to polarize the bonds and to lower its energy level.[26]

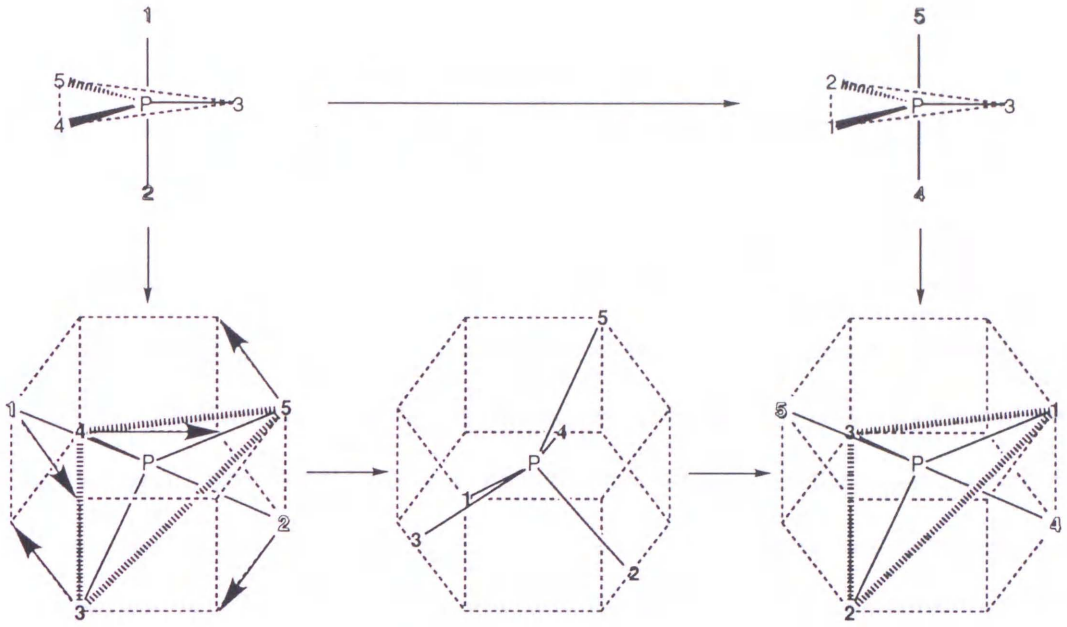
The permutation of pentacoordinate compounds has been found to be a very fast process in contrast with that of tetrahedral compounds which do not show such behavior. To account for this phenomenon two major mechanisms have been proposed, the pseudorotation process by Berry[27] and the turnstile process by Ugi.[28]

The former has its foundation on bond bending motions with the pair of apical substituents bending away from a pivotal equatorial atom and the remaining two equatorial substituents bending toward this pivotal atom to proceed via a transition state square pyramidal structure on to an isomer which has the apical atoms exchanged with the two moving equatorial positions.



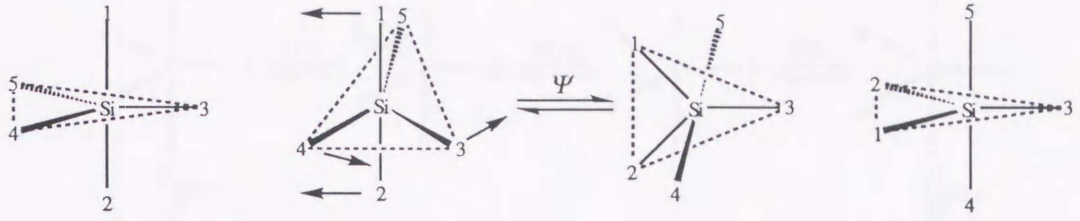
trigonal bipyramidal structure (TBP) — square pyramidal structure (SP) — trigonal bipyramidal structure (TBP)

On the other hand, according to the latter mechanism one apical and one equatorial substituent make up one group and the remaining three make up another. The members of the former group rotate 180° in the same direction while those of the other rotate 120° in the opposite direction just as a turnstile would to attain a new combination of substituents. Although the mode of motion is different between the two mechanisms, the overall result is the same and it is rather difficult to experimentally distinguish them.



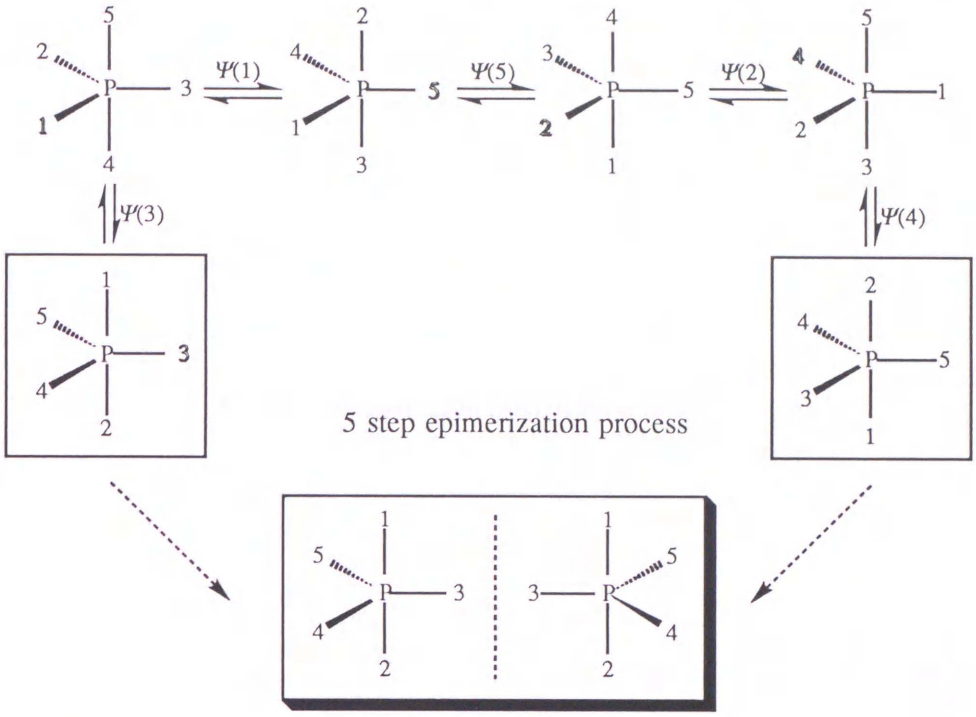
However theoretical calculations have shown that for simple systems the Berry process is energetically much more favorable and has thus become the more widely accepted mechanism for permutation in pentacoordinate compounds.[29] For simple compounds such as PH_5 the barrier for Berry pseudorotation has been calculated to be as low as 1-2 kcal/mol.

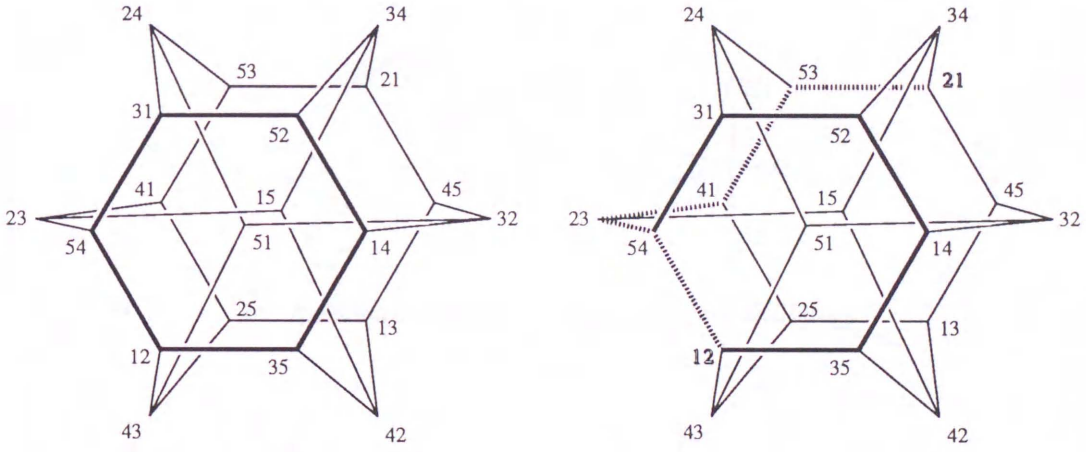
From the theoretical calculations of pentacoordinate silicate compound SiH_4F^- still another mechanism has been proposed by Gordon in which the direction of rotation of the moving equatorial substituents 3 and 4 is the same. In this case the pivotal equatorial substituent 5 becoming an apical substituent in the new configuration.[30] This alone shows that the permutation of pentacoordinate compounds is a much more perplex process than the widely accepted naive Berry process and implies that a lot has yet to be known of the true nature of the isomerization.



Theoretical calculations have also implied that the conventionally accepted square pyramidal structured species is not necessarily the transition state. For example according to calculations carried out by Wasada et al.[31] on PF_3H_2, the isomer with two apical hydrogens was found to be energetically less stable than the square pyramidal species usually perceived to be the transition state on the reaction coordinate, and those on monocyclic $P(OC_3H_6O)H_3$ also showed that having the five membered bidentate ligand in the diequatorial disposition was of more energy than the square pyramidal species. So in the case of bidentate ligands the permutation could actually pass through the usually unfavored turnstile mechanism in which strain energy might be relieved. Sophisticated calculations on the turnstile process in the presence of bidentate ligands are awaited to reveal the true nature.

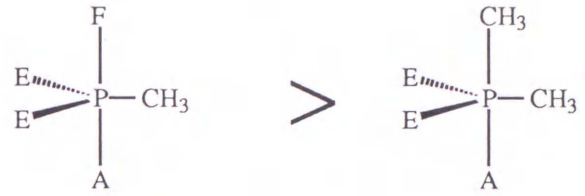
Since the real nature of permutation is not known with certainty we shall use the presently generally accepted Berry process to give a general picture of isomerization in pentacoordinate species. According to this mechanism when the five sites are unequally substituted at least five processes in which each substituent is used once as the pivotal atom are necessary to convert one isomer to its enantiomer. The interexchange processes has cleverly been summed up in a topological graph usually referred to as the Desargus-Levi graph.[32]



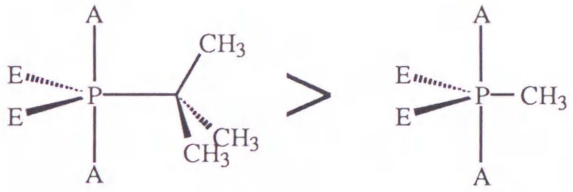


There are several guidelines for raising the permutation barrier which in principle is to differentiate the thermodynamic stability of topologically differing configurations.[33] One is to fit in substituents in which the difference in electronegativity between the apical and equatorial substituents is as large as possible. Another is to use bulky groups in the equatorial position. Still another (and of large effect) is to incorporate small rings (members of five or less) into the compound. Some others are to fix π donor equatorial

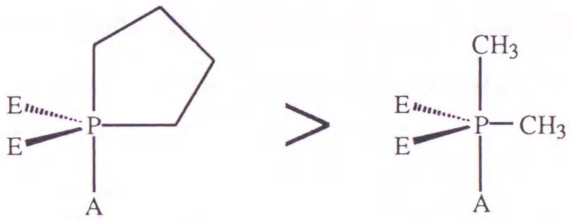
substituents perpendicular to the apical bond and π acceptor substituents parallel to the apical bond.



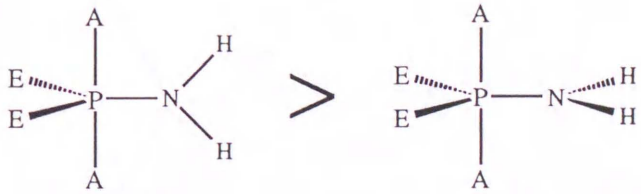
Use of substituents having large difference in electronegativity



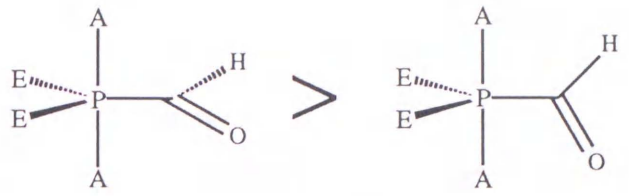
Use of equatorial prefering substituents of large steric hindrance



Incorporation of bidentate ligands which form small rings

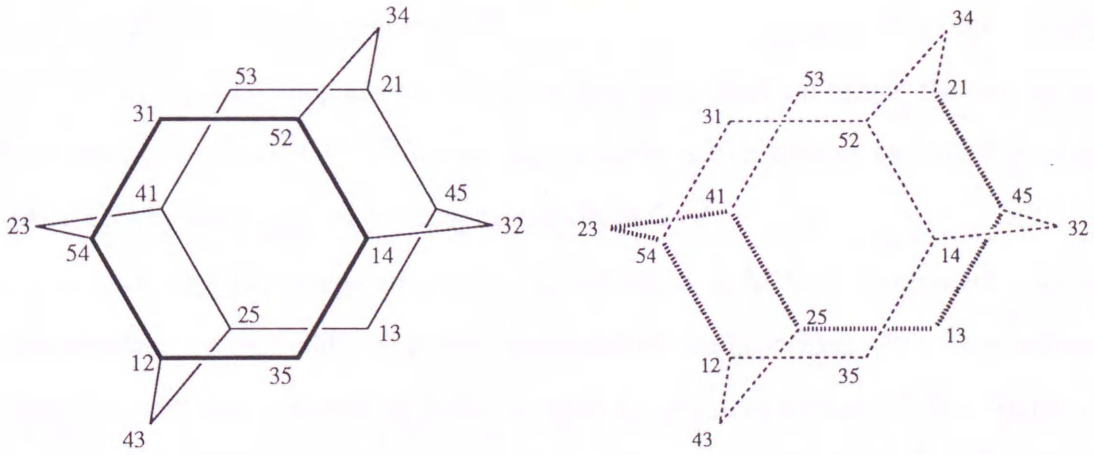


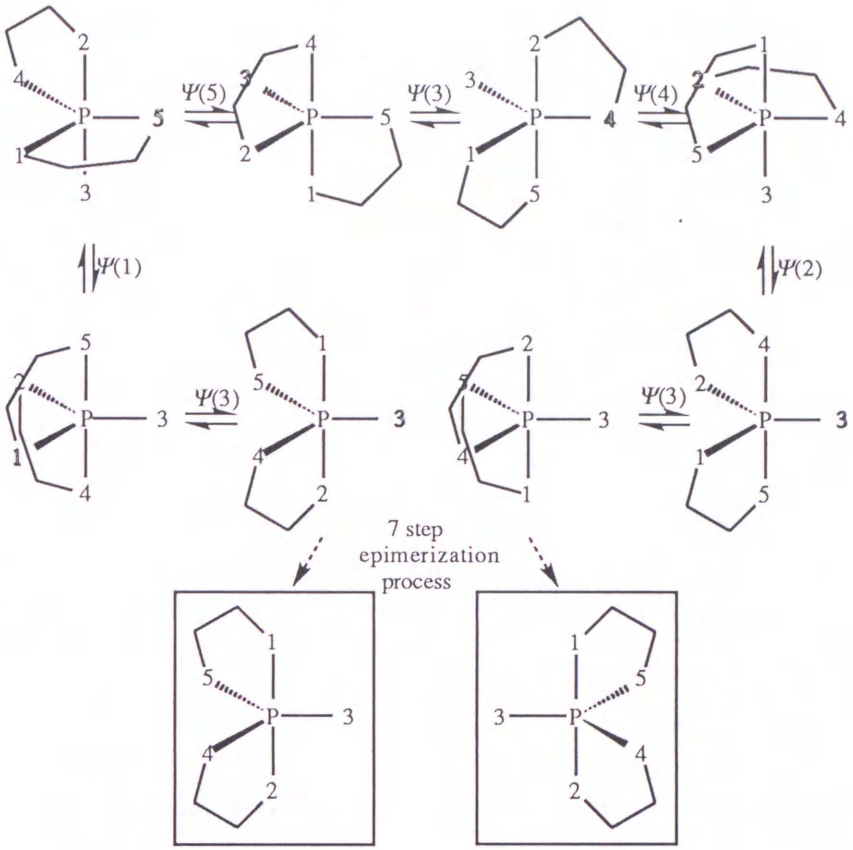
Perpendicular alignment of the apical bond and equatorial π donors



Parallel alignment of the apical bond and equatorial π acceptors

When two bidentate ligands are introduced into a pentacoordinate compound, for example if 1 and 5, and 2 and 4 are of the same ligand then the combinations of 15, 51, 24, and 42 are non-existent and therefore the Desargus-Levi graph is reduced to the following figure. Furthermore if 1 and 2 are differentiated from 4 and 5 as electron withdrawing groups, the highest energy intermediate according to the Desargus-Levi graph would be 34, 43, 35, and 53 in which one ligand is positioned diequatorial and two carbon atoms are placed at the apical positions. Therefore if we assume that the highest energy transition state is this intermediate or a square pyramid species leading to this structure then we can envision a seven step permutation process to account for epimerization in spiro compounds, in which out of the many possible configurations only a pair of enantiomers with the electronegative substituents in the apical positions are probable.

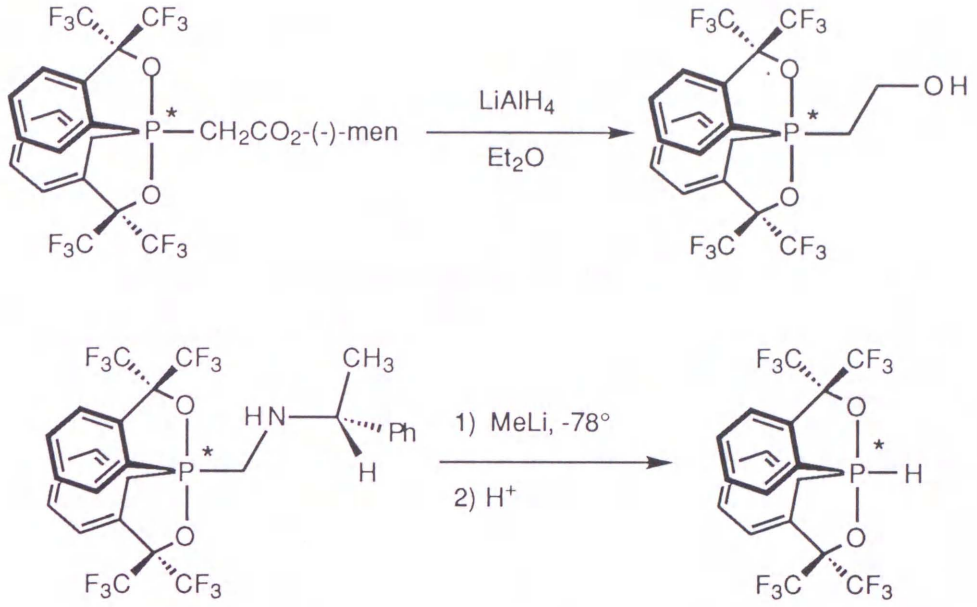




Among the isolated thermodynamically stable pentacoordinate compounds some optically active phosphoranes with backbone asymmetry have been reported. Besides one example which is monocyclic these compounds are all spiro compounds (bicyclic) with optically active alcohols or aminoalcohols as the chiral auxiliary.[34] As for optically active phosphorus compounds with phosphorus as the sole chiral center, the only report has been by Hellwinkel.[35] However this optically active species exhibited residual optical activity and could not be stereochemically defined.

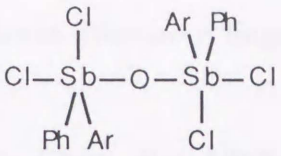
In chapter 2 the preparation and characterization of the first enantiomeric pairs of stereochemically definable 10-P-5[36] phosphoranes are described. We have utilized Martin's ligand that is known to stabilize many hypervalent species.[37] The feature of this ligand is that the trifluoromethyl groups raise the negativity of the oxygen atoms attached to phosphorus, the bidentate and phosphorus atom together form five

membered rings, and the trifluoromethyl groups exert a Thorpe-Ingold effect[38] to favor the formation of the five membered ring.

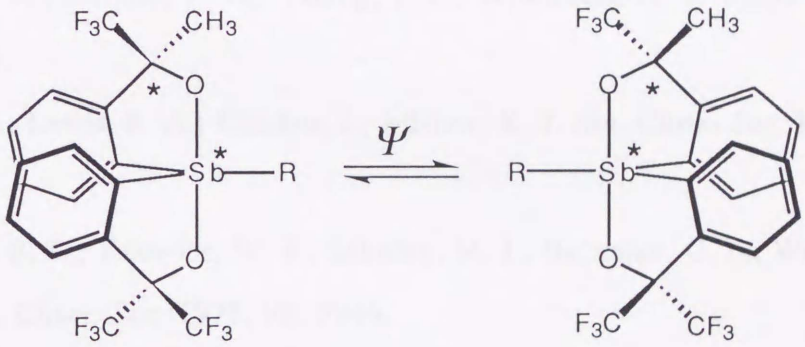


Assuming that the Berry pseudorotation mechanism, which has its foundation upon vibrational bending motions, is operative the strength of the bonds about the pentacoordinate atom would reflect the barrier to permutation. Thus, pentacoordinate compounds of elements of lower rows on the periodic table having weaker bonds would naturally be expected to have smaller permutation barriers compared with phosphorus, therefore making it difficult to obtain configurationally stable diastereomers. In fact, there is experimental evidence that is in good accordance with this assumption. For example, for spiro compounds with biphenylene group as bidentates and P, As, Sb as the central atom, the barriers for a multi-step permutation process between rapidly interconverting enantiomers have been determined by variable temperature NMR techniques to be 15.8, 15.4, 11.6 kcal/mol,[39] respectively. On the other hand, for compounds MCl_5 both measurements (3.6, 2.8, 1.6 kcal/mol, respectively)[40] and theoretical calculations (4.78, 2.80, 1.98 kcal/mol, respectively)[41] for a single step permutation process which exchange the apical and equatorial substituents support this tendency. In the case of antimony, Doak et al. have reported that in a certain case

diastereomeric species could be observed by VT-NMR,[42] but to our knowledge there have been no reports on the isolation of such compounds as configurationally stable species.



In chapter 3 the preparation, stereochemical characterization, and kinteic studies of the first stereochemically definable diastereomeric 10-Sb-5 stiboranes are described. A modified Martin's ligand was employed along with a Martin's ligand. The permutation of these compounds were found to be accelerated by the interaction of donative solvents such as pyridine and DMA.



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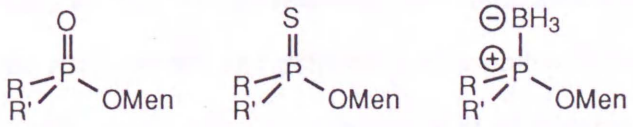
Chapter 1

Preparation of Optically Active Phosphine Oxides via Wittig Type Rearrangement and Phosphine Sulfides via Alkylation of Lithium Phosphinothioites

1. Introduction

Optically active phosphorus compounds have been utilized in the investigation of biological processes that involve phosphate transformation, such as enzymic activity.[1,2] They have also been utilized in the form of phosphines as ligands for metal catalyzed asymmetric synthesis. Phosphorus compounds have been put to practical use as agrochemicals and pharmaceuticals[3] Further advancement in these fields relies on the development of efficient and versatile methodology for preparing optically active phosphorus compounds.[4,5]

The interconversion between P-chiral phosphine chalcogenides with P-chiral phosphines has been thoroughly examined and efficient reactions have been found.[5] In contrast, the preparation of P-chiral phosphines and P-chiral phosphine chalcogenides themselves is not so straightforward. Efficient reactions of generality for the direct interconversion among P-chiral phosphine chalcogenides have also not been established. The most extensively used method of preparation for optically active phosphines is the one developed by Mislow[6] which utilizes the substitution reaction of the menthyl ester of phosphinic acid after separation of the diastereomers. Similar reactions utilizing O-menthyl phosphinothioates[7] and menthyl phosphinite-borane complexes[8] have also evolved. Other chiral auxiliaries have also been examined.

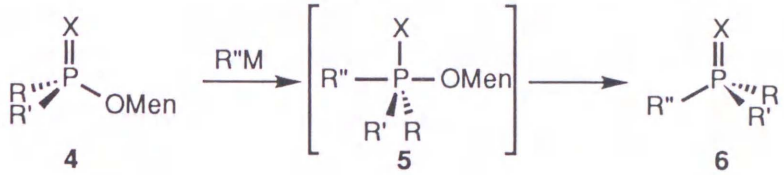


1 2 3

Some of the transformations of these compounds have been found to give the inverted product with excellent selectivity. However, many suffer from varying reaction selectivity probably due to permutation of the intermediate pentacoordinate adduct. Thus this method cannot be considered of full generality. Another effective method developed recently by Imamoto[9] utilizes the stereoselective reductive cleavage of the ester P-O

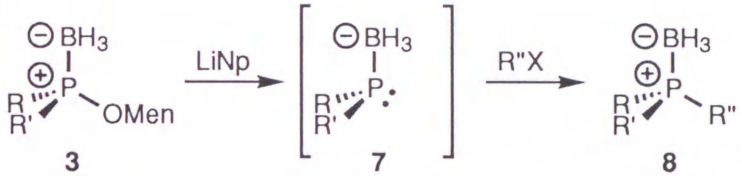
bond followed by reaction with electrophiles to give products with predominant retention. This serves as a complementary reaction to the Mislow reaction, since the enantiomeric product can be obtained from the same diastereomer .

Scheme 1



4 5 6

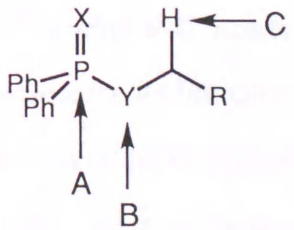
Scheme 2



3 7 8

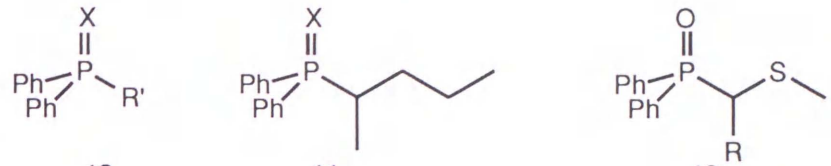
Among phosphorus compounds optically active phosphinothioic acids are known to be the most accessible by conventional optical resolution methods, namely fractional crystallization.[4] These compounds have found application in double displacement reactions and excellent results have been put forward by Corey.[10]

Phosphinates which have the general structure as **9** have three sites (A, B, and C) upon which nucleophilic attack could occur. Nucleophiles could attack the phosphorus atom as in path A and result in substitution accompanied by the elimination of alkoxide or thiolate, an $S_N2(P)$ type reaction, or it could attack atom Y as in path B when Y is not a first row element and generate a phosphinite anion, an $S_N2(Y)$ type reaction. Alternatively, nucleophiles can react as base and abstract a proton α to the sulfur atom as in path C.



9a: X=O, Y=O
9b: X=S, Y=O
9c: X=O, Y=S
9d: X=S, Y=S

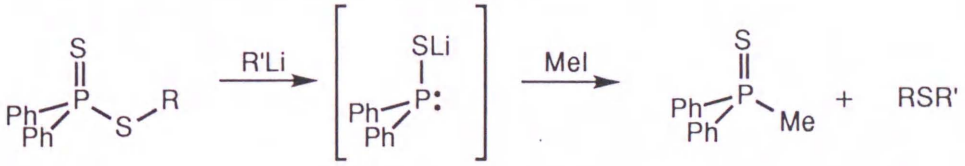
An examination of these possibilities was carried out with compounds **9a-d** by Inamoto et al.[11] and the following results were obtained. In the case of **9a** and **9b** reaction with alkyl and aryllithium reagents gave $S_N2(P)$ products, **10** , exclusively. When n-BuLi was used as the nucleophile, **11**, a species derived from a carbanion generated α to phosphorus in the initial substitution product was obtained predominantly upon treating the reaction mixture with MeI. This implies that attack upon phosphorus was slower than the deprotonation of the product.



10 **11** **12**

Reactions with **9c** also predominantly gave the $S_N2(P)$ products **10**. However when the carbon α to sulfur in the reactant was benzylic compound **12** which arises from a Wittig-type [1,2] rearrangement was also obtained as a side product in ca. 10 % yield. Phosphinodithioates **9d** were found to be completely different from the other three combinations and yielded phosphine sulfides and unsymmetric sulfides, quantitatively, upon treatment with MeI, via a $S_N2(S)$ reaction.

Scheme 3



13 **14** **15**

We anticipated that an efficient generation of a carbanion α to sulfur in the reaction of **9c** might raise the proportion of the Wittig rearrangement product and thus give a valid means of forming P-C bonds. To this end we made recourse to S-stannylmethyl esters, because the tin-lithium transmetallation reaction has been known to be a useful method for generating carbanions in cases where direct metallation with lithium metal or deprotonation with other organolithium reagents is difficult. The

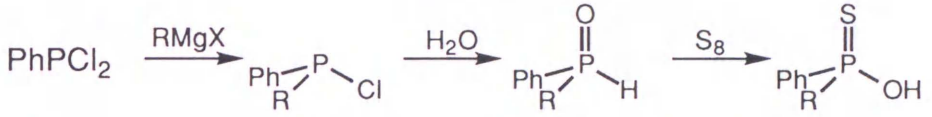
reaction of this ester with MeLi was found to be effective, and an application to optically active S-stannylmethyl esters gave the Wittig rearrangement product in high optical yield. We also found that the phosphinodithioates derived from optically active S-methyl phosphinothioates via sulfurization by Lawesson's reagent[12] give optically active phosphine sulfides upon reaction with organolithium reagents and subsequent treatment with alkylating agents. Herein we describe the details.

2. Results and Discussion

Preparation of Phosphinothioates and Phosphinodithioates.

The phosphinothioic acids **19a** (R=1-Np) and **19b** (R=t-Bu) were prepared by conventional methods as shown in Scheme 4 as one pot reactions. To a THF solution of dichlorophenylphosphine was added 1 equiv of the appropriate Grignard reagent. This solution was then treated with degassed aqueous NH_4Cl followed by elemental sulfur to give the acids in 70 % and 64 %, respectively.

Scheme 4



16

17a: R=1-Np
17b: R=t-Bu

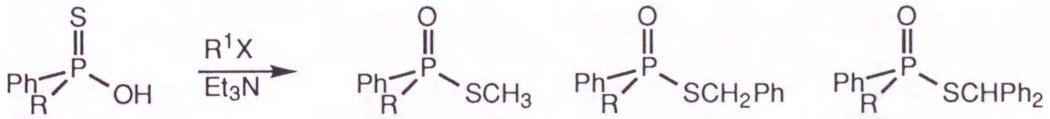
18a: R=1-Np
18b: R=t-Bu

19a: R=1-Np
19b: R=t-Bu

An excess amount of the Grignard reagent readily gave the disubstituted product in the case of 1-Np, however **17b** was found to be relatively inert. The hydrolysis of **9b** was also found to be very slow compared with **17a** under the weakly acidic conditions which were used to avoid the formation of phosphinic acid. Thus, when the hydrolysis was insufficient, (t-butyl)phenylphosphinyl chloride was obtained.

The preparation of the S-esters **20**, **21**, and **22** was achieved by the straightforward reaction of MeI, $PhCH_2Cl$, and Ph_2CHCl, respectively, in the presence of Et_3N.

Scheme 5



19a: R=1-Np
19b: R=t-Bu

20a: R=1-Np
20b: R=t-Bu

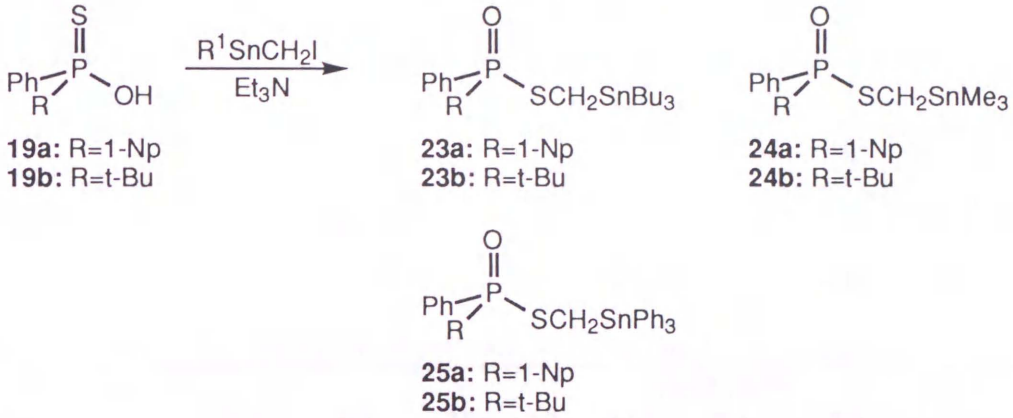
21a: R=1-Np
21b: R=t-Bu

22a: R=1-Np
22b: R=t-Bu

The S-stannylmethyl esters were prepared by treating the acids with Et_3N and R_3SnCH_2I (R=Bu, Me, Ph) which were prepared from the corresponding R_3SnCl and the Simmons-Smith reagent.[13]

Scheme 6

Scheme 7



19a: R=1-Np
19b: R=t-Bu

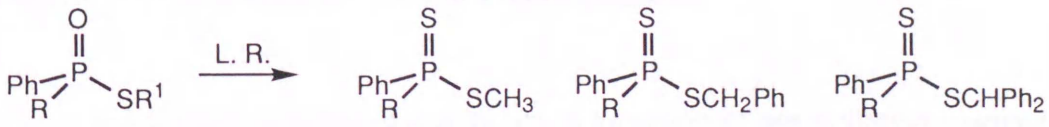
23a: R=1-Np
23b: R=t-Bu

24a: R=1-Np
24b: R=t-Bu

25a: R=1-Np
25b: R=t-Bu

Sulfurization of phosphinothioates **20-22** was carried out with the use of Lawesson's reagent.[13] The reagent has also been found to convert phosphine oxides to phosphine sulfides.[14] The esters with the t-butyl group generally required longer reaction times. The reaction itself was nearly quantitative for **20a**, **20b**, **21a**, and **22a**, but those for **21b** and **22b** were sluggish, probably due to steric hindrance, and afforded other side products as well that could not be identified.

Scheme 8



20a, 21a, 22a
20b, 21b, 22b

26a: R=1-Np
26b: R=t-Bu

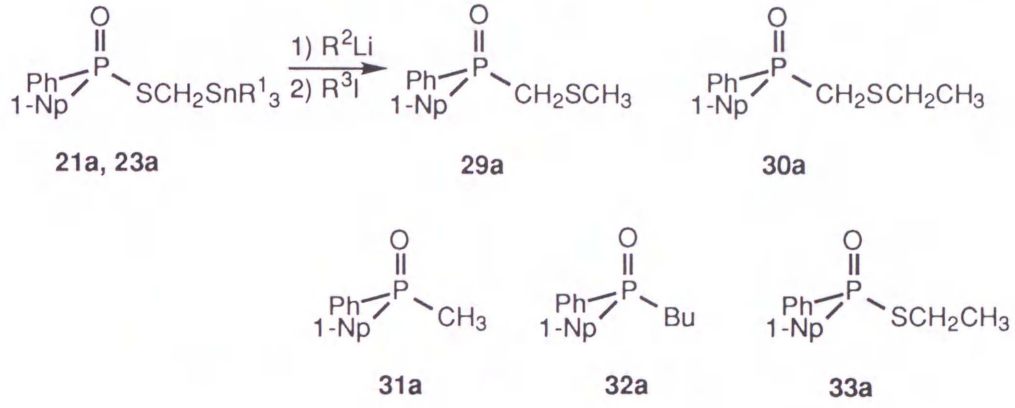
27a: R=1-Np
27b: R=t-Bu

28a: R=1-Np
28b: R=t-Bu

Reactions of S-Stannylmethyl Esters with Organolithium Reagents.

The results of the reactions between S-stannylmethyl esters and organolithium reagents are given in Table 1. The reaction was carried out at -78°C in THF and the reaction mixture was treated with alkyl iodides at -78°C or 0°C.

Scheme 9



21a, 23a **29a** **30a**

31a **32a** **33a**

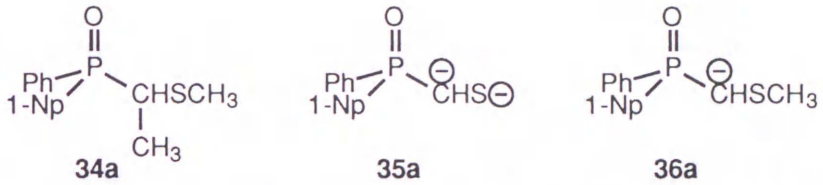
Table 1. Reactions of S-Stannylmethyl Esters with Organolithium Reagents.[a]

				yield (%)[b]			
run	R^1	R^2Li	R^3I	**29a, 30a**	**31a**	**32a**	**33a**
1	Bu	n-BuLi	MeI	34		66	
2	Bu	MeLi	MeI	79	11		
3	Bu	MeLi	EtI	74	9		
4	Bu	PhLi	MeI	70	28		
5	Ph	MeLi	MeI	50	18		
6	Ph	PhLi	MeI	15	20		47

[a]The reactions were carried out at -78°C and quenched at 0°C for runs 1-4 and at -78°C for runs 5, 6. [b]Yields based on consumed starting material.

It was preliminarily found that the use of an excess of organolithium resulted in the production of dimethylated compound **34a**, via either dianion **35a** or anion **36a** formed after initial monomethylation. Therefore a submolar amount of MeLi was used. When the ester was treated with n-BuLi the rearrangement product formed in a rather low yield and the $S_N2(P)$ product was predominant. Since we could attribute this result

to the strong nucleophilic nature of this lithium reagent we next examined MeLi. As shown in run 2 the use of MeLi was found to give the desired rearranged product **29a** in high yield along with methyl derivative **31a**. There are two possibilities that can account for the formation of **31a**, the alkylation of the phosphinite **37a** formed by the $S_N2(S)$ attack of the lithium reagent or the desulfurization of the initial rearrangement product to give the carbanion of **31a**. Quenching the reaction with EtI in the place of MeI gave only **30**a and **31a**, and no phosphinite adduct **38a**. Therefore we can conclude that the latter reaction has occurred.



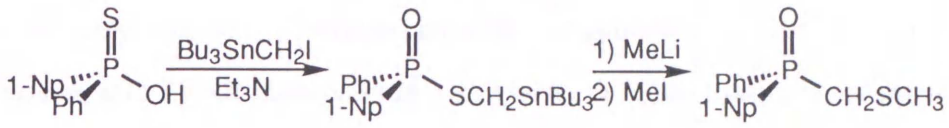
Quenching the reaction at low temperature (-78°C) gave similar results as run 2. Therefore it seems that the reaction proceeds at low temperatures. However the reaction of the triphenylstannylmethyl derivative **23a** quenched at low temperature gave a substantial amount of **33a**, a product directly formed from the initial transmetalation, in addition to **29a** and **31a**. This result implied that in the case of run 6 either the decomposition of the intermediate tin ate-complex was relatively slow or that the formation of the ate-complex itself is slow at low temperatures. In light of the report[15] that tin ate-complexes with the composition of Ph_nSnMe_{5-n} (n=0-5) can be observed by NMR and that stability rises as the value of n becomes larger, we attempted the observation of the intermediate ate complexes with ^{119}Sn VT-NMR using reactants **23**, **24**, and **25**. However in none of the measurements could the intermediate be observed, implying that there is no significant accumulation of the intermediate and the species exists in low concentration (< 10 %). The use of HMPA which has been reported to

stabilize ate complexes seemed to have accelerated the reaction, instead. Therefore, it should be that in the case of run 6 the formation of the ate complex itself is slow in addition to the slowness of decomposition and that the reaction of the initially formed carbanion with MeI is slightly more rapid than the ensuing rearrangement thus allowing the trapping of the carbanion. In the other cases rapid formation and decomposition seems to allow rearrangement to occur before the addition of MeI. Having optimized the reaction conditions we proceeded on to the use of optically active S-stannylmethyl esters.

Reactions of Optically Active S-Stannylmethyl Esters with Organolithium Reagents.

Optical resolution of acids **19a** and **19b** was carried out by resolving diastereomeric salts formed by treating the acids with quinine[16] and (+)-1-phenylethylamine,[17] respectively, and then treating the resolved salts with conc HCl to liberate the acids. In a typical resolution for **19a** optically active phosphinothioic acids of optical purities of 93 % ee (**19a-S**) and 98 % ee (**19a-R**) were obtained, while for **19b** those of 92 % ee (**19b-R**) and 98 % (**19b-S**) were obtained. The optical purity of **19a** was determined by converting the acids to their $NHEt_2$ salts.[16] These acids were then converted to their respective esters. Esterification of phosphinothioic acids are known to proceed with full retention, a fact to be expected.[18] The rearrangement reactions were carried out with MeLi as the organolithium reagent and were quenched with MeI. The optical rotation values for the products are shown in Schemes 10 and 11.

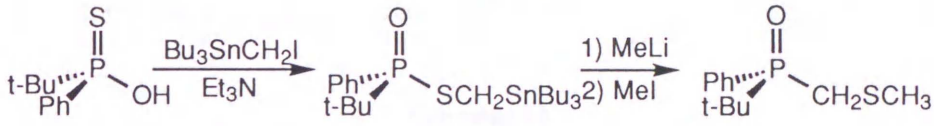
Scheme 10



19a-S, R **23a-S, R** **29a-R, S**

19a-S	**23a-S**	**29a-R**
$[\alpha]_D^{20}$ -93.3°	$[\alpha]_D^{19}$ +4.13°	$[\alpha]_D^{20}$ +8.22°
(*c* 1.07, PhH)	(*c* 1.62, $CHCl_3$)	(*c* 0.810, $CHCl_3$)
19a-R	**23a-R**	**29a-S**
$[\alpha]_D^{17}$ +96.8°	$[\alpha]_D^{16}$ -4.37°	$[\alpha]_D^{24}$ -8.07°
(*c* 0.283, PhH)	(*c* 2.93, $CHCl_3$)	(*c* 0.405, $CHCl_3$)

Scheme 11



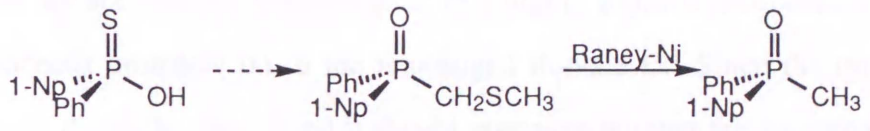
19b-R, S **23b-R, S** **29b-S, R**

19b-R	**23b-R**	**29b-S**
$[\alpha]_D^{18}$ +26.1°	$[\alpha]_D^{20}$ +57.9°	$[\alpha]_D^{19}$ +77.1°
(*c* 1.29, MeOH)	(*c* 4.40, $CHCl_3$)	(*c* 0.709, $CHCl_3$)
19b-S	**23b-S**	**29b-R**
$[\alpha]_D^{22}$ -27.8°	$[\alpha]_D^{18}$ -59.3°	$[\alpha]_D^{22}$ -81.0°
(*c* 2.35, MeOH)	(*c* 1.44, $CHCl_3$)	(*c* 0.639, $CHCl_3$)

In order to determine the optical yields of the rearrangement reactions the newly formed phosphine oxides presumed to be **29a-R** and **29b-R** were desulfurized with Raney-Ni W4 to yield phosphine oxides **31a-R** and **31b-R**. Since these transformations did not directly involve the chiral phosphorus centers we assumed that the absolute configurations would be unchanged. However in the case of **31a-R** prolonged exposure of the compound to reaction conditions resulted in partial racemization and thus this reaction could not be used for determination of optical purity. The reason for this racemization is not clear. For **31a-R** a comparison of optical rotations with the reported value of $[\alpha]_D$ +18.6° (*c* 5.494, MeOH)[19] for a sample of 95

% ee for the enantiomer of S configuration suggested that the optical purity was of 37 % ee and of R configuration. However, an NMR measurement using (-)-**19b** as a chiral shift reagent with **29a-R** showed only a single set of methyl protons for this sample, thus indicating that the sample was of high optical purity (>95 % ee). Therefore we could consider the optical purity of the product to be the same as the acid **19a-S** (93 % ee). It would follow that the optical purity of **29a-S** from **19a-R** was 90 % ee. Thus, the optical yield of this reaction can be considered to be of at least 90 %. Since the absolute stereochemistry of the initial acids **19a** have not been established in the literature a definite assignment could not be done. But assuming from the chemical correlation of the t-butyl analogs (vide infra), it could be concluded that the reaction proceeded with retention of configuration.

Scheme 12



19a-S **29a-R** **31a-R**

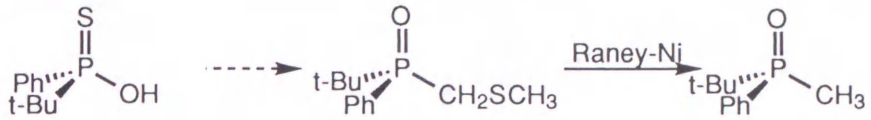
19a-S
$[\alpha]_D^{20}$ -93.3° (*c* 1.07, PhH)
o.p. 91 % ee

31a-R
$[\alpha]_D^{21}$ -7.3° (*c* 0.039, MeOH)

In the case of **31b-R** a comparison of optical rotations with the highest reported value of $[\alpha]_D$ +22.7° (*c* 1.0, MeOH)[20] for a sample of R configuration suggested that the optical purity was of 93 % ee and of R configuration. An NMR measurement using (-)-**19b** as a chiral shift reagent showed no signals due to the other enantiomer, thus indicating that the sample was of very high optical purity. A comparison of the optical rotation values of **23b** suggested 90 % ee and **29b** suggested 88 % ee for the reaction of the enantiomer. This corresponds to an optical yield of at least 96 % ee. Therefore overall the reaction can be considered to proceed with optical yield of at least 93 %.

According to the stereochemistry depicted in Scheme 13 the reaction could be determined to proceed with overall retention of configuration.

Scheme 13



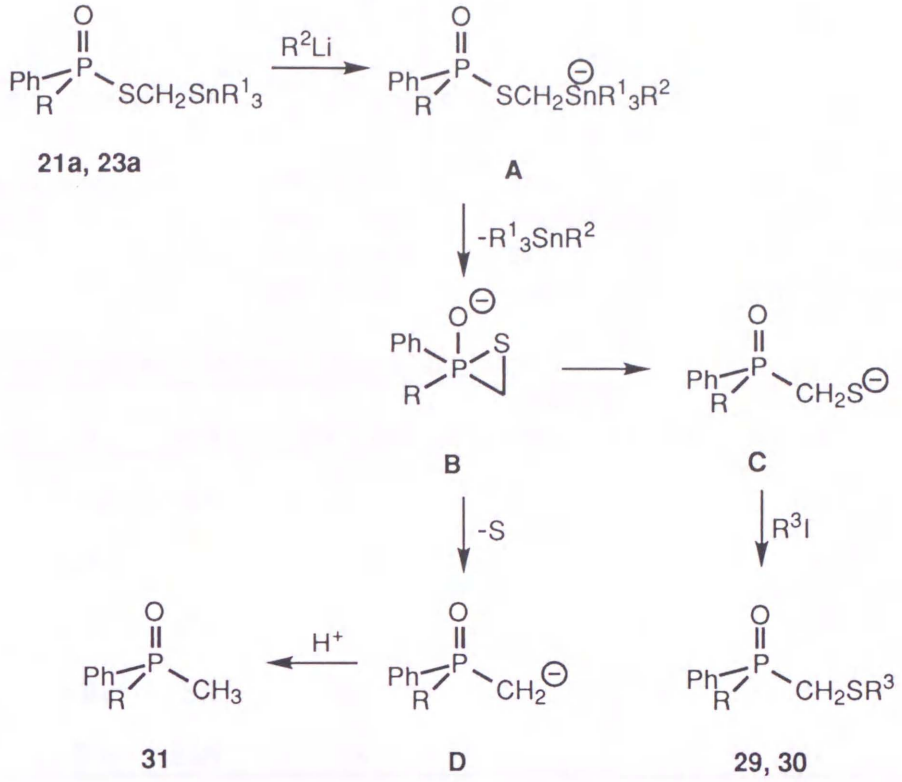
19b-S **29b-R** **31b-R**

19b-S
$[\alpha]_D^{22}$ -27.8° (*c* 2.35, MeOH)
o.p. 99 % ee

31b-R
$[\alpha]_D^{22}$ +21.0° (*c* 0.275, MeOH)
o.p. 93 % ee

A plausible mechanism of this reaction is summarized in Scheme 14. With the addition of methyllithium an ate complex such as A is initially formed. Upon the collapse of the ate complex the formation of a highly strained phosphorane B occurs which proceeds promptly on to the rearranged thiolate C. Since the intermediate phosphorane should be short-lived it should rearrange without the accompaniment of permutation upon phosphorus, thus giving the configurationally retained product. Treatment of the thiolate C with alkylating reagents would give the ultimate product. The side product **31** probably arises by the loss of sulfur either from the phosphorane B or thiolate C to give carbanionic species D, followed by protonation by species such as C in the reaction mixture. The fact that dialkylated product **34** was obtained even in reactions using submolar amounts of organolithium reagent support this speculation. We cannot rule out the possibility that thioformaldehyde eliminates from the initially formed carbanion followed by rapid recombination. However the high optical purity (if we believe the results from the NMR observations) indicates that its contribution must be small, if it exists at all. The fact that a compound derived from phosphinite described in the following reaction with LDA is obtained with complete racemization supports this interpretation (vide infra).

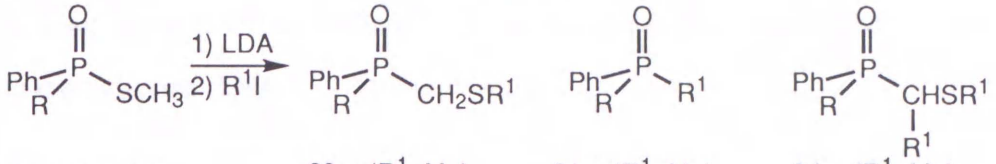
Scheme 14



Reactions of S-Methyl Phosphinothioates with Lithium Amide Bases.

We reasoned that if S-methyl phosphinothioates could be deprotonated efficiently, the rearranged product might be obtained in a more convenient matter. In order to examine this possibility we carried out deprotonation reactions using LDA a sterically hindered amide base of which nucleophilic substitution reactions are rare. The S-methyl esters were treated with lithium diisopropylamide (LDA) at -78°C and the mixture was allowed to warm to 0°C at which alkyl iodides were added.

Scheme 15



20a: R=1-Np
20b: R=t-Bu

29a: (R^1=Me)
30a: (R^1=Et)
29b: (R^1=Me)
30b: (R^1=Et)

31a: (R^1=Me)
38a: (R^1=Et)
31b: (R^1=Me)
38b: (R^1=Et)

34a: (R^1=Me)
39a: (R^1=Et)
34b: (R^1=Me)
39b: (R^1=Et)

Table 2. Reactions of S-Methyl Esters with LDA.[a]

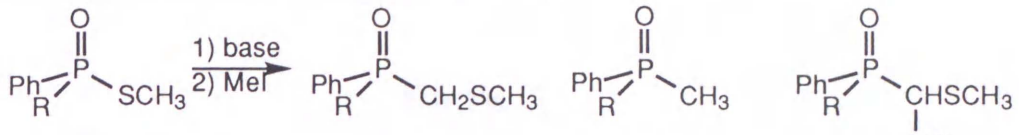
			yield (%)			
run	R	R^1I	**29, 30**	**31, 38**	**34, 39**	**20**
1	1-Np	MeI	39	12	7	12
2	1-Np	EtI	40	9	5	10
3	t-Bu	MeI	81		5	5
4	t-Bu	EtI	61		11	7
5	t-Bu[b]	MeI	58			39

[a]LDA (1.2 equiv) was added at -78°C and quenched at O°C. [b]0.8 equiv of LDA was used.

The rearranged product was obtained predominantly, but the reaction was found to be slightly different from that of S-stannylmethyl esters. Run 2 gave the ethyl incorporated product **38** in the place of **31**. This implies the intermediacy of phosphinite **37**,which was not found in the tin reaction. Interestingly, this product could not be found in the case of the t-Bu substituted compound. This can be explained from the difference in electronic effects of the substituents. The 1-Np group would serve to stabilize the phosphinite while the t-Bu group would destabilize it. A substantial amount of dialkylated products **34** and **39** were also obtained although unreacted starting material also remained. This implies that the acidity of the rearranged product is comparable to that of the starting material although a dianion is generated by deprotonation. The formation of the overreacted product could be diminished by using submolar amounts of base.

The effect of the size of the amide base was next examined using lithium dicyclohexylamide (LCHA), lithium 2,2,6,6-tetramethylpiperazide (LTMP), LDA, and lithium diethylamide (LEA).

Scheme 16



20a: R=1-Np
20b: R=t-Bu

29a
29b

31a
31b

34a
34b

Table 3. Reactions of S-Methyl Esters with Lithium Dialkylamides.[a]

			yield (%)[b]			
run	R	base	**29**	**31**	**34**	**20**
1	1-Np	LCHA	60	20	10	10
2	1-Np	LTMP	50	20	20	10
3	1-Np	LDA	64	9	18	9
4	1-Np	LEA	46		18	36
5	t-Bu	LCHA	83		11	5
6	t-Bu	LTMP	83		11	5
7	t-Bu	LDA	94		6	
8	t-Bu[b]	LEA	100			

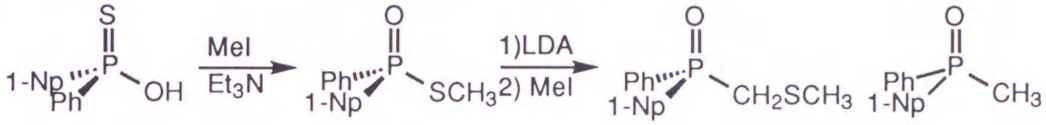
[a]The base (1.2 equiv) was added at -78°C and the mixture was quenched at O°C. [b]Relative ratio of crude mixture determined by NMR.

The results show that there is no significant difference between the bases and the size of the base is not a factor in the reaction. Therefore it can be concluded that the attack of the amide nucleophiles upon the sulfur atom does not play an important role in this reaction and the formation of the phosphinite anion is probably via the extrusion of thioformaldehyde from the carbanion initially formed upon deprotonation.

Reactions of Optically Active S-Methyl Phosphinothioates with LDA.

The stereochemistry of the present reaction was investigated using optically active compounds. Optically active S-methyl phosphinothioates were prepared from phosphinothioic acid of 93 % ee for **20a** and 92 % ee for **20b**. The reactions were carried out with submolar amounts of base.

Scheme 17

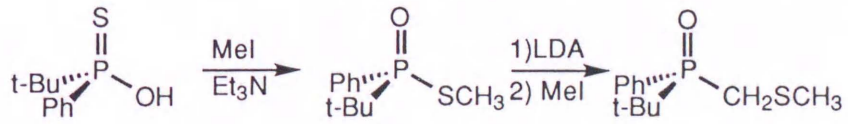


19a-S	**20a-S**	**29a-R**	**31a**
$[\alpha]_D^{25}$ -60.4°*	$[\alpha]_D^{24}$ -43.3°	$[\alpha]_D^{17}$ +6.45°	$[\alpha]_D^{17}$ ca.0°
(*c* 0.770, $CHCl_3$)	(*c* 0.878, $CHCl_3$)	(*c* 0.366, $CHCl_3$)	
o.p. 93 % ee		o.p. 73 % ee	

*optical rotation of $NHEt_2$ salt

The optical rotation of **31a-R** was found to be zero, thus indicating that (1-naphthyl)phenylphosphinite anion completely racemized before the reaction with MeI. This is in contrast with (t-butyl)phenylphosphinite anion which has been determined to be stable under similar conditions.[21] The optical purity of **29a-R** was found to be 73 % ee from comparison with the optical rotation value obtained in the reaction of the stannylmethyl ester. This corresponds to an optical yield of 78 %. The configuration was found to be retained.

Scheme 18



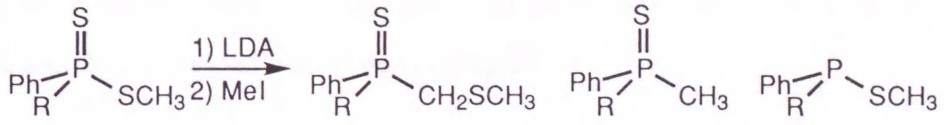
19b-R	**20b-R**	**29b-S**
$[\alpha]_D^{18}$ +26.1°	$[\alpha]_D^{17}$ +124°	$[\alpha]_D^{16}$ +62.0°
(*c* 1.29, MeOH)	(*c* 1.74, $CHCl_3$)	(*c* 0.793, $CHCl_3$)
o.p. 92 % ee		o.p. 71 % ee

The optical purity of **29b-S** was found to be 71 % ee from comparison with the optical rotation value obtained in the reaction of the stannylmethyl ester. This corresponds to an optical yield of 77 %. The configuration was found to be retained as with the **29a-R**. In both of these reactions the optical purities were found to be lower than those in the reactions with the stannylmethyl esters. The reason can be due to the participation of the phosphinite anion and recombination of the thioformaldehyde to the partial racemized anion. It could be that the racemization of the anion is accelerated by proton transfer to and from the phosphinite anion induced by the amine. An alternate explanation is that the rearrangement proceeds via a phosphorane as in the case of the stannylmethyl esters but that in this case hydrogen bonding with the amine serves to elongate the lifetime of the intermediate, thus allowing permutation and partial racemization to occur. Whichever is the case the presence of amine should be the reason for racemization.

Reactions of S-Alkyl Phosphinodithioates with LDA.

The scope of this reaction was examined with S-methyl phosphinodithioates.

Scheme 19

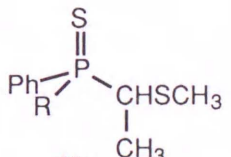


26a: R=1-Np
26b: R=t-Bu

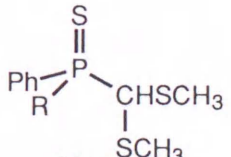
40a **40b**

41a **41b**

42a **42b**



43a
43b



44a
44b

Table 4. Reactions of S-Methyl Esters with LDA.[a]

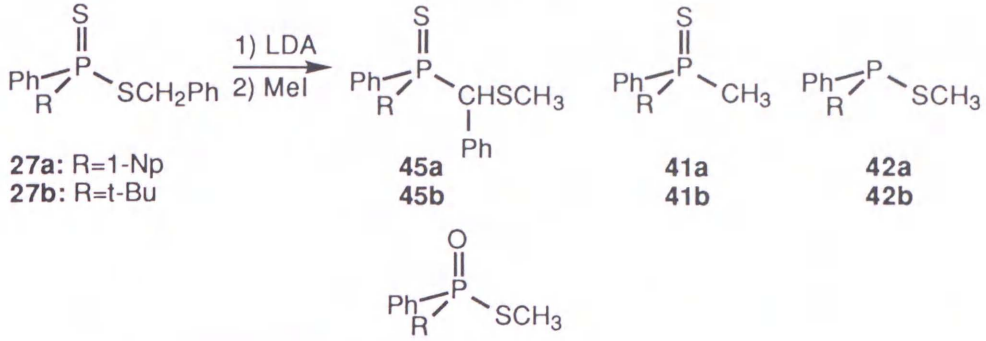
		yield (%)					
run	R	**40**	**41**	**42**	**43**	**44**	**26**
1	1-Np	7	45	30			
2	t-Bu	14	34		7	4	33

[a]LDA (1.2 equiv) was added at -78°C and the mixture was quenched at O°C.

The product distribution shows that the products resulting from rearrangement are obtained (**40**, **43**, and **44**), but in relatively low yields compared with the monothioates. Since LDA shows low nucleophilicity, the formation of **41** and **42** should be via the phosphinothioite anion generated by the extrusion of thioformaldehyde. The higher proportion of elimination compared with the oxide counterpart is probably due to the higher stability of the phosphinothioite anion compared with the phosphinite anion, thus enabling even the species with the t-butyl group to give products of elimination. The higher proportion of the overreacted species seen in run 2 reflects the fact that the initial proton abstraction is slower than its oxygen counterpart.

For **9c**, it has been reported that the rearranged product was obtained only when the abstracted proton was benzylic.[11] On the basis of this result we reasoned that raising the acidity of the site of deprotonation would raise the yield of the rearranged product and thus examined benzyl derivatives **27**.

Scheme 20



27a: R=1-Np
27b: R=t-Bu

45a **45b** **41a** **41b** **42a** **42b**

20a **20b**

Table 5. Reactions of S-Benzyl Esters with LDA.[a]

		yield (%)				
run	R	**45**	**41**	**42**	**20**	**27**
1	1-Np	42	11	7	3	27
2	t-Bu	51	9			36

[a]LDA (1.2 equiv) was added at -78°C and the mixture was quenched at O°C.

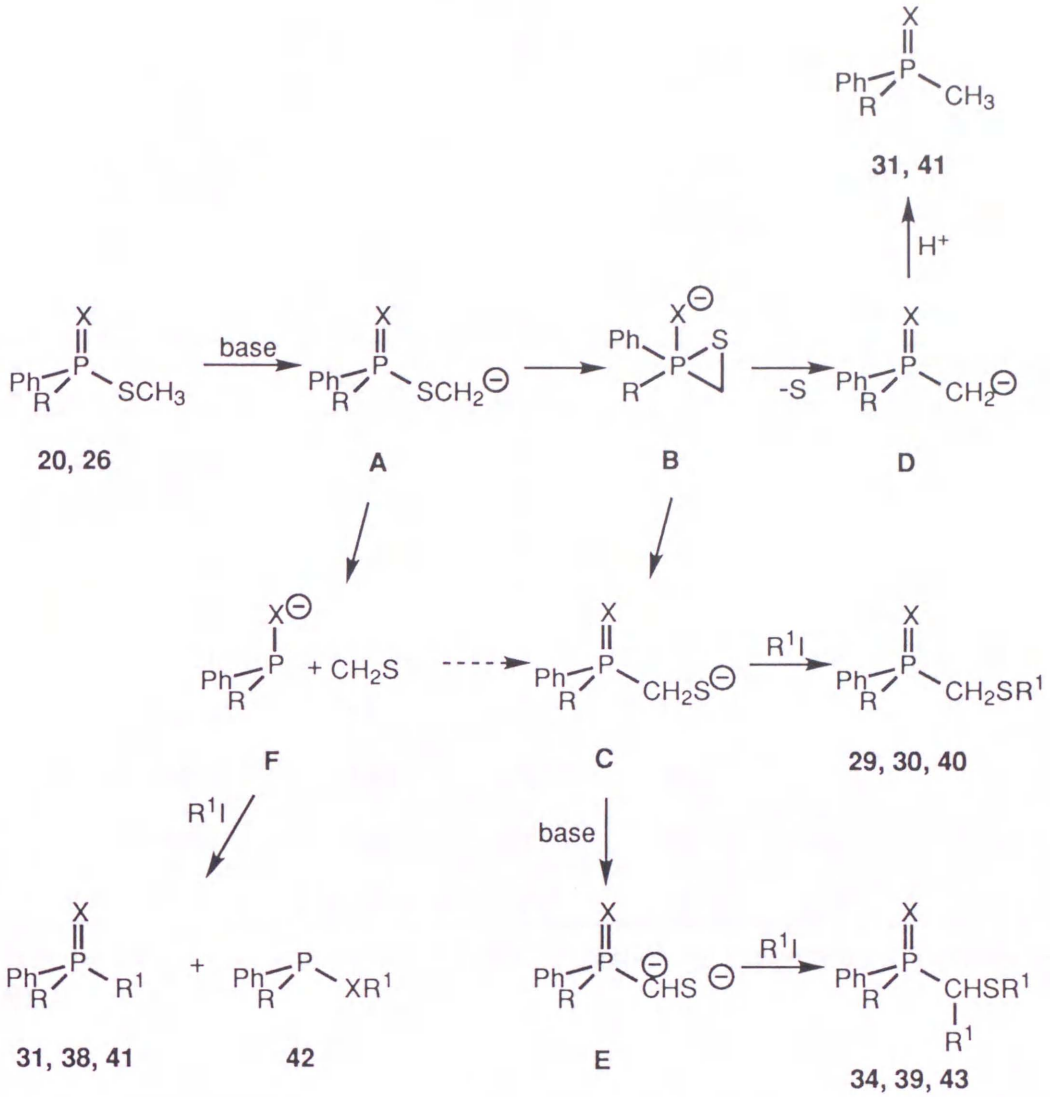
In accordance with expectations the proportion of the rearranged product to the elimination product was increased although the reaction itself turned out to be somewhat more sluggish probably due to the increase of steric bulk in the substrate. This view is supported by the fact that the overreacted species formed by deprotonation of the highly bulky carbanion center in the rearranged species could not be found. If the reaction were to proceed by elimination-recombination, the reaction involving the more bulky and thermodynamically more stable thiobenzaldehyde would have given more of the elimination product. However, since these results indicate otherwise it is reasonable to assume that at least the major path of the rearrangement is through the pentacoordinate intermediate, and that the less stable carbanion gives more of the elimination product

The reaction of benzhydryl derivatives **28** were also examined. However these compounds were found to be inert and gave only traces of reaction products even after stirring at room temperature. When the reaction was quenched with deuterated hydrochloric acid, only about 10 % of the substrate was found to incorporate deuterium.

Thus, in this case it seems that the bulkiness of the substrate decelerated carbanion formation and the stability of the carbanion retarded ensuing reactions.

The mechanism of the reactions involving amide bases can be summarized as in Scheme 21. Deprotonation of the esters to give A proceeds first of all. This carbanion A either cyclizes to B or eliminates thioformaldehyde to form phosphinite F. The intermediate B opens the ring to the rearranged intermediate C or desulfurizes to give D. As a minor path, phosphinite F could give the rearranged product by recombination with the thioaldehyde. These intermediates C, D, and E are directly quenched and/or alkylated, and C is further deprotonated to overreacted products. The difference between this reaction and that of stannylmethyl esters is probably due to the presence of amine which is known to cause hydrogen bonding in lithium mediated reactions.

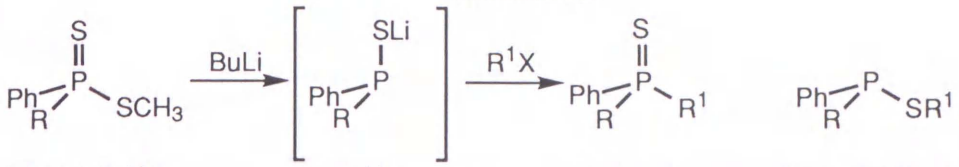
Scheme 21



Reactions of Methyl Phosphinodithioates with n-BuLi.

Since in the reactions of methyl phosphinodithioate with LDA the phosphinothioite was found to give the S-methylated product in addition to the P-methylated product, we made a reinvestigation of the reaction of methyl phosphinodithioate with n-BuLi by varying the quenching agent.

Scheme 22



26a: R=1-Np
26b: R=t-Bu

46a
46b

41a: R=Me
47a: R=Et
41b: R=Me
47b: R=Et

42a: R=Me
48a: R=Et
42b: R=Me
48b: R=Et

Table 6. Reactions of Methyl Phosphinodithioates with n-BuLi.[a]

				yield (%)	
run	R	R^1X	temp	**41, 47**	**42, 48**
1	1-Np	MeI	-78°C	55	34
2	1-Np	MeI	0°C	50	20
3	1-Np	EtI	0°C	48	37
4	1-Np	$(MeO)_2SO_2$	-78°C		100[b]
5	t-Bu	MeI	-78°C	92	
6	t-Bu	MeI	0°C	83	
7	t-Bu	EtI	0°C	72	26
8	t-Bu	$(MeO)_2SO_2$	-78°C	18	82[b]

[a]The reactions were carried out at -78°C. [b]Quenching temperature. [b]Determined by NMR.

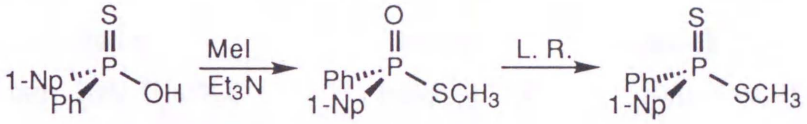
In the reaction with MeI it was found that the quenching temperature was not a factor and that in the case of the 1-Np substituted ester a substantial amount of the S-methylated product was obtained. The use of the less reactive ethyl iodide resulted in the increase of the portion of the S-methylated product and it could be found even in the case of the t-Bu ester. When methyl sulfate was used the S-methylated compound became predominant. This is probably because the phosphorus atom having a larger atom radius can be considered to be slightly softer than the sulfur atom. The difference between the 1-Np and the t-Bu series can be attributed to the larger electron density upon the phosphorus atom in the t-Bu series due to inductive effects. From the above results

it was concluded that the use of MeI would be appropriate for the reactions of optically active esters.

Reactions of Optically Active S-Methyl Phosphinodithioates with n-BuLi and Determination of Stereochemistry via Chemical Correlation.

The preparation of optically active S-methyl (1-naphthyl)phenyl-phosphinodithioate was carried out by using acid **19a-S** of optical purity of 93 % ee. The reaction using Lawesson's reagent required at least toluene reflux temperatures to allow the formation of the dithioate.

Scheme 23

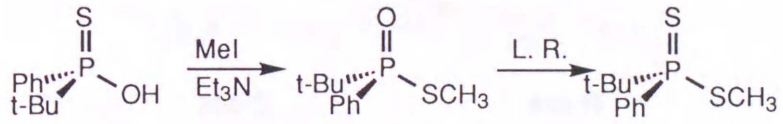


19a-S	**20a-S**	**26a-S**
$[\alpha]_D^{25}$ -60.4°*	$[\alpha]_D^{24}$ -43.3°	$[\alpha]_D^{22}$ +58.6°
(*c* 0.770, $CHCl_3$)	(*c* 0.878, $CHCl_3$)	(*c* 0.916, $CHCl_3$)
o.p. 93 % ee		

*optical rotation of $NHEt_2$ salt

The preparation of optically active S-methyl (t-butyl)phenylphosphinodithioate was carried out by using acid **19b-S** of optical purity of 93 % ee.

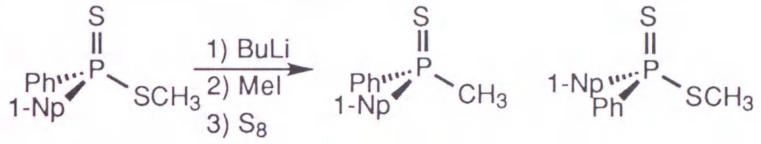
Scheme 24



19b-S	**20b-S**	**26b-S**
$[\alpha]_D^{22}$ -26.3°	$[\alpha]_D^{23}$ -138°	$[\alpha]_D^{22}$ -104°
(*c* 0.608, MeOH)	(*c* 1.064, $CHCl_3$)	(*c* 3.793, $CHCl_3$)
o.p. 93 % ee		

The reaction of optically active dithioates were carried at -78°C and treated with MeI after the elapse of the indicated time. It was necessary to add elemental sulfur to the reactions of **26a-S** because methyl phosphinothioite **42a** was rather susceptible to oxidation during separation procedures and **20a** was often found in preliminary runs, and because **42a** itself was sure to racemization upon treatment with SiO_2. The addition of sulfur to trivalent phosphorus had been established to proceed with full retention,[22] thus the stereochemical integrity of **42a** in the reaction mixture was sure to be retained.

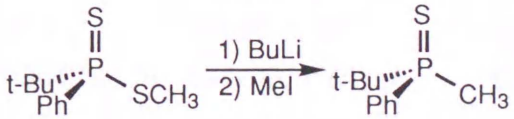
Scheme 25



	26a-S	**41a-R**	**26a-R**
-78°C, 15 min	$[\alpha]_D^{22}$ +58.6°	$[\alpha]_D^{21}$ +129°	$[\alpha]_D^{22}$ ca. 0
	(*c* 0.916, $CHCl_3$)	(*c* 0.445, $CHCl_3$)	
-78°C, 60 min	$[\alpha]_D^{22}$ +58.6°	$[\alpha]_D^{21}$ +99.6°	$[\alpha]_D^{21}$ ca. 0
	(*c* 0.916, $CHCl_3$)	(*c* 0.247, $CHCl_3$)	

The dithioate which was supposed to indicate the optical purity of methyl phosphinothioite **42a** was found to have completely racemized. Therefore **42a** could be considered to be stereochemically unstable.

Scheme 26



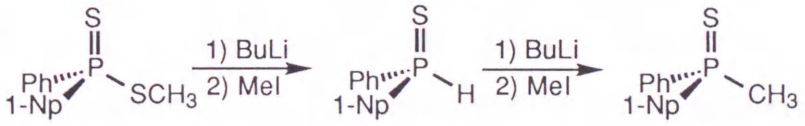
	26b-S	**41b-R**
-78°C, 30 min	$[\alpha]_D^{22}$ -104°	$[\alpha]_D^{20}$ +51.5°
	(*c* 3.793, $CHCl_3$)	(*c* 0.770, $CHCl_3$)
0°C, 2.5 h	$[\alpha]_D^{27}$ -100°	$[\alpha]_D^{20}$ +43.5°
	(*c* 0.84, $CHCl_3$)	(*c* 0.70, $CHCl_3$)

The decrease in optical rotation for **41a-R** with longer intervals till quenching indicated the susceptibility of lithium phosphinothioite towards racemization while that of the t-Bu series seemed rather stable at low temperatures, judging from the fact that there was practically no change in optical rotation with **41b-R** obtained in two steps (vide infra). However prolonged treatment at 0°C lead to gradual but evident racemization. This relative stability is in good agreement with the corresponding phosphinites (vide supra).

Using water in the place of MeI furnished secondary sulfides **49**, quantitatively in the reactions of racemic **26**. Prolonged exposure of this compound to the atmosphere led to gradual decomposition. This compound is of interest since it exists in equilibrium with its tautomer, phosphinothious acid.

The optically active dithioates were treated with water 30 min after addition of n-BuLi. The secondary phosphine sulfides were then converted to their corresponding tertiary phosphine sulfides with the same time interval, in order to determine their optical purities by means of comparison with the tertiary phosphine sulfides given in one step.

Scheme 27

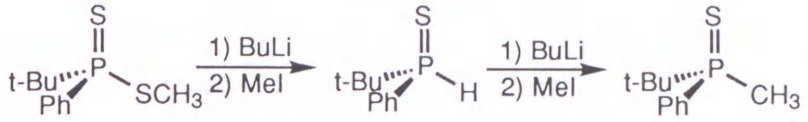


26a-S **49a-R** **41a-R**

26a-S	**49a-R**	**41a-R**
$[\alpha]_D^{22}$ +58.6°	$[\alpha]_D^{22}$ +104°	$[\alpha]_D^{25}$ +84.2°
(*c* 0.916, $CHCl_3$)	(*c* 0.73, PhH)	(*c* 0.60, $CHCl_3$)

The optical rotation value for **41a-R** was found to be 65 % of the largest value of +129°. Since the signs of the optical rotation values were the same, the transformations involving **49a** could be considered to be straightforward.

Scheme 28



26b-S	**49b-R**	**41b-R**
$[\alpha]_D^{27}$ -100°	$[\alpha]_D^{23}$ +82.9°	$[\alpha]_D^{20}$ +52.1°
(*c* 0.84, $CHCl_3$)	(*c* 0.62, PhH)	(*c* 0.53, $CHCl_3$)

The transformation in the t-Bu series proceeded with practically no change in optical purity judging from the value of optical rotation. Provided that protonation and alkylation could be assumed to take the same stereochemical course, it could be concluded that both processes proceed with retention of configuration since both the one step and the two step conversions to **41** result in products with the same optical rotation sign, a result which was highly expected.

In order to determine the configuration and optical purity of the tertiary sulfides transformation of the sulfides to oxides was examined, with the t-Bu series. Bis(trimethylsilyl)peroxide (BSPO) had been reported to convert sulfides to oxides in the presence of a catalytic amount of Lewis acid with nearly full inversion of configuration under mild conditions and short reaction times.[23] The use of BSPO without Lewis acids resulted in a clean conversion of the racemic sulfide to the oxide at room temperature. However the reaction turned out to be sluggish and accompanied unwanted formation of impurities when Lewis acids were present. The esters **26** were found not to react with BSPO.

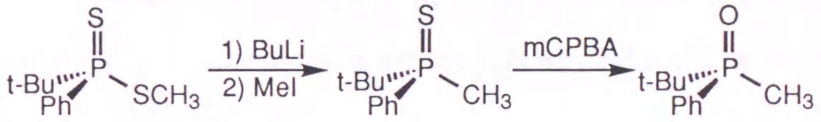
The optically active sulfide **41b-R** was found to give **31b-R** of low optical purity with retention of configuration, in conflict with reported results.

Scheme 29

41b-R	**31b-R**
$[\alpha]_D^{20}$ +51.5°	$[\alpha]_D^{21}$ +4.22°
(*c* 0.770, $CHCl_3$)	(*c* 0.860, MeOH)

Since BSPO did not live up to our expectations we made recourse to mCPBA which has been reported to convert sulfides to oxides with nearly full retention.[24] However, the optical rotation was again found to be low. The sign of the value confirmed that stereochemical course of the reaction with BSPO was of retention of configuration. It thus seems that neither BSPO nor mCPBA are effective for the transformation of sterically hindered tertiary sulfides.

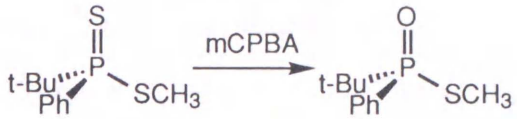
Scheme 30



26b-S	**41b-R**	**31b-R**
$[\alpha]_D^{15}$ -102°	$[\alpha]_D^{23}$ +53.9°	$[\alpha]_D^{22}$ +5.72°
(*c* 1.162, $CHCl_3$)	(*c* 1.178, $CHCl_3$)	(*c* 0.927, MeOH)

However, dithioate **26b** was found to react with mCPBA with stereochemical efficiency, although the reaction was accompanied by a significant amount of a single byproduct which could not be identified. A comparison with the values in Scheme 24 indicate that the O to S conversion by Lawesson's reagent proceeded with at least about 90 % optical yield. This is a very interesting result in light of the fact that somewhat harsh conditions (toluene reflux) were used in the sulfurization.

Scheme 31

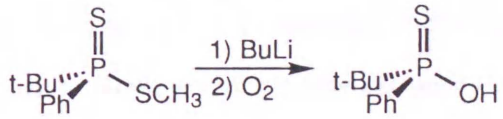


26b-S $[\alpha]_D^{15}$ -102° (*c* 1.162, $CHCl_3$)

20b-S $[\alpha]_D^{21}$ -123° (*c* 0.747, $CHCl_3$)

In order to establish the absolute optical purity of ester **26b-S**, oxidation of the stereochemically stable phosphinothioate with O_2 was next examined. Although the reaction with racemic **42b** was not a clean one, the reaction with the lithium phosphinothioate gave acid **11b** as the sole product. The optically active ester **26b-S** gave acid **11b** with inverted configuration compared with the incipient acid, which corresponds to overall retention of configuration since the oxygen and sulfur atoms are exchanged in the overall conversion. The optical yield of the phosphinodithioate forming reaction could be considered to be of at least 88 %. Since the oxidation reactions could accompany racemization, the true optical yield could be higher.

Scheme 32



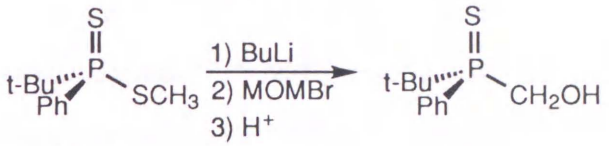
26b-S $[\alpha]_D^{15}$ -102° (*c* 1.162, $CHCl_3$)

19b-R $[\alpha]_D^{22}$ +23.0° (*c* 0.572, MeOH)

(t-Butyl)(hydroxymethyl)phenylphosphine sulfide **50b** prepared by the alkylation of lithium phosphinothioite from **26b-S** with methoxymethyl bromide and subsequent hydrolysis of (t-butyl)(methoxymethyl)phenylphosphine sulfide **51b** was found to be optically pure by NMR spectroscopy using $Eu(tfc)_3$. This coupled with the fact that the optical rotation values for **41b-R** were practically constant among the three

transformations implies that the optical purity of **41b-R** which could not be determined directly should be very high. The same type of analysis for **41a-R** could not be carried out because of the stereochemical unstability of the lithium phosphinothioite from **26a-S**.

Scheme 33



26b-S $[\alpha]_D^{22}$ -104° (*c* 3.793, $CHCl_3$)

50b-R $[\alpha]_D^{24}$ +15.6° (*c* 0.410, $CHCl_3$)

In conclusion we have presented a new general method of preparing phosphine oxides of high optical purity featuring the formation of a new P-C bond by a Wittig type rearrangement via tin-lithium transmetalation of a S-stannylmethyl phosphinothioate. The rearrangement reactions of simpler S-methyl phosphinothioates induced by deprotonation were also found to be nearly as effective. We have also found that the low temperature alkylation of phosphinothioites generated by the reaction of phosphinodithioates with BuLi serves as an effective method of preparing phosphine sulfides of high optical purity. However in this case the purity was highly dependent on the stereochemical stability of the lithium phosphinothioites. In the course of the investigation of phosphine sulfides, we also found that the sulfurization reaction utilizing Lawesson's reagent proceeds with high optical yield and retention of configuration.

3. Experimental

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H NMR spectra were measured with a JEOL FX-90Q, a JEOL EX-270 or a Bruker AM-500 spectometer using Me_4Si as internal standard. ^{13}C NMR spectra were taken with a JEOL EX-270 (68 MHz) or a Bruker AM-500 spectometer using Me_4Si as internal standard. ^{31}P NMR spectra were measured with a JEOL FX-90Q (36 MHz) spectrometer using 85% H_3PO_4 as external standard. Mass spectra were reported with a JEOL JMS-D300 or a JEOL JMX-SX 102 mass spectrometer Optical rotations were measured on a JASCO DIP-181 polarimeter. Dry column chromatography and preparative TLC were carried out with ICN silica DCC 60A and Merck Kieselgel 60 PF_{254}, respectively. All reactions were carried out under an argon atmosphere unless noted otherwise.

(1-Naphthyl)phenylphosphinothioic Acid (19a). To a dry THF (40 mL) solution of dichlorophenylphosphine (12.2 mL, 90.0 mmol) a THF Grignard solution of 1-NpMgBr (1.05 equiv) was added dropwise at -78°C. After removing the cooling bath and stirring at room temperature for 6 h, degassed aq NH_4Cl was added to the solution until the precipitate that had appeared completely dissolved. The organic layer was transferred to a flask containing sulfur (3.5 g, 1.2 equiv) via cannula and stirred overnight. The organic layer was concentrated and then redissolved in CH_2Cl_2. Alkaline extraction was done with 5 % NaOH, followed by treatment with dil HCl and extraction with CH_2Cl_2. The solution was dried with $MgSO_4$ and then evaporated dry. Recrystallization from benzene gave white crystals (16.4 g, 64 %). Mp 129-132°C. ^{1}H NMR ($CDCl_3$) δ 7.0-8.6 (m, 13H). ^{31}P NMR ($CDCl_3$) δ 74.2.

(1,1-Dimethylethyl)phenylphosphinothioic Acid (19b). To a dry THF (100 mL) solution of dichlorophenylphosphine (33 mL, 243 mmol) a THF Grignard solution of t-BuMgCl (1.05 equiv) was added dropwise at 0°C. After stirring at room temperature for 6 h, degassed aq NH_4Cl was added to the solution until the precipitate

that had appeared completely dissolved. The organic layer was transferred to a flask containing sulfur (10 g, 1.2 equiv) via cannula and stirred overnight. The organic layer was concentrated and then redissolved in CH_2Cl_2. Alkaline extraction was done with 5 % NaOH, followed by treatment with dil HCl and extraction with CH_2Cl_2. The solution was dried with $MgSO_4$ and then evaporated dry. Recrystallization from hexane gave white crystals (34.4 g, 70 %). Mp 94-95°C. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, J=17.6 Hz, 9H), 7.2-7.9 (m, 6H). ^{31}P NMR ($CDCl_3$) δ 97.6.

(1,1-Dimethylethyl)phenylthiophosphinyl Chloride. ^{1}H NMR ($CDCl_3$) δ 1.28 (d, J=20.4 Hz, 9H), 7.2-8.2 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 114.5.

S-Methyl (1-Naphthyl)phenylphosphinothioate (20a). To a solution of acid **19a** (4.30 g, 15.1 mmol) in dry benzene (70 mL) was added triethylamine (3.3 mL, 1.5 eq). After stirring for 30 min, iodomethane (2 mL, 2equiv) was added. After additionally stirring for 1 h the solution was treated with aq NH_4Cl and then worked up. Recrystallization from ethanol gave white crystals (3.43 g, 76 %). Mp 183.5-184.5°C. ^{1}H NMR ($CDCl_3$) δ 2.32 (d, J=12.2 Hz, 3H), 7.40-7.58 (m, 6H), 7.82-7.93 (m, 3H), 7.97-8.08 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 10.9 (d, ^2J=2.5 Hz), 124.2 (d, ^3J=14.7 Hz), 126.4 (s), 126.8 (d, ^3J=4.9 Hz), 127.2 (s), 128.3 (d, ^1J=103.7 Hz), 128.6 (d, ^3J=13.4 Hz), 128.7 (s), 131.5 (d, ^2J=11.0 Hz), 132.2 (d, ^4J=2.4 Hz), 132.9 (d, ^3J=9.7 Hz), 133.1 (d, ^2J=11.0 Hz), 133.1 (d, ^1J=107.4 Hz), 133.6 (d, ^4J=3.7 Hz), 133.8 (d, ^2J=9.7 Hz). ^{31}P NMR ($CDCl_3$) δ 46.4. HRMS (70 eV) Calcd for $C_{17}H_{15}OPS$: M, 298.0581. Found: *m/z* 298.0591. Calcd for $C_{17}H_{15}OPS$: C, 68.44; H, 5.07. Found: C, 68.23; H, 4.87.

S-Methyl (1,1-Dimethylethyl)phenylphosphinothioate (20b). The same method as for the preparation of **20a** was used. Acid **19b** (4.27 g, 19.9 mmol) gave **20b** as a colorless oil (3.48 g, 77 %). Bp 110°C (0.15-0.20 mmHg). ^{1}H NMR ($CDCl_3$) δ 1.19 (d, J=16.8 Hz, 9H), 2.14 (d, J=10.5 Hz, 3H), 7.36-7.64 (m, 3H), 7.73-8.06 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 9.3 (d, ^2J=3.0 Hz), 24.5, 36.8 (d, ^1J=70.6 Hz), 128.2 (d, ^3J=11.7 Hz), 129.8 (d, ^1J=91.6 Hz), 131.8 (d, ^4J=2.8 Hz), 132.9 (d,

^2J=9.0 Hz). ^{31}P NMR ($CDCl_3$) δ 67.8. HRMS (70 eV) Calcd for $C_{11}H_{17}OPS$: M, 228.0738. Found: *m/z* 228.0741.

S-Benzyl (1-Naphthyl)phenylphosphinothioate (21a). To a solution of acid **19a** (1.50 g, 5.28 mmol) in dry benzene (30 mL) was added triethylamine (0.91 mL, 1.2 eq), then benzyl chloride (0.81 mL, 1.3 equiv). After refluxing overnight, the solution was treated with aq NH_4Cl and then worked up. The crude mixture was subjected to column chromatography on SiO_2 (hexane-ethyl acetate) and recrystallized (hexane-CH_2Cl_2) to give colorless crystals (1.43 g, 72 %). Mp 142-143°C. ^{1}H NMR ($CDCl_3$) δ 4.15 (d, J=9.5 Hz, 2H), 7.1-8.9 (m, 17H). ^{31}P NMR ($CDCl_3$) δ 44.9.

S-Benzyl (1,1-Dimethylethyl)phenylphosphinothioate (21b). The same method as for the preparation of **21a** was used. From acid **19b** (1.50 g, 7.00 mmol) was obtained a colorless oil (1.58 g, 74°C). Bp 155°C (0.07 mmHg). ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J=17.1 Hz, 9H), 3.6-4.2 (m, 2H) 7.1-7.3 (m, 5H), 7.3-8.0 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 66.6. HRMS (70 eV) Calcd for $C_{23}H_{25}OPS$: M, 380.1363. Found: *m/z* 380.1363.

S-Benzhydryl (1-Naphthyl)phenylphosphinothioate (22a). To a solution of acid **19a** (1.70 g, 5.98 mmol) in dry benzene (30 mL) was added triethylamine (1.13 mL, 1.3 equiv), then benzhydryl chloride (1.55 mL, 1.4 equiv). After refluxing for 4 days, the solution was treated with aq NH_4Cl and then worked up. The crude mixture was subjected to column chromatography on SiO_2 (hexane-ethyl acetate) giving a colorless viscous oil (1.57 g, 58 %). ^{1}H NMR ($CDCl_3$) δ 5.94 (d, J=11.2 Hz, 1H), 6.9-8.7 (m, 22H). ^{31}P NMR ($CDCl_3$) δ 43.6.

S-Benzhydryl (1,1-Dimethylethyl)phenylphosphinothioate (22b). The same method as for the preparation of **22a** was used. From acid **19b** (2.09 g, 9.43 mmol) was obtained colorless crystals (2.66 g, 72°C) by recrystallization (hexane-CH_2Cl_2). Mp 106-107°C. ^{1}H NMR ($CDCl_3$) δ 1.15 (d, J=17.1 Hz, 9H), 5.68 (d, J=9.8 Hz, 1H) 6.9-7.8 (m, 15H). ^{31}P NMR ($CDCl_3$) δ 65.2.

(Iodomethyl)tributylstannane. To an aqua blue solution of cupric acetate monohydrate (0.11 g, 0.55 mmol) in glacial acetic acid (11 mL) kept at 80-100°C was added zinc (6.15 g, 94 mmol) and the mixture was stirred vigorously for 10 min. The solvent was removed by decantation and the mixture was repeatedly washed with fresh acetic acid at the same temperature until blueness could no longer be seen, then with ether to sufficiently remove the acetic acid. Drying under reduced pressure afforded brown coated copper-zinc couples. To a dry THF solution (100 mL) containing the Cu-Zn couples, a dry THF solution (15 mL) of diiodomethane (7.70 mL, 95 mmol) was added dropwise while maintaining a temperature of ca. 40°C. After stirring overnight the brownish solution was filtered under argon to remove solid particles remaining to yield a solution of iodo(iodomethyl)zinc. Chlorotributylstannane (18.1 mL, 66.6 mmol) diluted with THF (20 mL) was then added dropwise as 40°C and stirring was continued overnight. The mixture was extracted with pentane, washed with water, dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was subjected to column chromatography on SiO_2 (hexane) and distillation by Kugelrohr was carried out to yield a clear liquid (15.9 g, 59 %). ^1H NMR ($CDCl_3$) δ 0.4-2.2 (m, 29H).

(Iodomethyl)trimethylstannane. The same method as for the preparation of (iodomethyl)tributylstannane was used. From chlorotrimethylstannane (3.0 g, 15 mmol) was obtained a viscous oil after Kugelrohr distillation (1.61 g, 35 %). Bp 105°C (0.03 mmHg). ^1H NMR ($CDCl_3$) δ 0.21 (s, 9H, J_{Sn-H}=53 Hz), 1.93 (s, 2H, J_{Sn-H}=20 Hz).

(Iodomethyl)triphenylstannane. The same method as for the preparation of (iodomethyl)tributylstannane was used. From chlorotriphenylstannane (12.0 g, 31.1 mmol) was obtained a colorless crystal (10.4 g, 67 %). ^1H NMR ($CDCl_3$) δ 2.43 (s, 2H, J_{Sn-H}=22 Hz), 7.0-8.3 (m, 15H).

S-Tributylstannylmethyl (1-Naphthyl)phenylphosphinothioate (23a). To a solution of acid **19a** (1.20 g, 4.22 mmol) in dry benzene (30 mL) was added

triethylamine (0.92 mL, 1.5 equiv). After stirring for 30 min, a dry benzene solution (5 mL) of (iodomethyl)tributylstannane (1.82 g, 1.0 equiv) was added dropwise, then the solution was gently refluxed for 1 h. Workup was done by washing the solution with aq NH_4Cl, aq Na_2CO_3, then water. Drying with anhydrous $MgSO_4$, removal of the solvent by evaporation under reduced pressure and recrystallization (pentane) yielded colorless crystals (1.77 g, 71 %). Mp 71.5-73°C. ^1H NMR ($CDCl_3$) δ 0.4-2.4 (m, 27H), 2.1 (d, J=7.8 Hz, 2H), 7.2-8.9 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 46.9 (s, J_{Sn-P}=97.7 Hz). HRMS (70 eV) Calcd for $C_{29}H_{41}OPS^{120}Sn$: M, 588.1638. Found: *m/z* 588.1624. Calcd for $C_{29}H_{41}OPS^{118}Sn$: M, 586.1637. Found: *m/z* 586.1582.

S-Tributylstannylmethyl (1,1-Dimethylethyl)phenylphosphinothioate (23b). The same method as for the preparation of **23a** was used. From acid **19b** (0.75 g, 3.50 mmol) was obtained a colorless oil (1.64 g, 90 %). Bp 185°C (0.08 mmHg). ^1H NMR ($CDCl_3$) δ 0.4-2.4 (m, 29H), 1.18 (d, J=16.4 Hz, 9H), 7.4-8.1 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 69.3 (s, J_{Sn-P}=85.5 Hz). HRMS (70 eV) Calcd for $C_{23}H_{43}OPS^{120}Sn$: M, 518.1794. Found: *m/z* 518.1820. Calcd for $C_{23}H_{43}OPS^{118}Sn$: M, 516.1824. Found: *m/z* 516.1793.

S-Trimethylstannylmethyl (1,1-Dimethylethyl)phenylphosphinothioate (24b). The same method as for the preparation of **23a** was used. From acid **19b** (0.58 g, 2.7 mmol) was obtained a colorless oil (0.82 g, 78 %) after column chromatography on SiO_2 (hexane-ethyl acetate: 10:1). ^1H NMR ($CDCl_3$) δ 0.19 (s, 9H, J_{Sn-H}=54.7 Hz), 1.18 (d, J=16.6 Hz, 9H), 1.4-2.2 (m, 2H), 7.3-8.2 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 68.5 (s, J_{Sn-P}=95.2 Hz). HRMS (70 eV) Calcd for $C_{13}H_{25}OPS^{120}Sn$: M, 392.0386. Found: *m/z* 392.0398. Calcd for $C_{13}H_{25}OPS^{118}Sn$: M, 390.0384. Found: *m/z* 390.0401.

S-Triphenylstannylmethyl (1-Naphthyl)phenylphosphinothioate (25a). The same method as for the preparation of **23a** was used. From acid **19a** (0.65 g, 2.3 mmol) was obtained a colorless oil (1.28 g, 86 %) after column chromatography on SiO_2 (hexane-ethyl acetate: 10:1). ^1H NMR ($CDCl_3$) δ 2.71 (d, J=8.1 Hz, 2H, J_{Sn-}

$_H$=35.1 Hz), 6.9-8.6 (m, 27H). ^{31}P NMR ($CDCl_3$) δ 47.7 (s, J_{Sn-P}=124.5 Hz). HRMS (70 eV) Calcd for $C_{35}H_{29}OPS^{120}Sn$: M, 648.0697. Found: *m/z* 648.0672. Calcd for $C_{35}H_{29}OPS^{118}Sn$: M, 646.0696. Found: *m/z* 646.0679.

S-Triphenylstannylmethyl (1,1-Dimethylethyl)phenylphosphinothioate (25b). The same method as for the preparation of **23a** was used. From acid **19b** (0.70 g, 3.3 mmol) was obtained a colorless oil (1.10 g, 58 %) after column chromatography on SiO_2 (hexane-ethyl acetate: 10:1). ^{1}H NMR ($CDCl_3$) δ 1.13 (d, *J*=16.8 Hz, 9H), 2.0-2.9 (m, 2H), 7.1-8.0 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 69.9 (s, J_{Sn-P}=102.5 Hz).

2,4-Bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetidine 2,4-Disulfide. A solution of phosphorus pentasulfide (34.4 g, 77.4 mmol) in anisole (80 mL) was refluxed overnight in an anhydrous atmosphere. After the solution had cooled down, the precipitated yellow crystals were collected and washed thoroughly with hexane and dried in vacuo at ca. 50 °C overnight. This reagent was used without further purification (20.91 g, 33 %).

Methyl (1-Naphthyl)phenylphosphinodithioate (26a). A dry toluene solution (30 mL) of ester **20a** (1.93 g, 6.47 mmol) and L. R. (2.35 g, 1.8 equiv) was refluxed for 1 h. After the solution was cooled down, the excess L. R. which had precipitated was filtered off and the solvent was evaporated under reduced pressure. The residue was subjected to DCC on SiO_2 (CCl_4-CH_2Cl_2=4:1) followed by recrystallization (hexane-CH_2Cl_2) yielded colorless crystals (1.89 g, 93 %). Mp 151-153°C. ^{1}H NMR ($CDCl_3$) δ 2.38 (d, *J*=14.9 Hz, 3H), 7.2-8.7 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 64.2. HRMS (70 eV) Calcd for $C_{17}H_{15}PS_2$: M, 314.0351. Found: *m/z* 314.0346.

Methyl (1,1-Dimethylethyl)phenylphosphinodithioate (26b). A dry toluene solution (30 mL) of ester **20b** (1.35 g, 5.93 mmol) and L. R. (2.03 g, 1.7 equiv) was refluxed for 4 h. Workup and DCC on SiO_2 (hexane-ether=10:1) followed by recrystallization (hexane-CH_2Cl_2) yielded colorless crystals (1.09 g, 75 %). Bp 120°C (0.25 mmHg). ^{1}H NMR ($CDCl_3$) δ 1.21 (d, *J*=18.3 Hz, 9H), 2.19 (d, *J*=13.2 Hz,

3H), 7.40-7.57 (m, 3H), 7.91-8.22 (m, 2H). ^{31}P NMR ($CDCl_3$) δ 94.3. HRMS (70 eV) Calcd for $C_{11}H_{17}PS_2$: M, 244.0508. Found: *m/z* 244.0491.

Benzyl (1-Naphthyl)phenylphosphinodithioate (27a). The same method as for the preparation of **26b** was used. From ester **21a** (1.23 g, 3.29 mmol) was obtained colorless crystals (1.03 g, 80 %) upon recrystallization (hexane-CH_2Cl_2). Mp 120-121°C. ^1H NMR ($CDCl_3$) δ 4.27 (d, *J*=12.6 Hz, 2H), 7.2-8.6 (m, 17H). ^{31}P NMR ($CDCl_3$) δ 62.9. HRMS (70 eV) Calcd for $C_{23}H_{19}PS_2$: M, 390.0666. Found: *m/z* 390.0674.

Benzyl (1,1-Dimethylethyl)phenylphosphinodithioate (27b). The same method as for the preparation of **26b** was used. From ester **21b** (1.13 g, 3.71 mmol) was obtained a viscous oil (0.48 g, 40 %) upon Kugelrohr distillation. ^1H NMR ($CDCl_3$) δ 1.18 (d, *J*=18.6 Hz, 9H), 3.8-4.3 (m, 2H), 7.0-8.2 (m, 10H). ^{31}P NMR ($CDCl_3$) δ 92.4. HRMS (70 eV) Calcd for $C_{17}H_{21}PS_2$: M, 320.0822. Found: *m/z* 320.0817.

Benzhydryl (1-Naphthyl)phenylphosphinodithioate (28a). The same method as for the preparation of **26b** was used. From ester **22a** (0.478 g, 1.06 mmol) was obtained viscous oil (0.45 g, 90 %). ^1H NMR ($CDCl_3$) δ 6.11 (d, *J*=14.9 Hz, 1H), 6.9-8.6 (m, 22H). ^{31}P NMR ($CDCl_3$) δ 62.6. HRMS (70 eV) Calcd for $C_{29}H_{23}PS_2$: M, 466.0978. Found: *m/z* 466.0968.

Benzhydryl (1,1-Dimethylethyl)phenylphosphinodithioate (28b). The same method as for the preparation of **26b** was used. From ester **22b** (1.73 g, 4.51 mmol) was obtained a viscous oil (0.105 g, 6.1 %). ^1H NMR ($CDCl_3$) δ 1.15 (d, *J*=18.6 Hz, 9H), 5.93 (d, *J*=12.7 Hz, 1H), 6.8-7.9 (m, 15H). ^{31}P NMR ($CDCl_3$) δ 92.6. HRMS (70 eV) Calcd for $C_{23}H_{25}PS_2$: M, 396.1135. Found: *m/z* 396.1146.

Reactions of S-Stannylmethyl Phosphinothioates with Organolithium Reagents. The General Procedure is Given for the Reaction of 25a with PhLi. To a THF solution (20 mL) of stannyl ester **25a** (140. 7 mg, 0.217 mmol) was added PhLi (1.0 equiv) at -78°C. After stirring for 40 min MeI (in excess) was added

and then the solution was allowed to warm to room temperature. Workup followed by PTLC treatment on SiO_2 (hexane-ethyl acetate) yielded **29a** (15 %), **31a** (20 %), and **33a** (47 %).

(Methylthiomethyl)(1-naphthyl)phenylphosphine Oxide (29a): Mp 147-148°C (dec) (hexane-ether). ^1H NMR ($CDCl_3$) δ 2.21 (s, 3H), 3.34-3.50 (m, 2H), 7.42-7.58 (m, 6H), 7.78-7.94 (m, 4H), 8.04 (d, *J*=7.9 Hz, 1H), 8.50-8.58 (m, 1H). ^{31}P NMR ($CDCl_3$) δ 32.0. HRMS (70 eV) Calcd for $C_{18}H_{17}OPS$: M, 312.0738. Found: *m/z* 312.0734. Calcd for $C_{18}H_{17}OPS$: C, 69.21; H, 5.49; S, 10.26. Found: C, 68.95; H, 5.56; S, 10.51.

(Ethylthiomethyl)(1-naphthyl)phenylphosphine Oxide (30a): Colorless solid: ^1H NMR ($CDCl_3$) δ 1.19 (t, *J*=7.4 Hz, 3H), 2.64 (q *J*=7.4 Hz, 2H), 3.34-3.54 (m, 2H), 7.36-7.58 (m. 6H), 7.70-7.92 (m, 4H), 7.95-8.08 (m, 1H), 8.46-8.60 (m, 1H). ^{31}P NMR ($CDCl_3$) δ 32.1. HRMS (70 eV) Calcd for $C_{18}H_{17}OPS$: M, 326.0894. Found: *m/z* 326.0887.

Methyl(1-naphthyl)phenylphosphine Oxide (31a): Mp 152-153°C. (lit 150-153°C).[25] ^1H NMR ($CDCl_3$) δ 2.15 (d, *J*=12.9 Hz, 3H), 6.9-8.3 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 32.0.

n-Butyl(1-naphthyl)phenylphosphine Oxide (32a). ^1H NMR ($CDCl_3$) δ 0.3-2.2 (m, 9H), 6.9-8.2 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 34.7.

S-Ethyl (1-Naphthyl)phenylphosphinothioate (33a). ^1H NMR ($CDCl_3$) δ 1.37 (t, *J*=7.0 Hz, 3H), 4.0-4.3 (m, 2H), 7.2-8.6 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 32.1.

(1,1-Dimethylethyl)(methylthiomethyl)phenylphosphine Oxide (29b): Mp 153-154 °C (hexane-CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 1.17 (d, *J*=14.5 Hz, 9H), 2.28 (s, 3H), 3.07 (d, *J*=6.9 Hz, 2H), 7.44-7.60 (m, 3H), 7.69-7.80 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 18.0 (d, ^3J=2.4 Hz), 24.6, 26.4 (d, ^1J=59.8 Hz), 33.5 (d, ^1J=67.1 Hz), 128.1 (d, ^3J=11.0 Hz), 129.5 (d, ^1J=90.4 Hz), 131.6 (d, ^4J=2.4 Hz), 131.9 (d, ^2J=7.3 Hz). ^{31}P NMR ($CDCl_3$) δ 47.7. HRMS (70 eV) Calcd for $C_{12}H_{19}OPS$: M,

242.0894. Found: *m/z* 242.0900. Calcd for $C_{12}H_{19}OPS$: C, 59.48; H, 7.90; S, 13.23. Found: C, 59.20; H, 7.82; S, 13.58.

(1,1-Dimethylethyl)(ethylthiomethyl)phenylphosphine Oxide (30b): Mp 70-71°C (hexane-ether). ^1H NMR ($CDCl_3$) δ 1.16 (d, *J*=14.8 Hz, 9H), 1.22 (t, *J*=7.4 Hz, 3H), 2.59-2.86 (m, 2H), 3.09 (d, $^2J_{HP}$=16.6 Hz, 2H), 7.42-7.59 (m. 3H), 7.67-7.77 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 14.1, 24.1 (d, ^1J=63.5 Hz), 24.6, 28.1 (d, ^3J=2.4 Hz), 33.4 (d, ^1J=67.1 Hz), 128.1 (d, ^3J=11.0 Hz), 129.5 (d, ^1J=90.3 Hz), 131.5 (d, ^4J=2.4 Hz), 131.8 (d, ^2J=7.3 Hz). ^{31}P NMR ($CDCl_3$) δ 47.5. HRMS (70 eV) Calcd for $C_{13}H_{21}OPS$: M, 256.1051. Found: *m/z* 256.1044. Calcd for $C_{13}H_{21}OPS$: C, 60.84; H, 7.96; S, 12.62. Found: C, 60.91; H, 8.26; S, 12.51.

(1,1-Dimethylethyl)methylphenylphosphine Oxide (31b): ^1H NMR ($CDCl_3$) δ 1.13 (d, *J*=14.7 Hz, 9H), 1.73 (d, *J*=12.2 Hz, 3H), 7.3-7.9 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 47.3.

S-Ethyl (1,1-Dimethylethyl)phenylphosphinothioate (33b). ^1H NMR ($CDCl_3$) δ 1.20 (d, *J*=18.3 Hz, 9H), 1.22 (t, *J*=7 Hz, 3H), 2.6-3.1 (m, 2H), 7.1-8.0 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 91.5.

Optical Resolution of (1-Naphthyl)phenylphosphinothioic Acid (19a-R, S). Quinine (12.4 g, 38.2 mmol) and acid **19a** (10.7 g, 37.6 mmol) were dissolved in chloroform (70 mL) and the solution was allowed to stand at ca.10°C for one week. The white precipitate that resulted was collected by filtration and dried under vacuum overnight to yield a solid which was recrystallized from chloroform (6.62 g, 29 %). $[\alpha]_D$ -39.7° (*c* 1.07, $CHCl_3$). To determine the optical purity of the diastereomeric salt, it was converted to its diethylamine salt. Quinine was released by applying 4N HCl (100 mL), extracting with CH_2Cl_2 (100 mL), and washing succesively with 5% HCl and water. Workup furnished a yellow oil, which was dissolved in CH_2Cl_2 along with $NHEt_2$ (1.4 equiv) and the solution was stirred for a few minutes. After workup and recrystallization colorless crystals were obtained (2.07 g, 19 %). $[\alpha]_D$ +60.2° (*c* 0.57, $CHCl_3$), 93 % ee. The filtrate enriched with the other diastereomer was combined with

the filtrate of about the same composition of diastereomeric salts obtained on a different occasion and workup in a similar way and recrystallized from ethanol twice to give white crystals. $[\alpha]_D$ -158° (*c* 1.16, $CHCl_3$). Its $NHEt_2$ salt was obtained with the same procedure stated above. $[\alpha]_D$ -60.4° (*c* 0.770, $CHCl_3$), 93 % ee.

Optical Resolution of (1,1-Dimethylethyl)phenylphosphinothioic Acid (19b-R, S). A solution of acid **19b** (41.6 g, 194 mmol) in chloroform (200 mL) and a solution of (+)-1-phenylethylamine (23.93 g, 197 mmol) in chloroform (80 mL) were mixed together. After filtration to remove insoluble traces of material, benzene (160 mL) and hexane (500 mL) were added and the solution was allowed to stand overnight. The white precipitate which had appeared was collected by filtration and dried under vacuum overnight to gain a solid enriched with one of the diastereomeric salts (20.9 g, 32 %). ^{31}P NMR ($CDCl_3$) δ 78.8, 79.4 (13:1). The precipitate was dissolved in hot chloroform (180 mL) and ether (160 mL) was added to give a precipitate within 10 min, which was collected, washed with ether, and dried under vacuum. The precipitate consisted of only one diastereomer detectable by NMR (15.3 g, 23 %). ^{31}P NMR ($CDCl_3$) δ 79.1. $[\alpha]_D$ -22.3° (*c* 1.03, MeOH). Another crystallization showed no improvement in optical rotation (14.0 g, 21 %). This diastereomeric salt was dissolved in 10 % aqNaOH (150 mL) resulting in a slightly turbid solution which was extracted with CH_2Cl_2 to remove the released amine. The aqueous layer was acidified with conc HCl, extracted with CH_2Cl_2, washed with aq NH4Cl and worked up 8.28 (20 %). Repeated recrystallization ultimately yielded two crops of colorless crystals (4.20 g and 0.60 g, 10 %). $[\alpha]_D$ -27.4° (*c* 1.04, MeOH), 96 % ee, and $[\alpha]_D$ -28.1° (*c* 1.59, MeOH), 100 % ee. The mother filtrate was concentrated and dissolved in ether (200 mL) followed by addition of chloroform until the solid had dissolved with warming. After the solution was allowed to stand overnight the precipitated solid was collected and worked up as above. The resulting acid was dissolved in ether then hexane was added until a precipitate appeared. The solution was allowed to stand overnight the precipitate was discarded. The filtrate was concentrated and the resulting solid was recrystallized

from hexane to give a colorless solid (0.90 g, 2 %). $[\alpha]_D$ +22.3° (*c* 0.60, MeOH), 79 % ee.

S-Tributylstannylmethyl (1-Naphthyl)phenylphosphinothioate (23a-R). Quinine salt of acid **19a-R** (1.22 g, 2.00 mmol, $[\alpha]_D$ ^{17}+96.8° for acid) gave crystals (0.41 g, 35 %). Mp 68-70°C (pentane). HRMS (70 eV) Calcd for $C_{29}H_{41}OPS^{120}Sn$: M, 588.1638. Found: *m/z* 588.1651. $[\alpha]_D^{16}$ -4.37° (*c* 2.93, $CHCl_3$).

S-Tributylstannylmethyl (1-Naphthyl)phenylphosphinothioate (23a-S). Quinine salt of acid **19a-S** (1.90 g, 3.12 mmol, $[\alpha]_D^{20}$ -93.3° for acid) gave crystals (0.52 g, 27 %). Mp 69-70°C (pentane). HRMS (70 eV) Calcd for $C_{29}H_{41}OPS^{120}Sn$: M, 588.1635. Found: *m/z* 588.1625. Calcd for $C_{29}H_{41}OPS^{118}Sn$: M, 586.1636. Found: *m/z* 588.1658. $[\alpha]_D^{19}$ +4.13° (*c* 1.62, $CHCl_3$).

S-Tributylstannylmethyl (1,1-Dimethylethyl)phenylphosphinothioate (23b-R). From acid $[\alpha]_D^{18}$ +26.1° (*c* 1.29, MeOH). $[\alpha]_D^{20}$ +57.9° (*c* 4.40, $CHCl_3$).

S-Tributylstannylmethyl (1,1-Dimethylethyl)phenylphosphinothioate (23b-S). From acid $[\alpha]_D^{22}$ -27.8° (*c* 2.35, MeOH). $[\alpha]_D^{18}$ -59.3° (*c* 1.44, $CHCl_3$).

(Methylthiomethyl)(1-naphthyl)phenylphosphine Oxide (29a-S): Mp 152-154°C (dec) (hexane-ether). ^{1}H NMR ($CDCl_3$) δ 2.17 (d, ^4J=1 Hz, 3H), 3.41 (d, *J*=8.1 Hz, 2H), 7.28-8.11 (m, 11H), 8.43-8.66 (m, 1H). ^{31}P NMR ($CDCl_3$) δ 32.0. HRMS (70 eV) Calcd for $C_{18}H_{17}OPS$: M, 312.0736. Found: *m/z* 312.0731. $[\alpha]_D^{24}$ -8.07° (*c* 0.405, $CHCl_3$).

(Methylthiomethyl)(1-naphthyl)phenylphosphine Oxide (29a-R). $[\alpha]_D^{24}$ +8.22° (*c* 0.405, $CHCl_3$).

(1,1-Dimethylethyl)(methylthiomethyl)phenylphosphine Oxide (29b-S). $[\alpha]_D^{19}$ +77.1° (*c* 0.709, $CHCl_3$).

(1,1-Dimethylethyl)(methylthiomethyl)phenylphosphine Oxide (29b-R). $[\alpha]_D^{22}$ -81.0° (*c* 0.639, $CHCl_3$).

Desulfurization of 29a-S with Raney Ni. A solution of **29a-S** (41.4 mg, 0.133 mmol) and Raney Ni W-4 (large excess) in dry ethanol (15 mL) was stirred at room

temperature and monitored by TLC. After 8 h, the Ni was filtered off, the solvent removed, the residue redissolved in CH_2Cl_2, dried over anhydrous $MgSO_4$, and the solvent removed to give methyl(1-naphthyl)phenylphosphine oxide **31a-R** (10.3 mg, 29 %). $[\alpha]_D^{21}$ -7.3° (*c* 0.039, MeOH).

(1,1-Dimethylethyl)methylphenylphosphine Oxide (31b). $[\alpha]_D^{22}$ +21.0° (*c* 0.275, MeOH).

Reactions of S-Alkyl Phosphinothioates and Phosphinodithioates with Lithium Amides. The General Procedure is Given for the Reaction of 20b with LDA. To a solution of **20b** (196 mg, 0.858 mmol) in THF (20 mL) was added freshly prepared LDA (1.2 equiv) at -78°C, and the mixture was stirred at 0°C for 15 min. Then iodomethane (0.25 mL, ca. 4 equiv) was added to the solution. The mixture was stirred at room temperature overnight. The reaction mixture was treated with aq NH_4Cl, extracted with CH_2Cl_2, and the extracts were dried over anhydrous $MgSO_4$. After removal of the solvent the residue was subjected to dry column chromatography on SiO2 (hexane-ethyl acetate) to give t-butyl(methylthiomethyl)-phenylphosphine oxide (**29b**), t-butyl(1-methylthioethyl)phenylphosphine oxide (**34b**) in yields of 81 and 5 %, respectively, along with recovery of **20b** (9.8 mg, 5 %).

[(1-Methylthio)ethyl](1-naphthyl)phenylphosphine Oxide (34a): Diastreomeric mixture. HRMS (70 eV) Calcd for $C_{19}H_{19}OPS$: M, 326.0894. Found: *m/z* 326.0905. ^{31}P NMR ($CDCl_3$) δ 37.4, 37.9 (43:57).

Major diastereomer: ^1H NMR ($CDCl_3$) δ 1.61 (dd, J=7.3 Hz, $^3J_{PH}$=15.2 Hz, 3H), 1.95 (s, 3H), 3.99 (dq, J=7.3 Hz, $^2J_{PH}$=10.2 Hz, 1H), 7.40-7.60 (m, 6H), 7.75-8.10 (m, 5H), 8.66-8.76 (m, 1H).

Minor diastereomer: ^1H NMR ($CDCl_3$) δ 1.63 (dd, J=7.3 Hz, $^3J_{PH}$=15.2 Hz, 3H), 1.84 (s, 3H), 4.07 (dq, J=7.3 Hz, $^2J_{PH}$=10.1 Hz, 1H), 7.40-7.60 (m, 6H), 7.75-8.10 (m, 5H), 8.80-8.90 (m, 1H).

Ethyl(1-naphthyl)phenylphosphine Oxide (38a): Mp 143-144°C (dec) (ether). ^1H NMR ($CDCl_3$) δ 1.24 (dt, J=7.6 Hz, $^3J_{HP}$=17.4 Hz, 3H), 2.35-2.46 (m, 1H),

2.48-2.60 (m, 1H), 7.40-7.55 (m, 6H), 7.68-7.75 (m, 2H), 7.85-7.93 (m, 2H), 8.02 (d, J=8.2 Hz, 1H), 8.63 (d, J=8.3 Hz, 1H). ^{31}P NMR ($CDCl_3$) δ 36.1. HRMS (70 eV) Calcd for $C_{18}H_{17}OP$: M, 280.1017. Found: m/z 280.1024. Calcd for $C_{18}H_{17}OP$: C, 77.13; H, 6.11. Found: C, 76.90; H, 5.99.

[(1-Ethylthio)propyl](1-naphthyl)phenylphosphine Oxide (39a): Diastreomeric mixture. HRMS (70 eV) Calcd for $C_{19}H_{19}OPS$: M, 354.1207. Found: m/z 354.1197. ^{31}P NMR ($CDCl_3$) δ 36.8, 37.6 (49:51).

Major diastereomer: ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J=7.4 Hz, 3H), 1.19 (t, J=7.1 Hz, 3H), 1.62-1.78 (m, 2H), 2.15-2.28 (m, 1H), 2.49-2.59 (m, 1H), 3.22-3.28 (m, 1H), 7.40-7.58 (m, 6H), 7.65-7.75 (m, 2H), 7.98-8.09 (m ,3H), 8.87 (d, J=8.0Hz, 1H).

Minor diastereomer: ^{1}H NMR ($CDCl_3$) δ 1.03 (t, J=7.4 Hz, 3H), 1.20 (t, J=7.1 Hz, 3H), 2.02-2.12 (m, 1H), 2.15-2.28 (m, 2H), 2.36-2.43 (m, 1H), 3.10-3.17 (m, 1H), 7.40-7.58 (m, 6H), 7.65-7.75 (m, 2H), 7.98-8.09 (m ,3H), 8.73 (d, J=8.3Hz, 1H).

(1,1-Dimethylethyl)[(1-methylthio)ethyl]phenylphosphine Oxide (34b): Diastereomeric mixture. ^{31}P NMR ($CDCl_3$) δ 49.4, 50.4 (45:55). HRMS (70 eV) Calcd for $C_{13}H_{21}OPS$: M, 256.1051. Found: m/z 256.1053.

Major diastereomer: ^{1}H NMR ($CDCl_3$) δ 1.23 (d, J=14.2 Hz, 9H), 1.68 (dd, J=7.3 Hz, $^3J_{HP}$=13.4 Hz, 3H), 2.16 (s, 3H), 3.19 (dq, J=7.3 Hz, $^3J_{HP}$=9.2 Hz, 1H), 7.42-7.59 (m. 3H), 7.80-7.91 (m, 2H).

Minor diastereomer: ^{1}H NMR ($CDCl_3$) δ 1.29 (d, J=14.5 Hz, 9H), 1.40 (dd, J=7.3 Hz, $^3J_{HP}$=13.5 Hz, 3H), 2.36 (s, 3H), 3.12 (dq, J=7.3 Hz, $^3J_{HP}$=5.0 Hz, 1H), 7.42-7.59 (m. 3H), 7.69-7.78 (m, 2H).

(1,1-Dimethylethyl)[(1-ethylthio)propyl]phenylphosphine Oxide (39b): Diastereomeric mixture (ca. 1:1), was separated by preparative TLC (SiO_2, ether).

Less polar diastereomer: ^{1}H NMR ($CDCl_3$) δ 1.04 (t, J=7.3 Hz, 3H), 1.24 (t, J=7.5 Hz, 3H), 1.28 (d, ^3J=14.4 Hz, 9H), 1.50-1.79 (m, 2H), 2.74-2.84 (m, 2H), 3.01-3.09 (m, 1H), 7.40-7.52 (m, 3H), 7.68-7.77 (m, 2H). ^{31}P NMR ($CDCl_3$) δ 49.5. HRMS (70 eV) Calcd for $C_{15}H_{25}OPS$: M, 284.1364. Found: m/z 284.1354.

Polar diastereomer: ^{1}H NMR ($CDCl_3$) δ 1.10 (t, *J*=7.3 Hz, 3H), 1.14 (t, *J*=7.5 Hz, 3H), 1.24 (d, ^3J=14.3 Hz, 9H), 1.66-1.76 (m, 1H), 2.13-2.23 (m, 1H), 2.52-2.66 (m, 2H), 2.94-3.00 (m, 1H), 7.40-7.47 (m, 3H), 7.84-7.90 (m, 2H). ^{31}P NMR ($CDCl_3$) δ 48.3. HRMS (70 eV) Calcd for $C_{15}H_{25}OPS$: M, 284.1364. Found: *m/z* 284.1381.

(Methylthiomethyl)(1-naphthyl)phenylphosphine Oxide (29a-R). The reaction between ester **20a-S** (305 mg, 1.02 mmol, $[\alpha]_D^{22}$ -43.3°) and LDA gave **29a-R** (39 %) and **31a** (10 %). **29a-R**: $[\alpha]_D^{17}$ +6.45° (*c* 0.366, $CHCl_3$), **31a**: $[\alpha]_D^{17}$ ca.0°.

(1,1-Dimethylethyl)(methylthiomethyl)phenylphosphine Oxide (29b-S). The reaction between ester **20b-R** (53.3 mg, 0.233 mmol, $[\alpha]_D^{17}$ +124°) and LDA gave **29b-S** (15 mg, 27 %). $[\alpha]_D^{16}$ +62.0° (*c* 0.793, $CHCl_3$).

(Methylthiomethyl)(1-naphthyl)phenylphosphine Sulfide (40a): ^{1}H NMR ($CDCl_3$) δ 1.19 (d, *J*=16.9 Hz, 9H), 2.26 (s, 3H), 3.16 (d, *J*=5.6 Hz, 2H), 6.9-8.5 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 63.2.

Methyl(1-Naphthyl)phenylphosphine Sulfide (41a): ^{1}H NMR ($CDCl_3$) δ 2.30 (d, *J*=12.9 Hz, 3H), 7.1-8.5 (m, 12 H),. ^{31}P NMR ($CDCl_3$) δ 34.4.

Methyl (1-naphthyl)phenylphosphinothioite (42a). ^{1}H NMR ($CDCl_3$) δ 2.23 (d, *J*=11.6 Hz, 3H), 6.8-8.5 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 24.50.

(1,1-Dimethylethyl)(methylthiomethyl)phenylphosphine Sulfide (40b): ^{1}H NMR ($CDCl_3$) δ 1.20 (d, *J*=16.1 Hz, 9H), 2.31 (s, 3H), 3.0-3.7 (m, 2H), 7.2-8.2 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 63.2.

(1,1-Dimethylethyl)methylphenylphosphine Sulfide (41b). ^{1}H NMR ($CDCl_3$) δ 1.17 (d, *J*=16.6 Hz, 9H), 2.00 (d, *J*=12.5 Hz, 9H), 7.40-7.56 (m, 3H), 7.75-8.03 (m, 2H). ^{31}P NMR ($CDCl_3$) δ 55.9.

(1,1-Dimethylethyl)[(1-methylthio)ethyl]phenylphosphine Sulfide (43b): Diastereomeric mixture. ^{31}P NMR ($CDCl_3$) δ 69.7, 71.5 (ca. 1:1). ^{1}H NMR ($CDCl_3$)

δ 1.23 (d, J=16.1 Hz, 9H), 1.85 (s, 3H) or 2.25 (s, 3H), 3.4-4.1 (m, 1H), 7.3-8.2 (m, 5H).

(1,1-Dimethylethyl)[bis(methylthio)methyl]phenylphosphine Sulfide (44b): ^{1}H NMR ($CDCl_3$) δ 1.31 (d, J=16.1 Hz, 9H), 2.31 (d, J=18.7 Hz, 6H), 4.46 (d, J=9.0 Hz, 1H), 7.7-8.6 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 69.2.

[(Methylthio)phenylmethyl](1-naphthyl)phenylphosphine Sulfide (45a): Diastereomeric mixture. ^{31}P NMR ($CDCl_3$) δ 45.2, 46.5 (ca. 1:1). ^{1}H NMR ($CDCl_3$) δ 2.00 (s, 3H), 4.76 (d, J=11.2 Hz, 1H) or 4.96 (d, J=12.0 Hz, 1H), 6.7-8.6 (m, 12H).

(1,1-Dimethylethyl)[(methylthio)phenylmethyl]phenylphosphine Sulfide (45b): Diastereomeric mixture. ^{31}P NMR ($CDCl_3$) δ 65.6, 67.9 (ca. 1:1). ^{1}H NMR ($CDCl_3$) δ 0.92 (d, J=16.4 Hz, 9H) or 1.39 (d, J=16.6 Hz, 9H), 1.87 (s, 3H) or 1.99 (s, 3H), 4.63 (d, J=8.5 Hz, 1H), 6.9-8.3 (m, 5H).

Reactions of S-Methyl Phosphinothioates with n-BuLi. The General Procedure is Given for the Reaction of 26a. To a THF solution of **26a** (114.5 mg, 0.364 mmol) was added n-BuLi (1.3 equiv) at -78 °C. After allowing the solution temperature to rise to 0°C, the solution was stirred for 1 h, and then treated with MeI (>3 equiv). PTLC treatment on SiO_2 (CH_2Cl_2-CCl_4=1:5) afforded **41a** (55.1 mg, 50 %) and **42a** (21.7 mg, 20 %).

Ethyl (1-naphthyl)phenylphosphinothioite (48a). ^{1}H NMR ($CDCl_3$) δ 1.34 (d, J=11.6 Hz, 3H), 2.80 (dq, J=7.2 Hz, $^3J_{HP}$=11.2 Hz, 2H), 6.8-8.5 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 19.4.

(1,1-Dimethylethyl)ethylphenylphosphine Sulfide (47b). ^{1}H NMR ($CDCl_3$) δ 1.17 (d, J=16.0 Hz, 9H), 1.17 (dt, J=7.4 Hz, $^3J_{HP}$=18 Hz, 3H), 1.7-2.7 (m, 2H), 7.3-8.0 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 66.2.

(Methoxymethyl)(1-naphthyl)phenylphosphine Sulfide (51a): ^{1}H NMR ($CDCl_3$) δ 3.36 (s, 3H), 4.1-4.8 (m, 2H), 7.3-8.5 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 36.3.

(Hydroxymethyl)(1-naphthyl)phenylphosphine Sulfide (50a): ^{1}H NMR ($CDCl_3$) δ 3.12 (bs, 1H), 4.40 (dd, J=13.2 Hz, $^{3}J_{HP}$=19.2 Hz, 2H), 7.2-8.3 (m, 12H). ^{31}P NMR ($CDCl_3$) δ 41.6.

(1,1-Dimethylethyl)(methoxymethyl)phenylphosphine Sulfide (51b): ^{1}H NMR ($CDCl_3$) δ 1.22 (d, J=16.2 Hz, 9H), 3.48 (s, 3H), 4.21 (d, J=5.8 Hz, 2H), 7.3-8.0 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 54.7.

S-Methyl (1-Naphthyl)phenylphosphinothioate (20a-S). The $NHEt_2$ salt of acid **19a-S** (2.47 g, 6.91 mmol, $[\alpha]_D^{25}$ -60.4°, 93 % ee) was treated with MeI (excess) in benzene (50 mL) to give crystals (1.16g, 56 %) upon recrystallization (hexane-CH_2Cl_2). $[\alpha]_D^{22}$ -43.3° (*c* 0.878, $CHCl_3$).

S-Methyl (1,1-Dimethylethyl)phenylphosphinothioate (20b-S). To a benzene (30 mL) solution of acid **19b-S** (0.849 g, 3.96 mmol, $[\alpha]_D^{22}$ -26.3°, 93 % ee) was added MeI (excess). Workup followed by sublimation gave a solid (0.59 g, 65 %). $[\alpha]_D^{23}$ -138° (*c* 1.064, $CHCl_3$).

Methyl (1-Naphthyl)phenylphosphinodithioate (26a-S). Ester **20a-S** (0.59 g, 1.98 mmol, $[\alpha]_D^{24}$ -43.3°) was refluxed with L. R. in toluene for 3 h. Dry column chromatography on SiO_2 (hexane-ethyl acetate) gave a solid (0.581 mg, 94 %). $[\alpha]_D^{22}$ +57.6° ($CHCl_3$). Recrystallization gave crystals (0.47 g, 76 %) of essentially the same value. $[\alpha]_D^{22}$ +58.6° (*c* 0.916, $CHCl_3$). Calcd for $C_{17}H_{15}PS_2$: C, 64.95; H, 4.81. Found: C, 65.05; H, 4.54.

Methyl (1,1-Dimethylethyl)phenylphosphinodithioate (26b-S). Ester **20b-S** (0.57 g, 2.49 mmol, $[\alpha]_D^{23}$ -138°) was refluxed with L. R. in toluene for 4 h. Dry column chromatography on SiO_2 (hexane-ethyl acetate) followed by Kugelrohr distillation gave a solid (0.581 mg, 94 %). Mp 73.5-74.5°C. ^{1}H NMR ($CDCl_3$) δ 1.21 (d, J=18.3 Hz, 9H), 2.19 (d, J=13.2 Hz, 3H), 7.40-7.57 (m, 3H), 7.91-8.22 (m, 2H). ^{31}P NMR ($CDCl_3$) δ 94.3. HRMS (70 eV) Calcd for $C_{11}H_{17}PS_2$: M, 244.0508. Found: *m/z* 244.0491. $[\alpha]_D^{22}$ -104° (*c* 3.793, $CHCl_3$).

Methyl(1-Naphthyl)phenylphosphine Sulfide (41a-R). To a solution of **26a-S** (131.6 mg, 0.418 mmol, $[\alpha]_D^{22}$ +58.6°) cooled to -78°C was added n-BuLi (1.5 equiv) and stirred for 60 min. After iodomethane was added in excess stirring was continued for 10 min. The solution was then transfered to a THF solution of elemental sulfur via cannula and stirred overnight. Workup and dry column chromatography on SiO_2 (hexane-ethyl acetate) yielded **41a-R** (30.6 mg, 25 %) and **26a** (12.8 mg, 10 %). $[\alpha]_D^{21}$ +99.6° (*c* 0.60, $CHCl_3$). **26a**: $[\alpha]_D^{25}$ ca. 0°.

From **26a-S** (131.5 mg, 0.418 mmol, $[\alpha]_D^{22}$ +58.6°) and quenched after 15 min, **41a-R** (64.9 mg, 55 %) and **26a** (44.4 mg, 34 %). $[\alpha]_D^{21}$ +99.6° (*c* 0.60, $CHCl_3$). **26a**: $[\alpha]_D^{25}$ ca. 0°.

(1,1-Dimethylethyl)methylphenylphosphine Sulfide (41b-R). To a THF solution of **26b-S** (122.6 mg, 0.502 mmol, $[\alpha]_D^{22}$ -104°) was added n-BuLi (1.2 equiv) at -78°C. After stirring for 30 min, MeI was added and the solution was allowed to warm to room temperature. Workup and subsequent dry column chromatography on SiO_2 (hexane-ethyl acetate) gave a solid (98.3 mg, 92 %). Mp 78-79°C. ^{1}H NMR ($CDCl_3$) δ 1.17 (d, *J*=16.6 Hz, 9H), 2.00 (d, *J*=12.5 Hz, 9H), 7.40-7.56 (m, 3H), 7.75-8.03 (m, 2H). ^{31}P NMR ($CDCl_3$) δ 55.9. HRMS (70 eV) Calcd for $C_{11}H_{17}PS$: M, 212.0787. Found: *m/z* 212.0779. $[\alpha]_D^{20}$ +51.5° (*c* 0.770, $CHCl_3$).

From **26b-S** (49.0 mg, 0.201 mmol, $[\alpha]_D^{22}$ -100°) and quenching after stirring at 0°C for 2.5 h, **41b-R** (11.5 mg, 27 %). $[\alpha]_D^{20}$ +43.5° (*c* 0.70, $CHCl_3$).

(1-Naphthyl)phenylphosphine Sulfide (49a-R). To a solution of **26a-S** (89.0 mg, 0.283 mmol, $[\alpha]_D^{22}$ +58.6°) cooled to -78°C was added n-BuLi (1.5 equiv) and stirred for 15 min. Quenching with aq NH_4Cl diluted with THF and workup gave an oil (67.6 mg, 89 %). ^{1}H NMR ($CDCl_3$) δ 7.0-8.3 (m, 12 H), 8.45 (d, *J*=469 Hz, 1H). ^{31}P NMR ($CDCl_3$) δ 19.7. $[\alpha]_D^{20}$ +104° (*c* 0.73, PhH).

Methyl(1-Naphthyl)phenylphosphine Sulfide (41a-R) from 49a-R. To a THF solution of **49a-R** (40.7 mg, 0.152 mmol, $[\alpha]_D^{20}$ +104°) was added n-BuLi (1.2 equiv) at -78°C. After stirring for 15 min iodomethane was added in excess and stirring

was continued for 1 h. The solution was transfered to a THF solution of elemental sulfur via cannula and stirred overnight. Workup and dry column chromatography on SiO_2 (hexane-CH_2Cl_2) yielded **41a-R** (18.5 mg, 43 %) and **26a** (8.0 mg, 16 %). **41a-R**: ^1H NMR ($CDCl_3$) δ 2.30 (d, *J*=12.9 Hz, 3H), 7.1-8.5 (m, 12 H),. ^{31}P NMR ($CDCl_3$) δ 34.4. $[\alpha]_D^{25}$ +84.2° (*c* 0.60, $CHCl_3$). **26a**: $[\alpha]_D^{25}$ ca. 0°.

(1,1-Dimethylethyl)phenylphosphine Sulfide (49b-R). To a solution of **26b-S** (92.9 mg, 0.380 mmol, $[\alpha]_D^{27}$ -100°) in dry THF (10 mL) cooled to -78°C was added n-BuLi (1.5 equiv). After stirring for 30 min, aq NH4Cl diluted with THF was added dropwise without raising the temperature. Extraction with CH_2Cl_2, drying with anhydrous $MgSO_4$, removal of the solvent followed by drying under vacuum yielded a solid (62.7 mg, 83 %). Mp 72-76°C. ^1H NMR ($CDCl_3$) δ 1.18 (d, *J*=18.2 Hz, 9H), 6.89 (d, *J*=442 Hz, 1H), 7.40-7.90 (m, 5H). ^{31}P NMR ($CDCl_3$) δ 52.7. HRMS (70 eV) Calcd for $C_{10}H_{15}PS$: M, 198.0632. Found: *m/z* 198.0632. $[\alpha]_D^{23}$ +82.9° (*c* 0.62, PhH).

(1,1-Dimethylethyl)methylphenylphosphine Sulfide (41b-R) from 49b-R. n-BuLi (1.2 equiv) was added to a THF solution of **49b-R** (59.7 mg, 0.301 mmol) cooled to -78°C and stirred for 30 min. Iodomethane in large excess was added and stirring was continued for 1 h after which the temperature was allowed to warm to room temperature. Workup and subsequent DCC on SiO_2 (hexane-CH_2Cl_2) afforded a solid (43.3 mg, 68 %). $[\alpha]_D^{20}$ +52.1° (*c* 0.53, $CHCl_3$).

Bis(trimethylsilyl) Peroxide. To an ether solution (200 mL) of diazabicyclo[2.2.2]octane (DABCO) (11.25 g, 0.100 mol), 90 % H_2O_2 (5.4 mL, 2 equiv) was added at 0°C. After stirring for 1 h, the precipitate, DABCO-$2H_2O_2$, was collected, excessively washed with ether, and vacuum dried overnight to yield a solid (15.8 g, 87 %). To a dry CH_2Cl_2 suspension (120 mL) of DABCO-$2H_2O_2$ (14.4 g, 80 mmol) and DABCO (9.00 g, 1 equiv), chlorotrimethylsilane (34.3 mL, 3.4 equiv) was added at 0°C. After stirring for 1 h, the solution was stirred at room temperature overnight. The white precipitate was filterd off under argon, and excessively washed

with dry pentane. The solvent was carefully removed in vacuo at rt (100 mmHg). Fresh pentane (50 mL) was added to the residue and the insoluble solid was filtered off after which the solvent was removed. Distillation yielded a clear liquid (4.75 g, 20 % based on Me_3SiCl). Bp 42-43°C (35 mmHg). ^1H NMR ($CDCl_3$) δ 0.18 (s, 18H).

Oxidation of 41b-S with BSPO. To a solution of sulfide **41b-S** (45.3 mg, 0.213 mmol, $[\alpha]_D^{20}$ +51.5°) was slowly added BSPO (2 equiv). After stirring at room temperature for 24 h, the solution was treated with aq Na_2CO_3 then workup. The residue was chromatographed on SiO_2 (CH_2Cl_2) to give the oxide **31b-R** (31.6 mg, 75 %). $[\alpha]_D^{21}$ +4.22° (*c* 0.866, MeOH).

Oxidation of 41b-S with mCPBA. A CH_2Cl_2 solution (5 mL) of **41b-S** (44.5 mg, 0.210 mmol, $[\alpha]_D^{23}$ +53.9°) was added to a CH_2Cl_2 solution (10mL) of mCPBA (1.5 equiv) at 0°C, and stirred at room temperature overnight. Treatment of the solution with aq Na_2CO_3, subsequent workup, and PTLC on SiO_2 (hexane-ethyl acetate=1:1) gave oxide **31b-R** (14.1 mg, 34 %). $[\alpha]_D^{22}$ +5.72° (*c* 0.927, MeOH).

Oxidation of 26b-S with mCPBA. The same procedure as for **41b-R** was used. Ester **26b-S** (51.0 mg, 0.209 mmol, $[\alpha]_D^{21}$ -102°) gave **20b-S** and an unidentified compound (11 mg). **26b-S**: $[\alpha]_D^{21}$ -123° (*c* 0.747, $CHCl_3$). Unidentified compound: $[\alpha]_D^{22}$ -316° (*c* 0.787, $CHCl_3$).

Oxidation of 46b-R with O_2. To a solution of **26b-S** (78.7 mg, 0.322 mmol, $[\alpha]_D^{15}$ -102°) in dry THF (10 mL) cooled with an acetone-dry ice bath, was added n-BuLi (1.5 equiv) to give a light yellow solution. After stirring for 20 min, O_2 was passed through the solution via a needle and resulted in immediate decolorization. Alkaline extraction and subsequent workup yielded acid **19b-R** (40.0 mg, 58 %). $[\alpha]_D$ +23.0° (*c* 0.572, MeOH).

(1,1-Dimethylethyl)(hydroxymethyl)phenylphosphine Sulfide (50b-R). To a THF solution (20 mL) of **26b-S** (236.2 mg, 0.966 mmol, $[\alpha]_D^{22}$ -104°) was added n-BuLi (1.3 equiv) at -78°C. After stirring for 20 min the solution was treated with methoxymethyl bromide and stirring was continued overnight at 0°C. The solution

mixture was treated with dil HCl then worked up. Dry column chromatography on SiO_2 (hexane-CH_2Cl_2) gave a solid (154.6 mg, 70 %). Mp 85.0-88.0°C. ^1H NMR ($CDCl_3$) δ 1.20 (d, J=16.4 Hz, 9H), 3.09 (bs, 1H), 4.12 (dd, J=12.7 Hz, $^2J_{HP}$=1.2 Hz, 1H), 4.42 (d, J=12.7 Hz, 1H), 7.42-7.59 (m, 3H), 7.66-7.80 (m, 2H). ^{31}P NMR ($CDCl_3$) δ 63.9. HRMS (70 eV) Calcd for $C_{11}H_{17}OPS$: M, 228.0738. Found: m/z 228.0740. $[\alpha]_D^{24}$ +15.6° (c 0.410, $CHCl_3$). Only signals due to a single enantiomer were observed in ^1H, ^{13}C, and ^{31}P NMR spectra on adding chiral shift reagent, Eu(tfc)$_3$.

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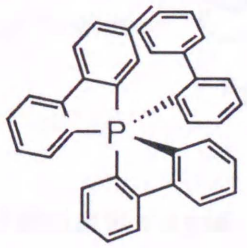
Chapter 2

Characterization of the First Enantiomeric Pairs of Stereochemically Definable Hypervalent 10-P-5 Phosphoranes with Asymmetry Only at Phosphorus

1. Introduction

Phosphorus compounds are of significance due to their important role in numerous biological processes involving phosphoryl transfer, and recently, artificial phosphorus compounds have seen application as herbicides, insecticides, and medicines.[2] Thus, the mechanism of reaction involving phosphorus compounds, particularly those having a P=O segment, has been a topic of interest for quite some time. Through the pioneering work of Westheimer and others it is now widely accepted that the reaction process involves a pentavalent phosphorus intermediate (or transition state) formed by nucleophilic attack upon the tetracoordinate phosphorus atom, and that the stability and stereochemistry (both steric and electronic effects combined) of the transient species (or transition state) greatly influence the outcome of the process.[3] Therefore to deduce basic understanding of the process much attention has been focused on the stereochemistry by using various model compounds and through these studies it has been found that the permutation of the intermediate is an important factor.[4] The permutation is usually interpreted in the terms of Berry pseudorotation.[5] Since the process only requires simultaneous bending of bonds, the energy barrier is generally very small. Recently, due to the advent of new theoretically interesting results based upon highly sophisticated calculations[6] and the emergence of advanced instrumentation, this field of research has gained renewed interest.[7] In investigations of the stereochemistry, isomers arising from different configurations upon asymmetric pentavalent phosphorus atoms have been utilized by introducing chirality into at least one of the substituents thus producing diastereomers which can be monitored by spectroscopic methods such as NMR. Among these compounds there are some phosphoranes in the literature that have been successfully isolated as optically active diastereomers. These compounds bear ligands derived from optically active alcohols or aminoalcohols which are available or can be prepared easily from the chiral pool.[8] But as for optically active pentacoordinate compounds

bearing chirality only at the central phosphorus atom, the only one example we are aware of is the pentaarylphosphorus compound **1**, which was prepared by Hellwinkel.[9] This fascinating compound exhibits residual optical activity, meaning that what is observed at ambient temperatures is the averaged spectroscopic properties among interconverting positional isomers of low conversion energy barriers, and that high energy barriers between the enantiomeric groups of isomers exist. So for optically active compounds with rigid and definable stereochemistry there was no precedence. However by utilizing Martin's phosphorane **2** which meets the substituent combination requirements which permit permutation but also slows it down by allowing in principle the existence of only one configuration (along with its enantiomer) about the phosphorus atom, we have succeeded in preparing and characterizing the first configurationally stable optically active phosphoranes **4-R$_P$** and **4-S$_P$**, and **2-R$_P$** and **2-S$_P$** which bear asymmetry only upon phosphorus. Compounds **4-R$_P$** and **4-S$_P$** were obtained from a diastereomeric pair of (o-$OC(CF_3)_2C_6H_4)_2P^*CH_2CO_2$(-)menthyl, through a transformation not directly involving chemical exchange upon the phosphorus atom, thus the stereochemistry being subject only to permutation. On the other hand, compounds **2-R$_P$** and **2 - S$_P$** were obtained from (o-$OC(CF_3)_2C_6H_4)_2P^*CH_2NHC^*HCH_3Ph$ (**10-R$_P$** and **10-S$_P$**), through a transformation directly involving the phosphorus atom, thus the stereochemistry being dependent not only on permutation but also on reaction stereoselectivity. Herein we describe the details of the transformations and the characterization of the optically active compounds.



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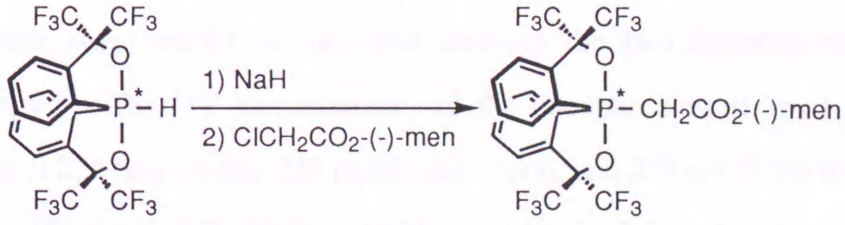
2. Results and Discussion

*R*P- and *S*P-(o-OC(CF3)2C6H4)2P*CH2CH2OH.

The preparation of diastereomers **3-RP** and **3-SP** was done as shown in Scheme 1. The chiral auxiliary (-)-menthol was converted to its chloroacetate by reacting the alcohol with chloroacetic chloride. Racemic phosphorane **2**[10] was prepared by treating phosphorus trichloride at -78°C with lithium 1,1,1,3,3,3-hexafluoro-2-(2-lithiophenyl)-2-propoxide prepared according to a published procedure[11] and then quenching the solution with 6N HCl. The use of acid was required to minimize the amount of oxidized product. The attachment of the chiral auxiliary to phosphorane **2** was achieved by treating the phosphorane with NaH in THF, followed by the addition of (-)-menthyl chloroacetate to furnish a 1:1 diastereomeric mixture of phosphoranes **3** in 87 % combined yield. While a small amount of the pair could be separated by repeated use of preparative TLC, fortunately for us they could also be resolved in larger quantities by fractional crystallization using MeOH-H_2O as solvent. The diastereomers crystallized out as prisms and needles, which could easily be separated by hand. The separated crystals were repeatedly recrystallized to assure diastereomeric purity ultimately giving the diastereomer later determined to be **3-RP** in 25 % yield and the diastereomer later determined to be **3-SP** in 22 % yield.

Scheme 1



2-racemic **3-RP, SP**

The diastereomers showed distinctive signals in both ^1H NMR (δ 4.53 for **3-RP** and 4.61 for **3-SP** in $CDCl_3$, respectively, for the methine proton geminal to the

oxygen atom in the (-)-menthyl moiety; Fig. 10) and ^{31}P NMR (δ -25.6 for **3-R$_P$** and -25.3 for **3-S$_P$** in acetone-d_6, respectively; Fig. 11) thus allowing facile determination of the diastereomeric ratio.

In order to determine the absolute stereochemistry of the diastereomers, X-ray crystal structure analysis was carried out on the diastereomer of the cubic crystal. The ORTEP structure of **3-R$_P$** is shown in Fig. 1 along with selected structural parameters in Table 1 and crystal parameters in Table 2. As the drawing shows the compound assumes a trigonal bipyramidal structure with the two oxygen atoms occupying the two apical positions and the three carbon atoms occupy the three equatorial positions. The angles around the phosphorus atom are nearly ideal with the apical O(1)-P(1)-O(2) angle being 177.4°, and the sum of the angles formed by the equatorial atoms and phosphorus being 359.9° implying coplanarity of the phosphorus atom and the three equatorial carbon atoms. The absolute stereochemistry of the phosphorus atom determined from its relative stereochemistry to the known (-)-menthyl moiety turned out to be **R$_P$**.[12]

The optical rotation values measured with 589 nm (Na-*D*) radiation were near zero, therefore the measurement was carried out with 436 nm (Hg). The values were $[\alpha]^{21}_{436}$ +11.1° (*c* 1.02, $CHCl_3$) for **3-R$_P$** and $[\alpha]^{21}_{436}$ -70.0° (*c* 1.02, $CHCl_3$) for **3-S$_P$**. Since benzene rings were attached directly to the asymmetric phosphorus atom in a C_2 symmetry style, it was speculated that opposite Cotton effects arising from the isoenergetic exiton dipole coupling of light polarization due to π-π* transition of the two benzene rings would be observed between the two diastereomers in CD spectroscopy.[13] The UV measurements of the phosphoranes showed absorption maximums at 224 (logε=4.26), 229 (4.26), 266 (3.16), and 273 nm (3.10) for **3-R$_P$** and 224 (4.32), 229 (4.32), 267 (3.23), and 274 nm (3.16) for **3-S$_P$** while the absorption of (-)-menthyl chloroacetate alone was observed as a shoulder at ca.220 nm (strong solvent absorption is inevitable in this low wavelength region).

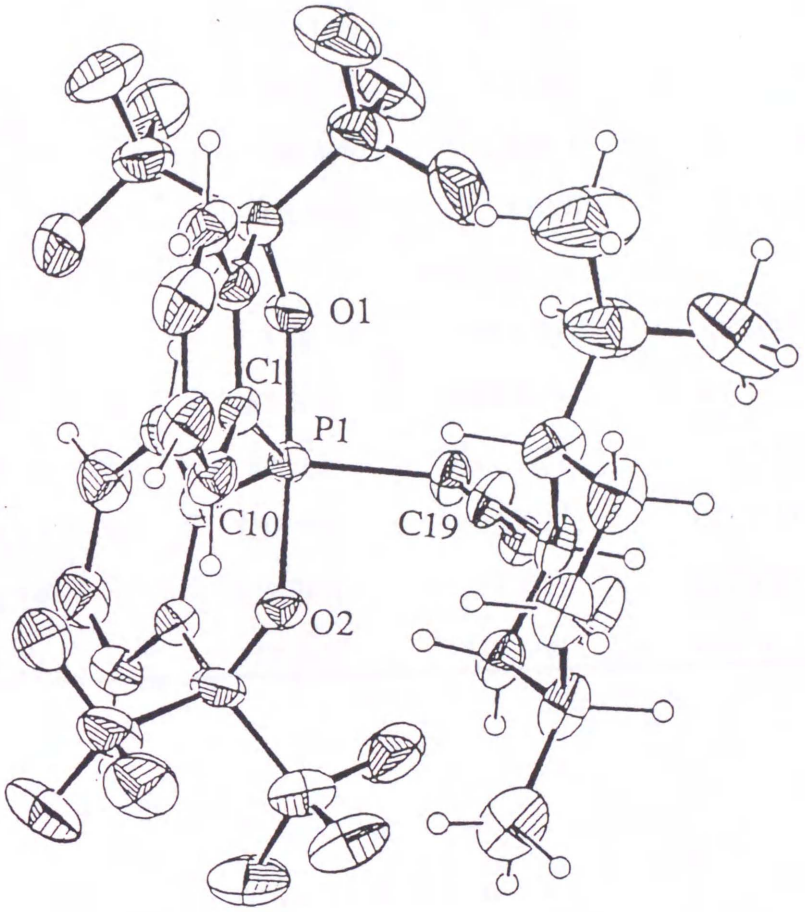


Figure 1. ORTEP drawing of **3-Rp** showing the thermal ellipsoids at the 30 % probability level.

Table 1. Selected Bond Lengths and Angles for **3-R$_P$**, **6-R$_P$** and **10-R$_P$**.

	3-R$_P$	**6-R$_P$**	**10-R$_P$**
		Bond Lengths (Å)	
P1-O1	1.747(4)	1.768(3)	1.754(3)
P1-O2	1.751(4)	1.753(3)	1.771(3)
P1-C1	1.816(6)	1.818(5)	1.825(4)
P1-C10	1.813(5)	1.808(5)	1.821(4)
P1-C19	1.849(6)	1.817(6)	1.834(3)
		Bond Angles (deg)	
O1-P1-O2	177.4(2)	178.1(2)	175.8(1)
O1-P1-C1	87.9(2)	87.5(2)	87.1(1)
O2-P1-C10	87.2(2)	87.8(2)	87.3(1)
C1-P1-C10	129.1(3)	123.8(2)	127.7(1)
C1-P1-C19	118.2(3)	118.8(2)	117.4(2)
C10-P1-C19	112.6(2)	117.6(2)	114.9(2)

The CD spectra of (-)-menthyl chloroacetate showed a single monotone positive peak at 221 nm ($\Delta\varepsilon$=+0.42), therefore implying a slight signal overlap in the positive region. The measured spectra of **3-R$_P$** and **3-S$_P$** have been calibrated so that the vertical coordinate gives the $\Delta\varepsilon$ values as shown in Fig. 2. The spectrum of **3-R$_P$** showed a negative Cotton effect (a negative primary Cotton effect and a positive secondary Cotton effect) with peaks at λ ($\Delta\varepsilon$) = 214 (+8.2), 229 (-5.4), 235 (+3.5), 265 (+1.7), and 271 nm (+1.3), while that for **3-S$_P$** exhibited a positive Cotton effect (a positive primary Cotton effect and a negative secondary Cotton effect) with peaks at 214 (-6.5), 229 (+8.2), 235 (-3.5), 265 (-2.0), and 272 nm (-1.5). The expected small differences in intensity due to the (-)-menthyl moiety could be observed at 214 and 229 nm. These Cotton effects imply that **3-R$_P$** has an overall left-handed helical electron transition moment, while that of **3-S$_P$** is the opposite.

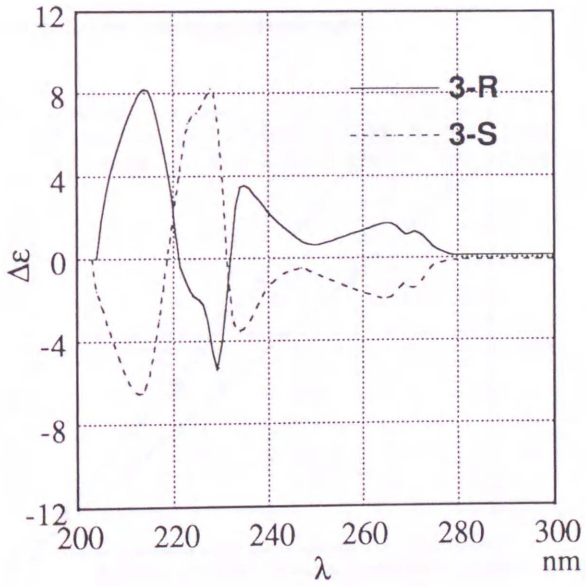


Figure 2. CD spectra of **3-R$_P$** (solid line, 4.98 x 10^{-5} M) and **3-S$_P$** (broken line, 5.38 x 10^{-5}) in cyclohexane. The original data has been replotted in terms of $\Delta\varepsilon$. The random noise level in the <230 nm region was $\Delta\varepsilon$= ca.±30 while in the >230 nm region it was $\Delta\varepsilon$= ca.±10.

Before proceeding on to the removal of the chiral auxiliary and subsequent reactions, the rates of epimerization of the compounds were measured at 100°C using toluene and pyridine as solvent by monitoring ^{31}P NMR. The observed change in diastereomer ratio is shown in Fig. 3. Martin et al. had already measured the permuation rate of a similar compound having a phenyl group in the equatorial position in the place of the chiral auxiliary in compound **3** and have come up with the value $\Delta G^{\neq}$=28.3 kcal mol^{-1} (424 K).[14] In our case the rates were found to be 1.3 x 10^{-7} s^{-1} in toluene, and 1.9 x 10^{-7} s^{-1} in pyridine, corresponding to activation free energies of $\Delta G^{\neq}$=33.8 kcal mol^{-1} (373 K) and 33.5 kcal mol^{-1} (373 K), respectively. These results show that the process is very slow and that there is little dependence of solvent polarity or donor ability upon the rate. This is in contrast with results obtained in kinetic studies of permutation of pentacoordinate antimony compounds, which showed strong solvent dependence with large rate acceleration when donating solvents were used.[15] Thus it was concluded that by avoiding high temperatures and prolonged reaction periods epimerization could be avoided.

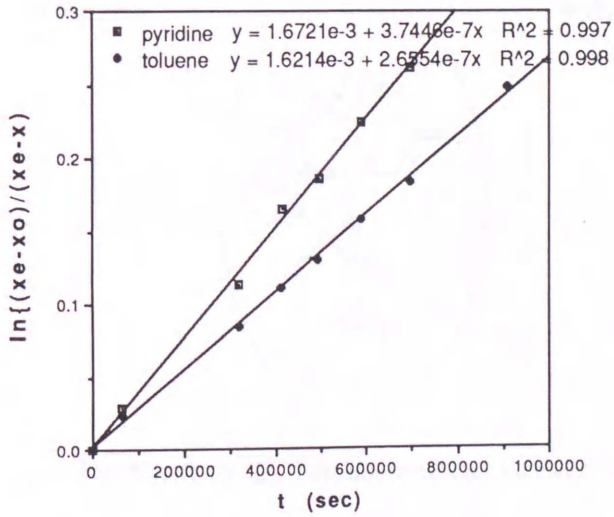
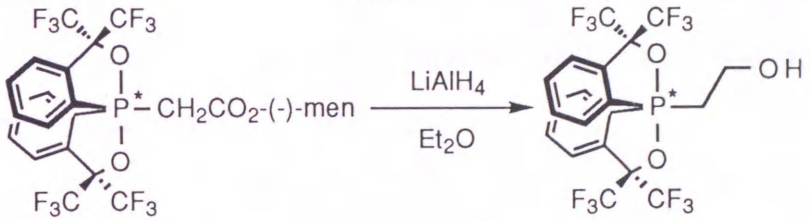


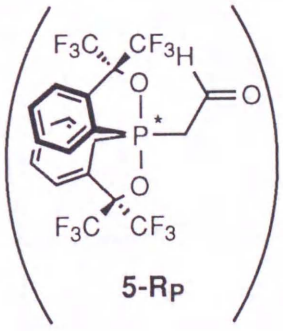
Figure 3. Plot of $\ln\{(x_e-x_o)/(x_e-x)\}$ vs time. (x_e=ratio at equilibrium, x_o=ratio observed at t=0, x=observed ratio at arbitrary intervals)

The removal of the chiral menthyl moiety was achieved by treating the diastereomers with an excess amount of $LiAlH_4$ in refluxed Et_2O as depicted in Scheme 2, thereby generating the first pair of rigid optically active phosphoranes with asymmetry only at phosphorus. The yields of **4-R$_P$** and **4-S$_P$** were 81 % and 84 %, respectively. Since it was found that complete removal of (-)-menthol from the product mixture was difficult using chromatographic means the final purification of the alcohols **4-R$_P$** and **4-S$_P$** was carried out by sublimation under reduced pressure at temperatures at or below 50°C. Since this process required a rather lengthy amount of time, partial epimerization could be detected when heating was carried out at temperatures over 50°C.

Scheme 2



3-R$_P$, S$_P$ **4-R$_P$, S$_P$**



5-R$_P$

^1H, ^{13}C, and ^{31}P NMR (δ -22.7 in acetone-d_6) showed identical spectra for the two compounds and were fully compatible with the assigned structure. The hydroxy proton could be observed at δ 1.86 as a broad singlet and the carbon bonded to this hydroxy group was observed at δ 58.2. The IR spectra also showed the presence of a hydroxy group with OH stretching at 3410 cm^{-1} and alcoholic CO stretching at 1197

cm^{-1}. The reaction of other nucleophilic reagents such as Grignard and alkyllithium reagents turned out to be sluggish probably due to steric hindrance and were not suitable for the conversion. In the reaction of **3-R$_P$**, the use of less amounts of $LiAlH_4$ led to partial formation of aldehyde **5-R$_P$** (aldehyde proton at δ 9.63; carbonyl stretching at 1719 cm^{-1}), the partially reduced product.

The optical rotation values of **4-R$_P$** and **4-S$_P$** were $[\alpha]^{21}_{436}$ +108° (*c* 1.02, $CHCl_3$) and $[\alpha]^{21}_{436}$ -107° (*c* 0.83, $CHCl_3$), respectively. The UV spectra showed λ_{max} (log ε) at 223 (4.36), 228 (4.38), and 266 (3.21) nm. The CD spectra (Fig. 4) of **4-R$_P$** showed the expected negative Cotton effect with peaks at λ (Δε) = 210 (+10.2), 227 (-10.9), 264 (+1.8), and 270 (+1.3), while that of **4-S$_P$** showed the expected positive Cotton effect with peaks at the same wavelengths with identical absolute intensities and opposite signs. The small intensity differences could be ascribed primarily to uncertainty of measurement, therefore implying the high enantiomeric purities of the compounds.

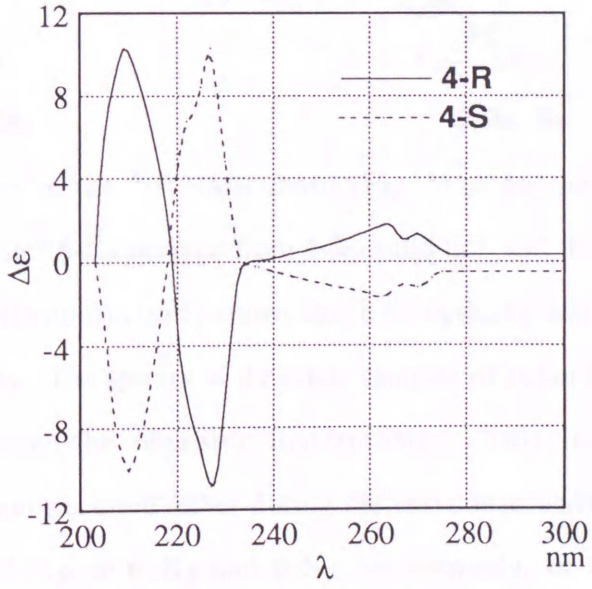
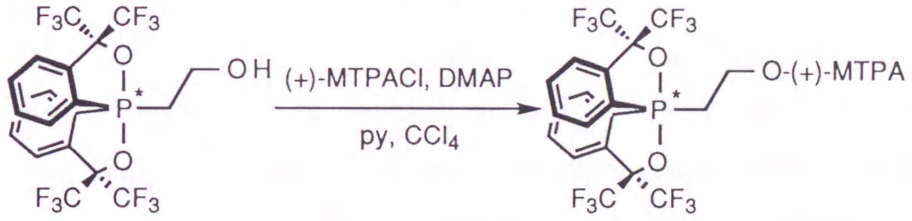


Figure 4. CD spectra of **4-R$_P$** (solid line, 1.73 x 10^{-5} M) and **4-S$_P$** (broken line, 1.26 x 10^{-5}) in cyclohexane. The original data has been replotted in terms of Δε. The random noise level in the <230 nm region was Δε= ca.±30 while in the >230 nm region it was Δε= ca.±10.

In order to assure the high enantiomeric purity of the chiral alcohols, the alcohols **4** were converted to their *R*-(+)-Mosher ester as described in Scheme 3, using the acid chloride derived from (R)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid. The isolated yields were at best 54 and 31 %, respectively, and were not optimized. To facilitate assignments and make comparisons a mixture of **3-R$_P$** and **3-S$_P$** was exposed to the same sequence of reactions, to give **4** in 92 % yield and the following **6** in 57 %. Resolution of the ^{31}P NMR signals could be achieved in acetone (δ -24.5 for **6-R$_P$** and δ -24.7 for **6-S$_P$**). ^{1}H NMR of the protons of the benzene ring ortho to phosphorus (δ 8.38 for **6-R$_P$** and δ 8.28 for **6-S$_P$**) and the methoxy protons (δ 3.37 for **6-R$_P$** and δ 3.26 for **6-S$_P$**) could also be distinguished. Other common solvents were not appropriate.

Scheme 3



4-R$_P$, S$_P$ **6-R$_P$, S$_P$**

A comparison of the ^{31}P NMR charts (Fig. 5) of the diastereomeric mixture (top), the Mosher ester **6-S$_P$** derived from **4-S$_P$** (middle), and the Mosher ester **6-R$_P$** derived from **4-R$_P$** (bottom) clearly shows that both optically active esters are of high diastereomeric purity. The spectra of the crude samples of either **6-S$_P$** or **6-R$_P$** did not show the presence of the opposing diastereomer. This implies the fact that epimerization had not occurred either during the two consecutive transformations of esters **3-R$_P$** and **3-S$_P$** to **6-R$_P$** and **6-S$_P$**, respectively, or during purification procedures. Thus we could confirm the high enantiomeric purity of the alcohols **4-R$_P$** and **4-S$_P$**.

Recrystallization of **6-R$_P$** from hexane-CH_2Cl_2 afforded single crystals, and were thus structurally analyzed. Figure 6 shows the ORTEP drawing and selected parameters are listed in Tables 1 and 2 along side those of **3-R$_P$**. Compound **6-R$_P$** was found to have a nearly ideal trigonal bipyramidal structure just as **3-R$_P$**. The R configuration of the phosphorus atom was determined from its relative stereochemistry to that of the Mosher moiety of known absolute stereochemistry. Through analogy the absolute stereochemistry of the alcohols **4-R$_P$** and **4-S$_P$** were again affirmed. The structural features of the two compounds are quite similar in principle, but **3-R$_P$** was found to have a rather longer P(1)-C(19) bond length (1.849 Å to 1.817 Å; Δ=0.032 Å) and smaller sum of apical bond lengths (3.498 Å to 3.521 Å; Δ=-0.023 Å). The former is probably due to the steric bulk of the equatorial ligand moiety in **3-R$_P$** and the presence of the electron withdrawing carbonyl group, whereas the latter is due to the counter balance of the electron density upon the phosphorus atom, i.e., **3-R$_P$** having shorter bonds due to the presence of the carbonyl group, a kind of push-pull effect.

Thus, we were able to establish the absolute stereochemistry and high enantiomeric purity of the first single structured chiral pentacoordinate phosphorus compound with asymmetry located solely on the phosphorus atom through successive conversions, i.e., reduction and esterification, under rather mild conditions without the accompaniment of epimerization (racemization).

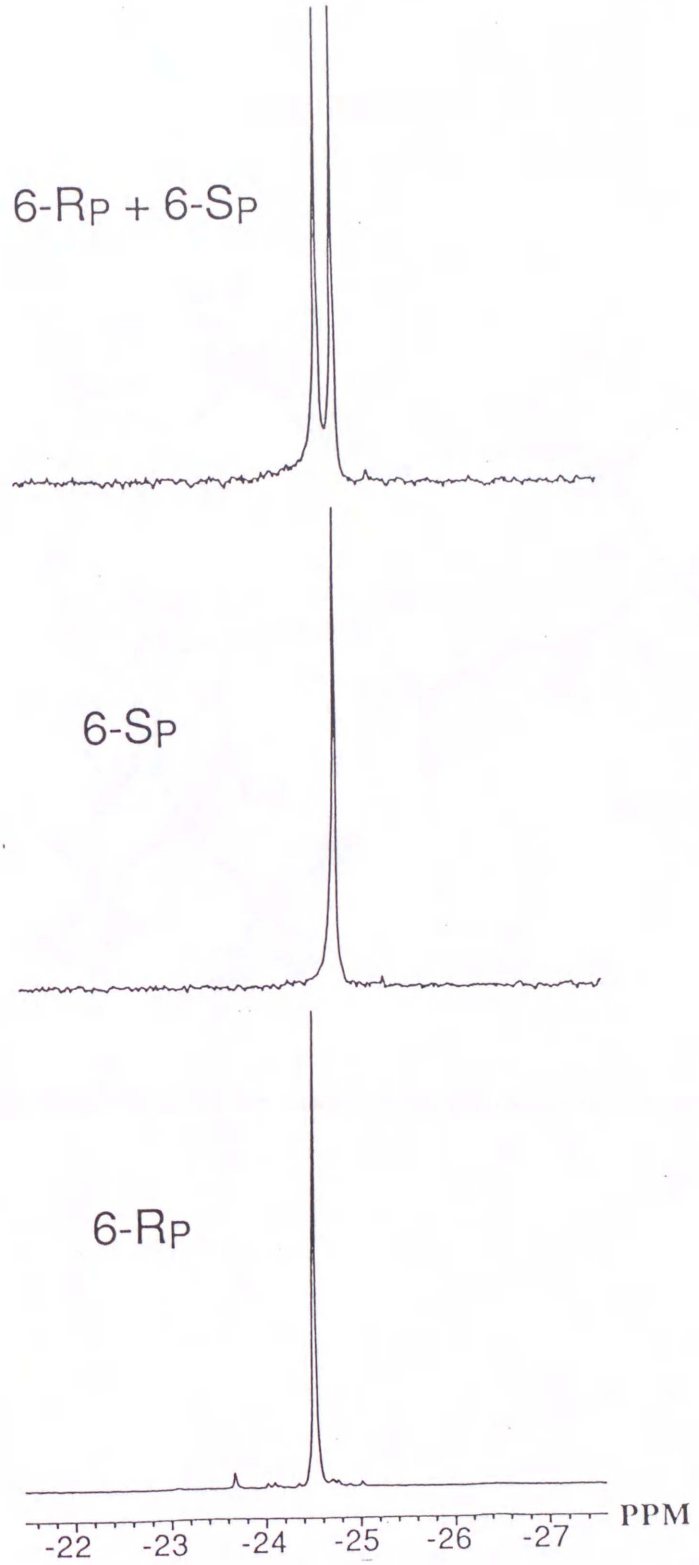


Figure 5. ^{31}P NMR of a mixture of **6-RP+6-SP** (upper chart), **6-SP** derived from **4-SP** (middle chart), and **6-RP** derived from **4-RP** (lower chart).

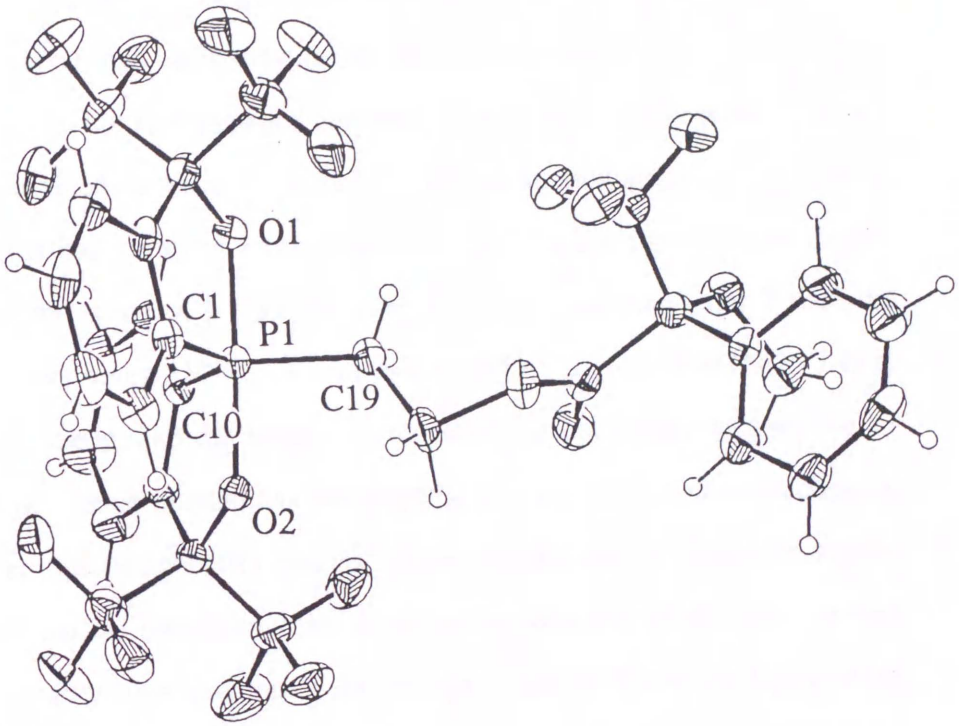
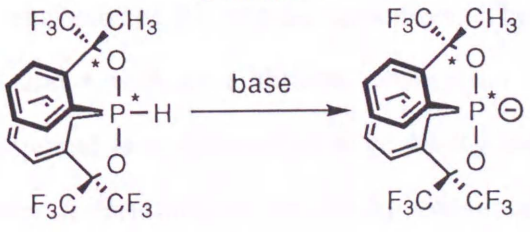


Figure 6. ORTEP drawing of **6-Rp** showing the thermal ellipsoids at the 30 % probability level.

***R*P- and *S*P-(o-OC(CF$_3$)$_2$C$_6$H$_4$)$_2$P*H.**

To further gain a general picture of the nature of optically active phosphoranes we reasoned that it would be desirable to have a larger amount of available optically active compounds with differing functionalities. In order to do so a parent compound that would allow transformation without losing optical activity was required. To this end we turned our attention to hydrophosphorane **2** because the hydrogen could potentially be replaced with other substituents, and the compound itself is unique due to the possibility of giving a ring opened tautomer. Before seeking the optically active compound we examined the stereochemical features of an analogous diastereomeric compound **7** which has a methyl group in place of one of the four trifluoromethyl groups.[16] The permutation of **7** was found to be much faster than ester **3** with the activation parameters being $\Delta H^{\neq}$=24.3 kcal mol^{-1}, $\Delta S^{\neq}$=-4.5 eu, and $\Delta G^{\neq}$=25.7 kcal mol^{-1} (298K) in toluene, and the values were essentially unchanged in pyridine or acetic acid although the compound has the potential to undergo proton abstraction or tautomerize to an open-ring P(III) species. This implied that it would be highly desirable to carry out the transformations at as low temperature as possible. It was also found that the alkylation reaction of the conjugate base of **7**, namely **8** proceeded with full retention of configuration provided that the reaction temperature was kept at or below ambient temperature (Scheme 4).

Scheme 4

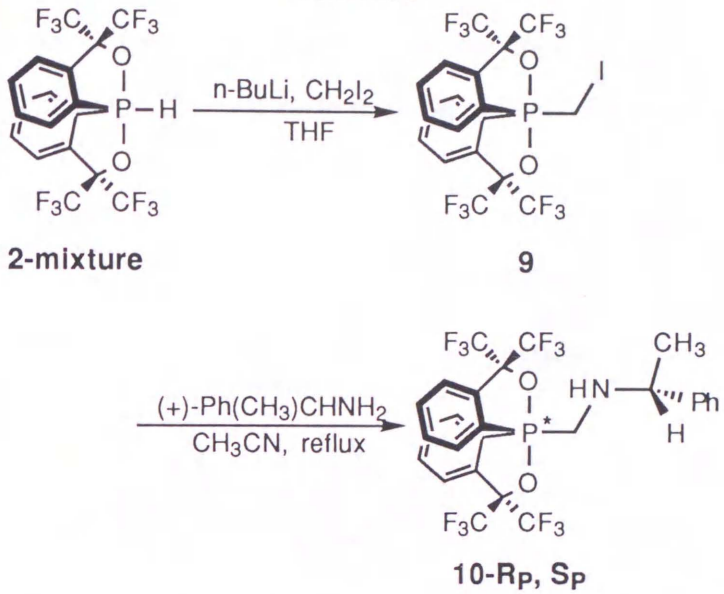


7 **8**

The attachment of the chiral auxiliary to phosphorane **2** was achieved in two steps (Scheme 5). Phosphorane **2** was first treated with CH_2I_2 after deprotonation

with NaH to give **9** [^{31}P NMR ($CDCl_3$) -24.6] in 82 % yield. This compound was found to gradually decompose on standing. Compound **9** was then treated with optically active (+)-phenylethylamine in acetonitrile to give a diastereomeric mixture of **10** in 56 % combined yield.

Scheme 5



Fortunately, recrystallization from hexane gave each diastereomer as differently shaped crystals. The diastereomer of the flat plate like crystal [^{31}P NMR ($CDCl_3$) δ -25.1] was obtained in 11 % overall yield, while the diastereomer of the prism shaped crystal [^{31}P NMR ($CDCl_3$) δ -26.9] was obtained in 20 % overall yield. ^{1}H NMR of almost all of the protons of the monodentate amine moiety were characteristically different between the two diastereomers. The UV spectra was very similar to those of **3** and **4** with an additional absorption maximum at 203 nm (logε=4.37) for the compound later determined to be **10-R$_P$** and 208 nm (logε=4.39) for the compound later determined to be **10-S$_P$** presumably arising from the absorbance of the phenyl group of the amine moiety. The optical rotation values were $[\alpha]_{436}^{20}$ +73° (c=1.22, $CHCl_3$) for **10-R$_P$** and $[\alpha]_{436}^{20}$ +104°(c=0.66, $CHCl_3$) for **10-S$_P$**. The fact that the values both turned out to be large with the same plus sign implied that the optically active amine moiety would have a large bearing on the CD

spectra. The CD charts calibrated to give the $\Delta\varepsilon$ values are shown in Fig. 7. The spectrum for **10-R$_P$** could be considered to have a negative Cotton effect with an overlap from the amine moiety in the positive region. The peaks were at λ ($\Delta\varepsilon$) = 211 (+3.6), 228 (-9.9), 242 (-1.0), 245 (-0.9), 260 (+1.9), 265 (+2.46), and 272 (+2.4) nm. However it was rather difficult to tell for the **10-S$_P$** compound with peaks at λ ($\Delta\varepsilon$) = 221 (+6.8), 225 (+6.2), 232 (-0.4), 245 (+2.8), 260 (-0.5), 266 (-0.5), 271 (+1.3), and 278 (+3.1). Therefore the absolute stereochemistry upon phosphorus could not be determined with certainty. Thus we made recourse to X-ray crystallographic analysis.

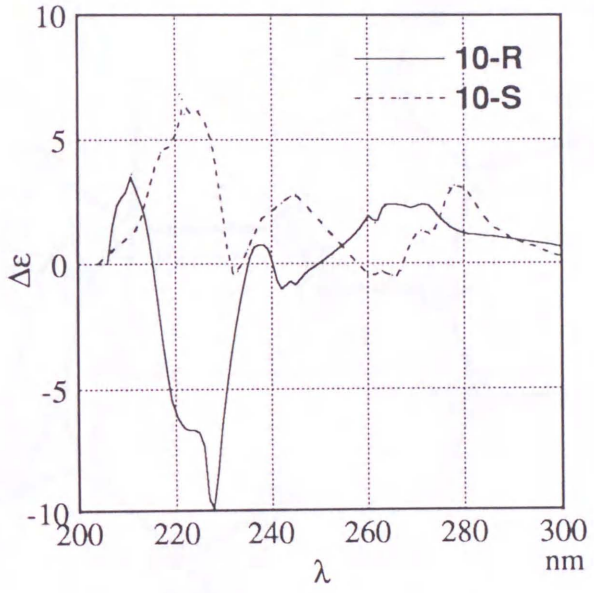


Figure 7. CD spectra of **10-R$_P$** (solid line, 3.85 x 10^{-5} M) and **10-S$_P$** (broken line, 5.41 x 10^{-5}) in cyclohexane. The original data has been replotted in terms of $\Delta\varepsilon$. The random noise level in the <230 nm region was $\Delta\varepsilon$= ca.±1 while in the >230 nm region it was $\Delta\varepsilon$= ca.±0.3.

X-Ray crystallographic analysis was conducted with the diastereomer of the plate-like crystals. The ORTEP structure is shown in Fig. 8 with selected structural parameters in Table 1.

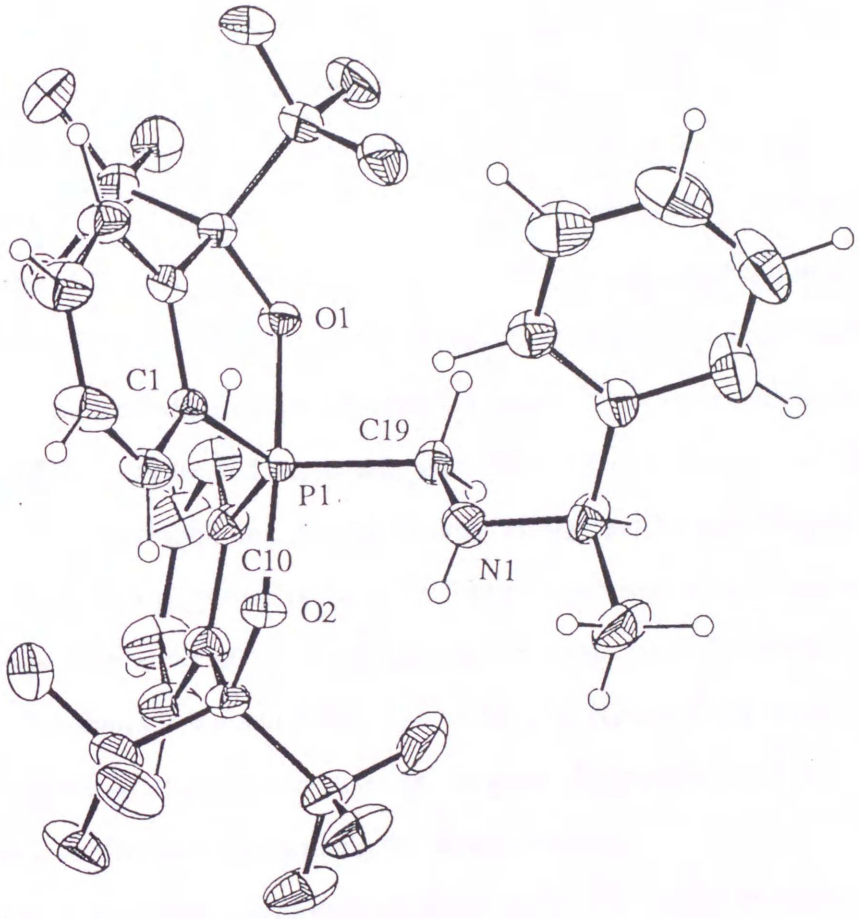


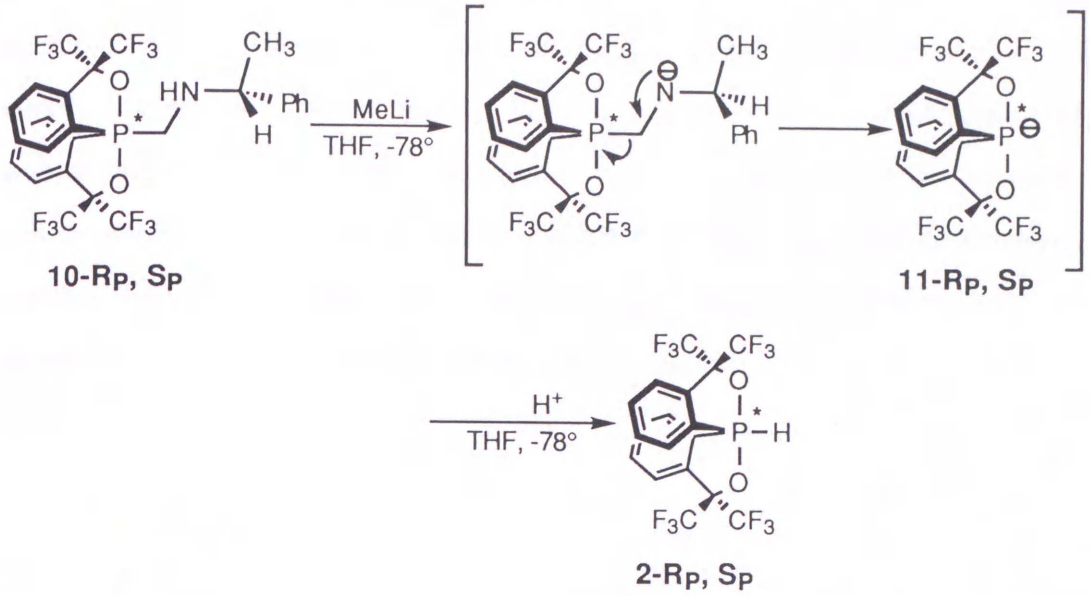
Figure 8. ORTEP drawing of **10-Rp** showing the thermal ellipsoids at the 30 % probability level.

The above compound was also found to have a trigonal bipyramidal structure and the absolute stereochemistry of the phosphorus atom determined from its relative stereochemistry to the known (+)-phenylethylamine moiety turned out to be **R_P**, i. e., **10-R_P**. The bond angle between the two apical bonds was somewhat more acute (175.8°) than the corresponding angles in **3-R_P** (177.4°) and **6-R_P** (178.1°) . This implies that compound **10-R_P** has slightly more of a square pyramidal nature compared with the other two compounds, thus leading to slight overall elongation of the bonds about phosphorus in comparison with **6-R_P**.

We anticipated that the generation of phosphoranide **11** would be effected by deprotonation of the proton upon the nitrogen atom followed by spontaneous imine elimination. A similar type of reaction has been applied in the generation of a simple germanium anion[17]. However, there also existed the possibility that a phosphoramide would be produced via a Brook-type rearrangement.[18] When each diastereomer **10-R_P** and **10-S_P** was treated separately with MeLi (3 eq) at -78°C as illustrated in Scheme 6, the corresponding phosphoranides **11-R_P** and **11-S_P** [^{31}P NMR (THF) δ +43 for the Li^+ salt], respectively, were formed quantitatively. Treatment of these compounds with aqNH_4Cl without raising the temperature furnished the desired hydrophosphoranes **2-R_P** and **2-S_P**. The yields of **2-R_P** and **2-S_P** were 67 % and 87 %, respectively, after chromatographic purification. Less amounts of base or use of n-BuLi was less effective in generating the phosphoranides.

The enantiomers both exhibited identical ^{1}H, ^{13}C, and ^{31}P NMR spectra with racemic **2** used as the starting material. The optical rotation values were $[\alpha]_{436}^{20}$ -16°(c=1.07, $CHCl_3$) for **2-R_P** and $[\alpha]_{436}^{20}$ +17° (c=1.09, $CHCl_3$) or **2-S_P**. The CD spectrum showed peaks for **2-R_P** at λ (Δε) = 214 (+5.3), 225 (-5.3), 267 (+1.5), 269 and (+1.0), corresponding to a negative Cotton effect. The enantiomer **2-S_P** showed a mirror image spectrum with a positive Cotton effect. Thus the handedness of the Cotton effect could be considered the same as the amine reactant.

Scheme 6



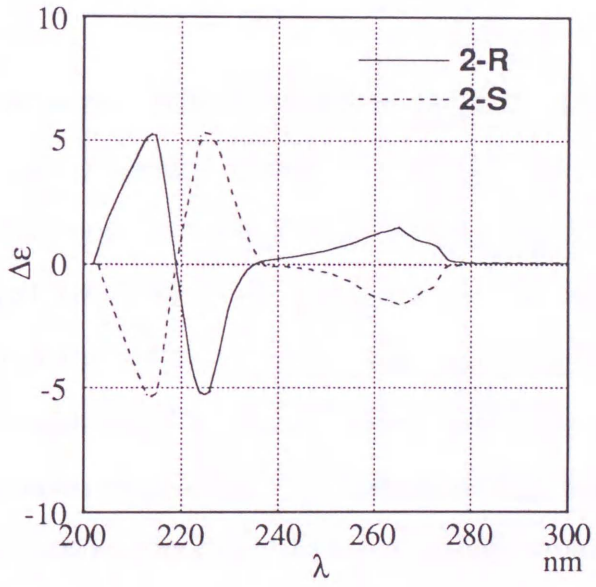
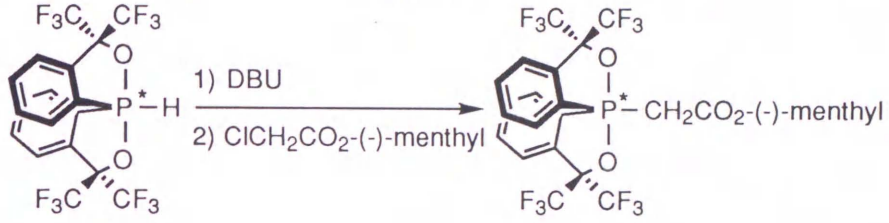


Figure 9. CD spectra of **2-Rp** (solid line, 1.09 x 10^{-5} M) and **2-Sp** (broken line, 1.49 x 10^{-5}) in cyclohexane. The original data has been replotted in terms of Δε. The random noise level in the <230 nm region was Δε= ca.±1 while in the >230 nm region it was Δε= ca.±0.3.

As described in Scheme 7 the optical purities and the stereochemistries of the enantiomers were confirmed by converting the hydrophosphoranes **2-Rp** and **2-Sp** to

their menthyl esters, **3-R$_P$** and **3-S$_P$**, the stereochemistry of which we had already established as mentioned above. The use of DBU as base turned out to give most satisfactory results, giving **3-R$_P$** and **3-S$_P$** in 80 % and 95% yields, respectively, without the accompaniment of racemization. The use of metal-oriented bases such as n-BuLi and NaH resulted in partial racemization. However, it could not be determined whether the result was due to permutation of the intermediate phosphoranide or to stereochemical leakage in the sequential alkylation process.

Scheme 7



2-R$_P$, S$_P$ **3-R$_P$, S$_P$**

Figure 10 shows the ^{1}H NMR spectra of the methine proton geminal to the oxygen atom in the (-)-menthyl moiety. A comparison of the charts of the diastereomeric mixture (top), the menthyl ester derived from **2-S$_P$** (middle), and the menthyl ester derived from **2-R$_P$** (bottom) clearly shows that the former ester is **3-S$_P$** and the latter ester is **3-R$_P$**, and not a trace of the other diastereomer could be observed in the chart of either diastereomer. The same can be concluded from the comparison of the ^{31}P NMR spectra shown in Fig. 11. These facts imply that **2-R$_P$**, **2-S$_P$**, **3-R$_P$**, and **3-S$_P$** are all stereochemically pure. Thus no racemization had occurred during the two conversion processes or during their purification procedures and the stereochemistry upon the phosphorus atom was completely retained. In other words, the stereochemical identity of the first enantiomeric pair of optically active hydrophosphoranes with only a single stereocenter could be established as designated in the text having >99 % enantiomerical purity. We could also conclude that there is a

tendency for these compounds with an R configuration to have a negative Cotton effect while those of S configuration have a positive Cotton effect.

In summary, we have successfully obtained and characterized the first enantiomeric pair of stereochemically definable 10-P-5 phosphoranes **4a** and **4b**, and hydrophosphoranes **2a** and **2b**. It was also found that the hydrophosphoranes could be converted to alkylated derivatives with complete retention of configuration via the optically active phosphoranide intermediates **7a** and **7b** to give optically pure derivatives. Phosphoranes with other ligand combinations are currently under investigation.

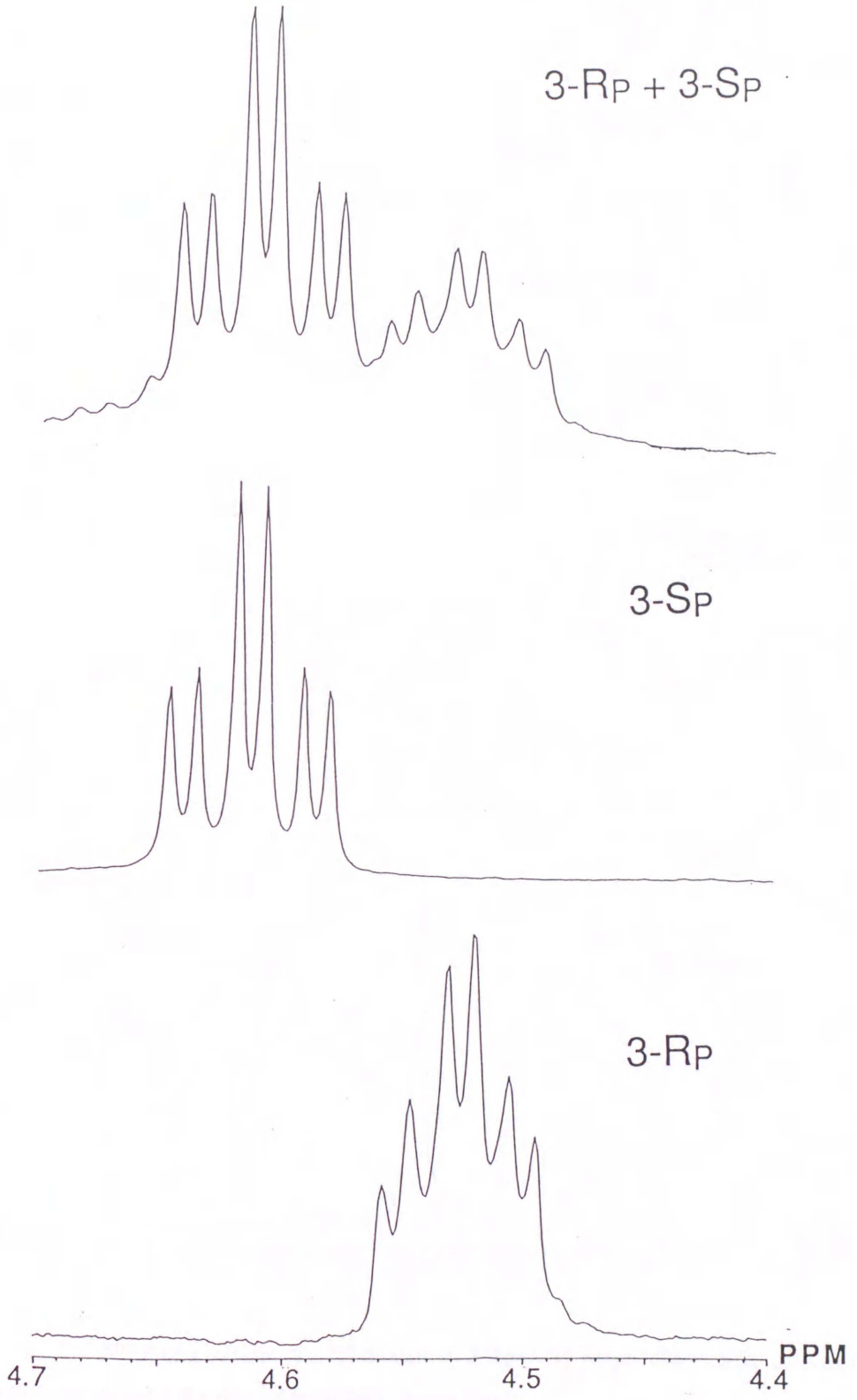


Figure 10. ^{1}H NMR of the methine proton of the (-)-menthyl moiety. From top to bottom, a 3:7 mixture of **3-RP+3-SP**, **3-SP** derived from **2-SP**, and **3-RP** derived from **2-RP**.

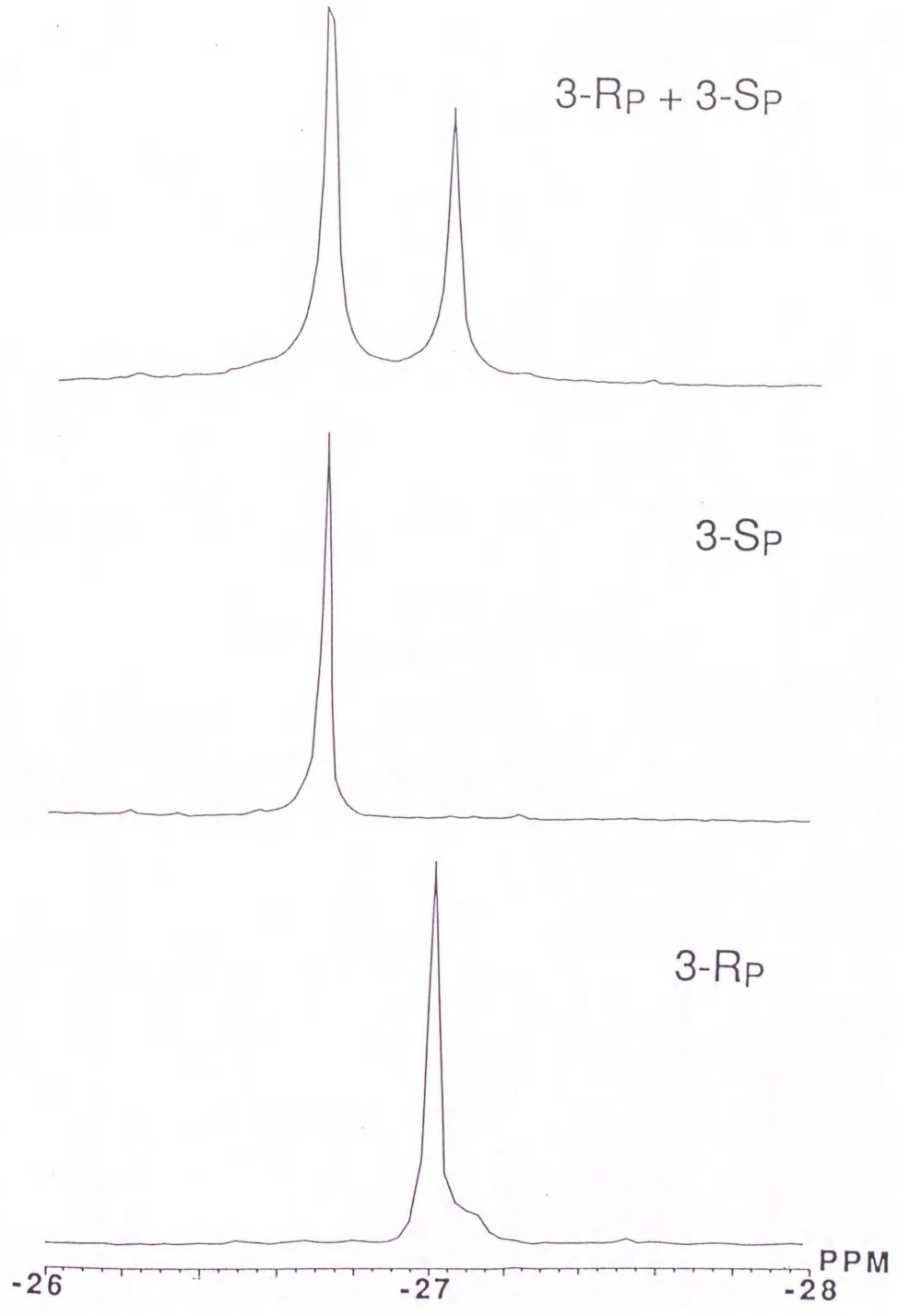


Figure 11. ^{31}P NMR of a mixture of a 3:7 mixture of **3-Rp+3-Sp** (upper chart), **3-Sp** derived from **2-Sp** (middle chart), and **3-Rp** derived from **2-Rp** (lower chart).

Table 2. Crystal Data for **3-RP**, **6-RP** and **10-RP**.

	3-RP	**6-RP**	**10-RP**
formula	C30H29F12O4P	C30H20F15O5P	C27H20F12NO2P
mol wt	712.5	776.4	649.40
cryst syst	orthorhombic	orthorhombic	monoclinic
space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
cryst dimens, mm	0.30 x 0.30 x 0.20	0.70 x 0.20 x 0.20	0.70 x 0.60 x 0.60
a, Å	16.922(4)	13.019(5)	14.402(2)
b, Å	19.322(7)	25.90(1)	8.949(2)
c, Å	10.036(3)	8.980(3)	10.961(2)
α, deg	90	90	90
β, deg	90	90	102.88
γ, deg	90	90	90
V, Å^3	3281(2)	3028(2)	1377.2(4)
Z	4	4	2
D_{calc}, g cm^{-3}	1.43	1.70	1.57
abs coeff (ν), cm^{-1}	1.38	1.70	1.58
$F(000)$	1456	1560	656
radiation; λ, Å	Mo Kα, 0.71073	Mo Kα, 0.71073	Mo Kα, 0.71073
temp, °C	23±1	23±1	23±1
$2\theta_{max}$, deg	55.0	50.0	55.0
scan rate, deg/min	3.0	3.0	3.0
linear decay,%	-	-	-
data collected	$+h, +k, +l$	$+h, +k, +l$	$\pm h, +k, +l$
total no. of data collcd, unique,obsd	4375, 4217, 3059 ($I>1.5\sigma(I)$)	3115, 3049, 2670 ($I>1.0\sigma(I)$)	3584, 3373, 3005 ($I>3\sigma(I)$)
R_{int}	0.00	0.00	0.03
no of params refined	494	526	393
R, R_w, S	0.075, 0.057, 1.27	0.058, 0.044, 1.18	0.047, 0.059, 1.54
max shift in final cycle	0.17	1.53	0.15
final diff map, max, e/Å^3	0.53	0.35	0.52

3. Experimental Section

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H NMR (400 MHz), ^{13}C (100 MHz), ^{19}F (376 MHz), and ^{31}P (162 MHz) spectra were recorded on a JEOL EX-400 spectrometer. ^{1}H NMR (90 MHz) and ^{19}F NMR (85 MHz) spectra were also routinely recorded on a Hitachi R-90H spectrometer. ^{1}H NMR chemical shifts (δ) are given in ppm downfield from internal Me_4Si, or from residual chloroform (δ = 7.26) or acetone (δ = 2.0). ^{13}C NMR chemical shifts (δ) are given in ppm downfield from internal Me_4Si, or from internal chloroform-*d* (δ = 77.0), benzene-d_6 (δ=128.0) or acetone-d_6 (δ = 30.3).^{19}F NMR chemical shifts (δ) are given in ppm downfield from internal $CFCl_3$. ^{31}P NMR chemical shifts (δ) are given in ppm downfield from external 85% H_3PO_4. Elemental analyses were performed on a Perkin Elmer 2400CHN elemental analyzer. IR spectra were measured on a Shimadzu IR-460 spectrometer. UV spectra were measured on a Shimadzu UV-160A spectrometer Optical rotations were measured on a JASCO J-40CS polarimeter. CD spectra were measured on a Union Giken PM-71 polarimeter.

All reactions were carried out under N_2. THF and Et_2O were freshly distilled from Na-benzophenone, and benzene was freshly distilled from CaH_2 prior to use. All other liquid solvents and reagents were distilled from CaH_2. (-)-Menthol (Wako Chemicals), (R)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (Aldrich), and (+)-1-phenylethylamine (Tokyo Kasei) were used as received. Preparative thin layer chromatography was carried out on plates of Merck silica gel 60 GF254.

(-)-Menthyl Chloroacetate. Chloroacetyl chloride (12.0 mL, 151 mmol) was added to (-)-menthol (23.6g, 151 mmol) in benzene (60 mL) and the solution was refluxed for one day. Removal of the solvent under reduced pressure, followed by distillation (161°C, 13mmHg) yielded **1** (32.4 g, 86 %) as a colorless liquid. $[\alpha]^{21}_{436}$ -159° (*c* 0.99, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 4.70 (dt, *J* = 4.4, 11.0 Hz, 1 H), 3.97 (d, *J* =14.7

Hz, 1 H), 3.96 (d, J = 14.7 Hz, 1 H), 1.96-1.32 (m, 6 H), 1.04-0.94 (m, 2 H), 0.91-0.76 (m, 1 H), 0.85 (d, J = 5.9 Hz, 3 H), 0.83 (d, J = 7.8 Hz, 3 H), 0.70 (d, J = 7.3 Hz, 3 H).

3,3,3',3'-Tetrakis(trifluoromethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole]. Lithium 1,1,1,3,3,3-hexafluoro-2-(2-lithiophenyl)-2-propoxide prepared according to a reported procedure from n-BuLi (c 1.62 mol L^{-1}, 143 mL, 233 mmol), TMEDA (3.52 mL, 23.3 mmol), and hexafluorocumyl alcohol (23.6 ml, 116 mmol) in THF (50 mL) was transferred dropwise via cannula to a THF (30 mL) solution of PCl_3 (5.08 mL, 58.2 mmol) at -78°C. After removal of the cooling bath, the solution was stirred at rt for 24 h. The solution was quenched with 6N HCl (20 mL), extracted with Et_2O (3 x 200 mL), dried with $MgSO_4$, and concentrated in vacuo. Recrystallization (hexane) of the residue gave the product (17.6 g, 59 %) as white powder. Mp 162°C. ^1H NMR ($CDCl_3$) δ 8.41-8.27 (m, 2H), 8.38 (d, J_{PH}=729 Hz, 1H), 7.79-7.68 (m, 6H). ^{13}C NMR ($CDCl_3$) δ 137.4 (d, $^2J_{PC}$=22.0 Hz), 136.7 (d, $^3J_{PC}$=11.0 Hz), 134.4, 131.8 (d, $^2J_{PC}$=14.7 Hz), 126.4 (d, $^1J_{PC}$=158.1 Hz), 125.3 (d, $^3J_{PC}$=16.6 Hz), 122.6 (q, $^1J_{FC}$=286.8 Hz), 122.4 (q, $^1J_{FC}$=286.8 Hz), 82.0 (sept, $^2J_{FC}$=31.3 Hz). ^{19}F NMR ($CDCl_3$) -75.0 (q, J=9.8 Hz, 3F), -76.2 (q, J=9.8 Hz, 3F). ^{31}P NMR ($CDCl_3$) δ -45.8.

[(1'*R*, 2'*S*, 5'*R*)-1*R*]- and [(1'*R*, 2'*S*, 5'*R*)-1*S*]-1-[5-Methyl-2-(1-methylethyl)cyclohexyl]oxycarbonylmethyl-3,3,3',3'-tetrakis(trifluoromethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole] (3-R_P and 3-S_P). Phosphorane **2** (4.00 g, 7.75 mmol) was added to a suspension of NaH (0.205 g, 8.54 mmol) in THF (50 mL) at 0°C. After removing the cooling bath and stirring for 30 m, (-)-menthyl chloroacetate (1.93 g, 7.75 mmol) was added to the suspension. After stirring for one hour at rt, the mixture was quenched with 1N HCl (30 mL). Extraction with Et_2O (3 x 40 mL), followed by washing with brine, drying with $MgSO_4$, and removal of solvent under reduced pressure gave a diastereomeric mixture of **3** as a white solid (4.81 g, 87 %). Recrystallization from MeOH-H_2O (repeated 5 times) furnished **3-R_P** (1.38 g, 25 %) as prisms and **3-S_P** (1.19 g, 22 %) as needles in diastereomerically pure state. **3-R_P**: mp 127-128°C; $[\alpha]^{21}_{436}$ +11.1° (*c* 1.02, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.41-8.37

(m, 2 H), 7.75-7.70 (m, 6 H), 4.53 (dt, J = 4.4, 10.8 Hz, 1 H), 3.53 (dd, $^2J_{PH}$ = 18.1 Hz, J = 14.7 Hz, 1 H), 3.36 (dd, $^2J_{PH}$ = 17.1 Hz, J = 14.7 Hz, 1 H), 2.02 (d, J = 12.2 Hz, 1 H), 1.65-1.48 (m, 5 H), 0.94-0.80 (m, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 0.66 (d, J = 6.8 Hz, 3 H), 0.60 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (C_6D_6) δ 164.8 (d, $^2J_{PC}$ = 7.4 Hz), 137.8 (d, $^3J_{PC}$ = 9.2 Hz), 136.4 (d, $^2J_{PC}$ =20.2 Hz), 134.3 (d, $^4J_{PC}$ = 3.6 Hz), 133.5 (d, $^2J_{PC}$ = 14.7 Hz, P-C1-*C6*), 129.6 (d, $^1J_{PC}$ = 165.4 Hz, P-*ipsoC*), 125.0 (d, $^3J_{PC}$ = 16.6 Hz), 123.2 (q, $^1J_{FC}$ = 288.6 Hz), 123.1 (q, $^1J_{FC}$ = 288.6 Hz), 82.2 (sept, $^2J_{FC}$ = 31.3 Hz), 75.5, 47.1, 46.7 (d, $^1J_{PC}$ = 123.1 Hz, P-*C*H2-CO), 40.8, 34.5, 31.4, 26.0, 23.4, 22.1, 20.8, 16.2. ^{19}F NMR ($CDCl_3$) -74.7 (q, J=9.8 Hz, 3F), -75.1 (q, J=9.8 Hz, 3F). ^{31}P NMR (acetone-d_6) δ -25.6 ; IR (KBr, cm^{-1}) 1735 (ν_{CO}); UV (*c*-hexane) [λ_{max}, nm (log ε)] 224 (4.26), 229 (4.26), 266 (3.16), 273 (3.10). Anal. Calcd for $C_{30}H_{29}F_{12}O_4P$: C, 50.57; H, 4.10. Found: C, 50.40; H, 4.03. **3-S$_P$**: mp 125-127°C; $[\alpha]^{21}_{436}$ -70.0° (*c* 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.40-8.35 (m, 2 H), 7.75-7.67 (m, 6 H), 4.61 (dt, J= 4.4, 10.8 Hz, 1 H), 3.55 (dd, $^2J_{PH}$ = 18.1 Hz, J = 14.7 Hz, 1 H), 3.36 (dd, $^2J_{PH}$ = 16.6 Hz, J = 14.7 Hz, 1 H), 1.96-1.93 (m, 1 H), 1.78-1.75 (m, 1 H), 1.62-1.54 (m, 2 H), 1.42-1.30 (m, 1 H), 1.16-1.10 (m, 1 H), 1.01-0.95 (m, 1 H), 0.90 (d, J = 7.3 Hz, 3 H), 0.82 (d, J = 6.8 Hz, 3 H), 0.76-0.69 (m, 1 H), 0.71 (d, J = 6.8Hz, 3 H), 0.57-0.48 (m, 3 H); ^{13}C NMR (C_6D_6) δ 165.1, 137.8 (d, $^3J_{PC}$ = 9.2 Hz), 136.3 (d, $^2J_{PC}$ =22.2 Hz), 134.3, 131.5 (d, $^2J_{PC}$ = 14.7 Hz, P-C1-*C6*), 130.0 (d, $^1J_{PC}$ = 165.5 Hz, P-*ipsoC*), 125.0 (d, $^3J_{PC}$ = 14.7 Hz), 123.2 (q, $^1J_{FC}$ = 288.6 Hz), 123.1 (q, $^1J_{FC}$ = 288.6 Hz), 87.0 (sept, $^2J_{FC}$ = 31.3 Hz), 75.5, 47.2, 46.9 (d, $^1J_{PC}$ = 125.0 Hz, P-CH2-CO), 40.7, 34.3, 31.3, 26.0, 23.3, 22.0, 20.9, 16.2. ^{19}F NMR ($CDCl_3$) -74.7 (q, J=9.8 Hz, 3F), -75.1 (q, J=9.8 Hz, 3F). ^{31}P NMR (acetone-d_6) δ -25.3; IR (KBr, cm^{-1}) 1735 (ν_{CO}); UV (*c*-hexane) [λ_{max}, nm (log ε)] 224 (4.32), 229 (4.32), 266 (3.23), 273 (3.16). Anal. Calcd for $C_{30}H_{29}F_{12}O_4P$: C, 50.57; H, 4.10. Found: C, 50.43; H, 3.91.

***R*-3,3,3',3'-Tetrakis(trifluoromethyl)-1-(2-hydroxyethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole] (4-R$_P$).** Compound **3-R$_P$** (500 mg, 0.702 mmol) in Et_2O (30 mL) was added to a suspension of $LiAlH_4$ (79.7 mg, 2.10 mmol) in Et_2O. After refluxing

for 2 h, the mixture was quenched with 1N HCl , extracted with Et_2O (3 x 30 mL) and washed with brine. Drying with $MgSO_4$ followed by removal of solvent under reduced pressure and preparative TLC separation (hexane-CH_2Cl_2, 1:2) gave **4-R$_P$** (320 mg, 81 %) as a white solid. An analytical sample was prepared by sublimation (50 °C, ca. 0.1 mmHg) of the separated product.

4-R$_P$: mp 103-105°C; $[\alpha]^{21}_{436}$ +108° (*c* 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.42-8.38 (m, 2 H), 7.74-7.67 (m, 6 H), 3.84 (ddt, $^3J_{PH}$ = 4.88 Hz, *J* = 13.7, 6.8 Hz, 2 H), 2.75 (ddt, $^2J_{PH}$ = 17.1 Hz, *J* = 13.7, 6.8 Hz, 1 H), 2.60 (ddt, $^2J_{PH}$ = 13.2 Hz, *J* = 13.7, 6.8 Hz, 1 H), 1.79 (bs, 1 H); ^{13}C NMR (acetone-d_6) δ 138.3 (d, $^3J_{PC}$ = 9.2 Hz), 137.1 (d, $^2J_{PC}$ = 20.2 Hz), 135.9, 133.3 (d, $^2J_{PC}$ = 12.9 Hz), 131.3 (d, $^1J_{PC}$ = 160 Hz), 126.4 (d, $^3J_{PC}$ = 14.7 Hz), 124.1 (q, $^1J_{FC}$ = 288.6 Hz), 123.9 (q, $^1J_{FC}$ = 288.6 Hz), 82.8 (sept, $^2J_{FC}$ = 31.3 Hz), 58.2 ,44.0 (d, $^1J_{PC}$ = 114.0 Hz). ^{19}F NMR ($CDCl_3$) -74.9 (q, *J*=9.8 Hz, 3F), -75.1 (q, *J*=9.8 Hz, 3F).^{31}P NMR (acetone-d_6) δ -22.7, ($CDCl_3$) δ -21.5; IR (KBr, cm^{-1}) 3410 (ν_{OH}), 1197 (ν_{CO}); UV (*c*-hexane) [λ_{max}, nm (log ε)] 223 (4.36), 228 (4.38), 266 (3.21). Anal. Calcd for $C_{20}H_{13}F_{12}O_3P$: C, 42.88; H, 2.34. Found: C, 43.16; H, 2.17.

***S*-3,3,3',3'-Tetrakis(trifluoromethyl)-1-(2-hydroxyethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole] (4-S$_P$).** Following the procedure of **4-R$_P$**, **3-S$_P$** (300 mg, 0.421 mmol) and $LiAlH_4$ (47.9 mg, 1.26 mmol) yielded **4-S$_P$** (198 mg, 84 %) as a white solid. Sublimation (*vide supra*) gave an analytical sample. **4-S$_P$**: mp 103-105°C; $[\alpha]^{21}_{436}$ -107° (*c* 0.83, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.42-8.38 (m, 2 H), 7.74-7.67 (m, 6 H), 3.84 (ddt, $^3J_{PH}$ = 4.88 Hz, *J* = 13.7, 6.8 Hz, 2 H), 2.75 (ddt, $^2J_{PH}$ = 17.1 Hz, *J* = 13.7, 6.8 Hz, 1 H), 2.60 (ddt, $^2J_{PH}$ = 13.2 Hz, *J* = 13.7, 6.8 Hz, 1 H), 1.86 (bs, 1 H); ^{13}C NMR (acetone-d_6) δ 138.3 (d, $^3J_{PC}$ = 9.2 Hz), 137.0 (d, $^2J_{PC}$ = 20.2 Hz), 136.0, 133.4 (d, $^2J_{PC}$ = 12.9 Hz), 131.2 (d, $^1J_{PC}$ = 160 Hz), 126.3 (d, $^3J_{PC}$ = 14.7 Hz), 124.1 (q, $^1J_{FC}$ = 288.6 Hz), 123.9 (q, $^1J_{FC}$ = 288.6 Hz), 82.7 (sept, $^2J_{FC}$ = 31.3 Hz), 58.1 ,43.9 (d, $^1J_{PC}$ = 114.0 Hz). ^{19}F NMR ($CDCl_3$) -74.9 (q, *J*=9.8 Hz, 3F), -75.1 (q, *J*=9.8 Hz, 3F). ^{31}P NMR (acetone-d_6) δ -22.7, ($CDCl_3$) δ -21.5; IR (KBr, cm^{-1}) 3410 (ν_{OH}), 1197

(ν_{CO}); UV (*c*-hexane) [λ_{max}, nm (log ε)] 223 (4.38), 228 (4.40), 266 (3.21). Anal. Calcd for $C_{20}H_{13}F_{12}O_3P$: C, 42.88; H, 2.34. Found: C, 43.00; H, 2.61.

Under similar conditions, a diastereomeric mixture of **3** (800 mg, 1.12 mmol) and $LiAlH_4$ (128 mg, 3.36 mmol) gave **4** (577 mg, 92 %) as a mixture of enantiomers. **4-Rac**: mp 133-134°C; ^1H NMR ($CDCl_3$) δ 8.42-8.38 (m, 2 H), 7.74-7.67 (m, 6 H), 3.84 (ddt, $^3J_{PH}$ = 4.88 Hz, *J* = 13.7, 6.8 Hz, 2 H), 2.75 (ddt, $^2J_{PH}$ = 17.1 Hz, *J* = 13.7, 6.8 Hz, 1 H), 2.60 (ddt, $^2J_{PH}$ = 13.2 Hz, *J* = 13.7, 6.8 Hz, 1 H), 1.86 (bs, 1 H); ^{19}F NMR ($CDCl_3$) -74.9 (q, *J*=9.8 Hz, 3F), -75.1 (q, *J*=9.8 Hz, 3F). ^{31}P NMR (400 MHz, acetone-d_6) δ -22.7 , ($CDCl_3$) δ -21.5.

5-R$_P$: mp 154-157°C; ^1H NMR 9.63 (s, 1H), 8.33-8.23 (m, 2H), 7.70-7.65 (m, 6H), 3.67 (ddd, $^2J_{PH}$= 23.9 Hz, *J* = 13.7, 2.4 Hz, 1H), 3.17 (ddd, $^2J_{PH}$= 18.6 Hz, *J* = 14.2, 3.4 Hz, 1H),^{31}P NMR ($CDCl_3$) δ -28.6; IR (KBr, cm^{-1}) 1719 (ν_{CO}).

(1*R*,1'*R*)-[2-(2,2,2-Trifluoro-1-methoxy-1-phenylethyl)carbonyloxyethyl]-3,3,3',3'-tetrakis(trifluoromethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole] (6-R$_P$). A mixture of (R)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (63 mg, 0.268 mmol), thionyl chloride (1mL) and a trace of NaCl was refluxed for 50 h. After removing the excess thionyl chloride *in vacuo*, a mixture of **4-R$_P$** (100 mg, 0.179 mmol), DMAP (38.6 mg, 0.357 mmol), pyridine (0.5 mL), and CCl_4 (0.5 mL) was added to the crude (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride and the solution was stirred for 24 h. Quenching with sat.NH_4Cl followed by extraction with Et_2O (3 x 30 ml), washing with brine, drying with $MgSO_4$, and removal of solvent under reduced pressure yielded a crude product, which was subjected to preparative TLC (hexane-CH_2Cl_2, 1:1). **6-R$_P$** (75.6 mg, 54 %) was obtained as a white solid. Recrystallization from hexane-CH_2Cl_2 gave an X-ray sample. **6-R$_P$**: mp 128-130°C; ^1H NMR (acetone-d_6) δ 8.38 (dd, *J* = 11.2, 7.8 Hz, 2 H), 7.91-7.88 (m, 2 H), 7.84-7.79 (m, 3 H), 7.38-7.37 (m, 4 H), 4.70 (dddd, $^3J_{PH}$ = 14.7 Hz, *J* = 11.2, 8.8, 5.9 Hz, 1 H), 4.43 (dddd, $^3J_{PH}$ = 15.6 Hz, *J* = 11.2, 8.8, 6.8 Hz, 1 H), 3.37 (s, 3 H), 3.05 (dddd, $^2J_{PH}$ = 20.0Hz, *J* = 14.2, 8.8, 5.9 Hz, 1 H), 2.68 (dddd, $^2J_{PH}$ = 21.0 Hz, *J* = 14.2, 8.8, 6.8

Hz, 1 H); ^{13}C NMR (acetone-d_6) δ 167.2, 138.7 (d, $^3J_{PC}$ = 12.9 Hz), 137.0 (d, $^2J_{PC}$ = 20.3 Hz), 136.3, 133.6 (d, $^2J_{PC}$ = 12.8 Hz), 133.4, 131.1, 130.4 (d, $^1J_{PC}$ = 159.9 Hz), 130.0, 128.6, 126.4 (d, $^3J_{PC}$ = 14.7 Hz), 124.2 (q, $^1J_{FC}$ = 288.6 Hz), 124.1 (d, $^1J_{FC}$ = 288.6 Hz), 85.9 (q, $^1J_{FC}$ = 27.6 Hz), 82.6 (sept, $^2J_{FC}$ = 31.3 Hz), 64.4, 62.9 (d, J_{FC} = 23.9 Hz), 55.8 (d, $^2J_{PC}$ = 9.3 Hz), 39.4 (d, $^1J_{PC}$ = 119.5 Hz). ^{19}F NMR ($CDCl_3$) -72.2 (s, 3F), -74.9 (q, *J*=9.8 Hz, 3F), -75.2 (q, *J*=9.8 Hz, 3F).^{31}P NMR (acetone-d_6) δ -24.5 ; IR (KBr, cm^{-1}) 1719 (ν_{CO}). Anal. Calcd for $C_{30}H_{20}F_{15}O_5P$: C, 46.41; H, 2.60. Found: C, 46.53; H, 2.29.

(1*S*,1'*R*)-[2-(2,2,2-Trifluoro-1-methoxy-1-phenylethyl)carbonyloxyethyl]-3,3,3',3'-tetrakis(trifluoromethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole] (6-S$_P$). From (R)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (prepared from (R)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (50.1 mg, 0.214 mmol), thionyl chloride (1 mL), NaCl (trace)), **4-S$_P$** (60.0 mg, 0.107 mmol), DMAP (26.1 mg, 0.214 mmol), pyridine (0.5 mL), and CCl_4 (0.5 ml) was obtained **6-S$_P$** (26.2 mg, 31 %). **6-S$_P$**: mp 128-129°C; ^1H NMR (acetone-d_6) δ 8.28 (dd, *J* = 11.2, 7.8 Hz, 2H), 7.91-7.87 (m, 2H), 7.80-7.75 (m, 3H), 7.46-7.41 (m, 4H), 4.67 (dddd, $^3J_{PH}$ = 14.7 Hz, *J* = 11.2, 8.8, 5.9 Hz, 1H), 4.45 (dddd, $^3J_{PH}$ = 15.6 Hz, *J* = 11.2, 8.8, 6.8 Hz, 1H), 3.26 (s, 3 H), 3.05 (dddd, $^2J_{PH}$ = 20.0 Hz, *J* = 14.2, 8.8, 5.9 Hz, 1H), 2.74 (dddd, $^2J_{PH}$ = 21.0 Hz, *J* = 14.2, 8.8, 6.8 Hz, 1H); ^{13}C NMR (acetone-d_6)[19] δ 167.2, 138.3 (d,$^3J_{PC}$ = 14.7 Hz), 136.9 (d, $^2J_{PC}$ = 18.4 Hz), 135.6, 132.9 (d, $^2J_{PC}$ = 14.7 Hz), 131.9, 130.5 (d, $^1J_{PC}$ = 163.6 Hz), 130.5, 129.3, 127.1 (d, $^3J_{PC}$ = 12.9 Hz), 83.0 (sept, $^2J_{FC}$ = 31.3 Hz), 64.5, 63.0 (d, $^1J_{FC}$ = 29.4 Hz), 55.7 (d, $^2J_{PC}$ = 9.3 Hz), 39.3 (d, $^1J_{PC}$ = 139.9 Hz). ^{19}F NMR ($CDCl_3$) -72.6 (s, 3F), -74.9 (q, *J*=9.8 Hz, 3F), -75.1 (q, *J*=9.8 Hz, 3F). ^{31}P NMR (acetone-d_6) δ -24.7 ; IR (KBr, cm^{-1}) 1719 (ν_{CO}). Anal. Calcd for $C_{30}H_{20}F_{15}O_5P$: C, 46.41; H, 2.60. Found: C, 46.50; H, 2.21.

3,3,3',3'-Tetrakis(trifluoromethyl)-1-(iodomethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole] (9). To a THF (30 mL) solution of hydrophosphorane **2** (3.0 g, 5.81 mmol) was added n-BuLi (3.63 mL, 5.81mmol) at -78°C. After stirring at rt for 1

hr, CH_2I_2 (0.47 mL, 5.83 mmol) was added and stirring was continued for 24hr. The mixture was quenched with water, extracted with Et_2O (30 mL x 3). The combined ethereal layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. Recrystallization of the residue from n-hexane gave the product (3.13 g, 82 %) as a white solid. Mp 101-102°C. ^1H NMR ($CDCl_3$) δ 8.44-8.33 (m, 2H), 7.76-7.71 (m, 6H), 3.62 (dd, $^2J_{PH}$=7.3 Hz, *J*=9.8 Hz, 1H), 3.48 (dd, $^2J_{PH}$=3.9 Hz, *J*=9.8 Hz, 1H). ^{13}C NMR δ 137.5 (d, $^3J_{PC}$=12.9 Hz), 136.3 (d, $^2J_{PC}$=20.3 Hz), 134.4 (d, $^4J_{PC}$=6.5 Hz), 131.4 (d, $^1J_{PC}$=173.8 Hz), 131.4 (d, $^2J_{PC}$=20.2 Hz), 125.9 (d, $^3J_{PC}$=16.5 Hz), 119.6 (q, $^1J_{FC}$=286.8 Hz), 119.4 (q, $^1J_{FC}$=286.8 Hz), 81.1 (sept, $^2J_{FC}$=31.3 Hz), 25.2 (d, $^1J_{PC}$=125 Hz). ^{19}F NMR δ -75.1 (q, *J*=9.8 Hz, 6F), -75.5 (q, *J*=9.8 Hz, 6F). ^{31}P NMR δ -24.6.

(1R,1R') and (1S,1R')-3,3,3',3'-Tetrakis(trifluoromethyl)-1-(1-phenylethylaminomethyl)-1,1'-spirobi[3*H*,2,1,λ^5-benzoxaphosphole] (10-R$_P$ and 10-S$_P$). To a CH_3CN solution (30 mL) of **9** (2.32 g, 3.54 mmol) was added (+)-1-phenylethylamine (0.46 mL, 3.544 mmol) and the resulting solution was stirred for 14 d. The solution was quenched with aqNH_4Cl, and exacted with ether (30 mLx3). After drying the combined solution the solvent was removed under reduced pressure. Treatment of the residue on silica gel column chromatography (hexane-CH_2Cl2=1:1) gave the desired product (1.29 g, 56 %) as a 1:1 diastereomeric mixture. Recrystallization from hexane gave colorless plates (250 mg, 11 %) and prisms (456 mg, 20 %). **10-R$_P$**: mp 124-126°C; $[\alpha]^{20}_{436}$ +73° (*c* 1.22, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.42-8.38 (m, 2H), 7.71-7.68 (m, 6H), 7.23-7.16 (m, 5H), 3.74 (dq, *J*=6.8, 2.4 Hz, 1H), 3.61 (dd, $^2J_{PH}$=14.7 Hz, *J*=7.3 Hz, 1H), 3.53 (dd, $^2J_{PH}$=14.7 Hz, *J*=7.3 Hz, 1H), 2.09 (bs, 1H), 1.12 (d, *J*=6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 136.9 (d, $^3J_{PC}$=9.2 Hz), 136.1 (d, $^2J_{PC}$=20.3 Hz), 133.8, 131.5 (d, $^4J_{PC}$=14.7 Hz), 131.4, 130.1 (d, $^1J_{PC}$=154.4 Hz), 128.2, 126.9, 126.5, 124.8 (d, $^3J_{PC}$=14.7 Hz), 122.6 (q, $^3J_{FC}$=288.6 Hz), 122.4 (q, $^3J_{FC}$=288.6 Hz), 81.6 (sept, $^3J_{FC}$=31.3 Hz), 58.1 (d, $^3J_{PC}$=12.9 Hz), 55.7 (d, $^1J_{PC}$=114.0 Hz), 22.9. ^{19}F NMR ($CDCl_3$) δ -74.8 (q, *J*=9.8 Hz, 6F), -75.1 (q, *J*=9.8

Hz, 6F). ^{31}P NMR ($CDCl_3$) δ -24.6, (THF) δ -23.7, (CH_3CN) δ -23.3; UV (*c*-hexane) [λ_{max}, nm (log ε)] 223 (4.32), 227 (4.33), 267 (3.59), 274 (3.54). Anal. Calcd for $C_{27}H_{20}F_{12}NO_2P$: C, 49.94; H, 3.10; N, 2.16. Found: C, 49.82; H, 3.02; N, 2.10. **10-S$_P$**: mp 134-137°C; $[\alpha]^{20}_{436}$ +104° (*c* 0.66, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.43-8.39 (m, 2H), 7.73-7.71 (m, 6H), 7.10 (m, 3H), 6.81-6.79 (m, 2H), 3.92 (dq, *J*=5.4, 5.4 Hz, 1H), 3.65 (dd, $^2J_{PH}$=15.6 Hz, *J*=5.4 Hz, 1H), 3.33 (bd, $^2J_{PH}$=15.6 Hz, 1H), 2.21 (bs, 1H), 1.25 (d, *J*=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 136.7 (d, $^3J_{PC}$=11.0 Hz), 136.0 (d, $^2J_{PC}$=18.4 Hz), 133.6, 131.5 (d, $^4J_{PC}$=12.9 Hz), 130.1, 129.1 (d, $^1J_{PC}$=152.6 Hz), 128.1, 126.8, 126.7, 124.8 (d, $^3J_{PC}$=14.7 Hz), 122.6 (q, $^1J_{FC}$=286.8 Hz), 122.4 (q, $^1J_{FC}$=288.6 Hz), 81.7 (sept, $^2J_{FC}$=31.2 Hz), 57.4 (d, $^3J_{PC}$=5.6 Hz), 55.0 (d, $^1J_{PC}$=99.3 Hz), 24.6. ^{19}F NMR ($CDCl_3$) δ -74.8 (q, *J*=9.8 Hz, 6F), -75.0 (q, *J*=9.8 Hz, 6F). ^{31}P NMR ($CDCl_3$) δ -26.9, (THF) δ -25.8, (CH_3CN) δ -25.2; UV (*c*-hexane) [λ_{max}, nm (log ε)] 223 (4.37), 227 (4.38), 267 (3.64), 274 (3.59). Anal. Calcd for $C_{27}H_{20}F_{12}NO_2P$: C, 49.94; H, 3.10; N, 2.16. Found: C, 49.75; H, 2.92; N, 2.05.

Reaction of 10-R$_P$ with MeLi. MeLi (*c*1.14 in n-hexane, 0.49 mL, 0.558 mmol) was added to a solution of amine **10-R$_P$** (100.4 mg, 0.155 mmol) in THF (10 mL) at -78°C and the solution was stirred for 15 min. After quenching with aqNH_4Cl (10 mL), the solution was extracted with ether (30 mLx3), washed with brine, and dried with $MgSO_4$. Purification of the residue obtained after removal of the solvent was carried out on TLC (hexane) to give **2-R$_P$** (53.7 mg, 67 %) as white powder. Mp: 127-128°C; $[\alpha]^{20}_{436}$ -16° (*c* 1.07, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.36 (d, J_{PH}=729 Hz, 1H), 8.31-8.26 (m, 2H), 7.79-7.68 (m, 6H). ^{13}C NMR ($CDCl_3$) δ 137.4 (d, $^2J_{PC}$=22.1 Hz), 136.7 (d, $^3J_{PC}$=9.2 Hz), 134.4, 131.8 (d, $^2J_{PC}$=14.8 Hz), 126.4 (d, $^1J_{PC}$=158.1 Hz), 125.3 (d, $^3J_{PC}$=17.6 Hz), 122.6 (q, $^1J_{FC}$=286.8 Hz), 122.4 (q, $^1J_{FC}$=286.7 Hz), 81.9 (sept, $^2J_{FC}$=31.3 Hz). ^{19}F NMR ($CDCl_3$) -75.0 (q, *J*=9.8 Hz, 6F), -76.2 (q, *J*=9.8 Hz, 6F). ^{31}P NMR ($CDCl_3$) δ -45.9. UV (*c*-hexane) [λ_{max}, nm (log ε)] 223 (4.32), 228 (4.38), 267 (3.30), 274 (2.97). Anal. Calcd for $C_{18}H_9F_{12}O_2P$: C, 41.88; H, 1.76. Found: C, 41.86; H, 1.58.

Reaction of 10-Spwith MeLi. Using the same procedure described above, **10-SP** (160 mg, 0.247 mmol) treated with MeLi (1.14 M, 0.78 mL, 889 mmol) furnished **2-SP** (111 mg, 87%). Mp: 129-130°C; $[\alpha]^{20}_{436}$ +17° (*c* 1.09, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.36 (d, J_{PH}=729 Hz, 1H), 8.32-8.27 (m, 2H), 7.79-7.69 (m, 6H). ^{13}C NMR ($CDCl_3$) δ 137.3 (d, $^2J_{PC}$=22.1 Hz), 135.9 (d, $^3J_{PC}$=9.2 Hz), 134.4, 131.7 (d, $^2J_{PC}$=18.4 Hz), 126.4 (d, $^1J_{PC}$=156.3 Hz), 125.3 (d, $^3J_{PC}$=14.7 Hz), 122.6 (q, $^1J_{FC}$=286.8 Hz), 122.4 (q, $^1J_{FC}$=286.8 Hz), 81.9 (sept, $^2J_{FC}$=31.3 Hz). ^{19}F NMR ($CDCl_3$) δ -75.0 (q, *J*=9.8 Hz, 6F), -76.2 (q, *J*=9.8 Hz, 6F). ^{31}P NMR ($CDCl_3$) δ -45.9. UV (*c*-hexane) [λ_{max}, nm (log ε)] 223 (4.36), 228 (4.41), 267 (3.37), 274 (3.36). Anal. Calcd for $C_{18}H_9F_{12}O_2P$: C, 41.88; H, 1.76. Found: C, 41.92; H, 1.36.

Reaction of a Mixture of 10-RP and 10-SP with MeLi. A diastereomeric mixture (R:S=26:74) of **10** (450 mg, 0.693 mmol) treated with MeLi (1.14 M, 2.58 mL, 2.49 mmol) gave **2**, quantitatively. Mp: 162°C; ^1H NMR ($CDCl_3$) δ 8.36 (d, J_{PH}=729 Hz, 1H), 8.31-8.26 (m, 2H), 7.79-7.68 (m, 6H). ^{19}F NMR ($CDCl_3$) δ -75.0 (q, *J*=9.8 Hz, 6F), -76.2 (q, *J*=9.8 Hz, 6F). ^{31}P NMR ($CDCl_3$) δ -45.9.

3-RP from 2-RP. To **2-RP** (37.7 mg, 0.073 mmol) in CH_3CN (10 mL) was added DBU (0.02 mL, 0.14 mmol) at rt. After stirring for one minute **2-RP** (17.0 mg, 0.073 mmol) in THF (1 mL) was added and the solution was stirred for 30 m. The solution was quenched with aqNH_4Cl and extracted with ether (30 mL x 3). The residue obtained after drying with $MgSO_4$ and removal of solvent was subjected to PTLC (hexane:CH_2Cl_2=1:1) to yield **3-RP** (52 mg, 99 %) slightly contaminated with **2**. ^1H NMR ($CDCl_3$) δ 8.40-8.36 (m, 2 H), 7.74-7.69 (m, 6 H), 4.52 (dt, *J* = 4.4, 10.8 Hz, 1 H), 3.53 (dd, $^2J_{PH}$ = 18.1 Hz, *J* = 14.7 Hz, 1 H), 3.36 (dd, $^2J_{PH}$ = 17.1 Hz, *J* = 14.7 Hz, 1 H), 2.01 (d, *J* = 12.2 Hz, 1 H), 1.67-1.42 (m, 5 H), 0.92-0.80 (m, 3 H), 0.90 (d, *J* = 5.9 Hz, 3 H), 0.66 (d, *J* = 6.8 Hz, 3 H), 0.59 (d, *J* = 6.8 Hz, 3 H); ^{31}P NMR ($CDCl_3$) δ -27.0

3-SP from 2-SP In the same manner, **2-SP** (87.5 mg, 0.17 mmol) in CH_3CN (15 mL), DBU (0.05 mL, 0.33 mmol), and (-)-menthyl chloroacetate (39.4 mg, 0.17 mmol) in

THF (2 mL) gave **3-S$_P$** (106 mg, 87 %) slightly contaminated with (-)-menthyl chloroacetate. ^{1}H NMR ($CDCl_3$) δ 8.40-8.36 (m, 2 H), 7.74-7.67 (m, 6 H), 4.62 (dt, *J* = 4.4, 10.7 Hz, 1 H), 3.55 (dd, $^2J_{PH}$ = 18.1 Hz, *J* = 15.1 Hz, 1 H), 3.37 (dd, $^2J_{PH}$ = 15.6 Hz, *J* = 15.1 Hz, 1 H), 1.97-1.94 (m, 1 H), 1.78-1.75 (m, 1 H), 1.68-1.60 (m, 2 H), 1.34-1.26 (m, 1 H), 1.17-1.14 (m, 1 H), 1.11-0.96 (m, 2 H), 0.90 (d, *J* = 7.3 Hz, 3 H), 0.82 (d, *J* = 6.4 Hz, 3 H), 0.72 (d, *J* = 6.8 Hz, 3 H), 0.58-0.49 (m, 1H); ^{31}P NMR ($CDCl_3$) δ -26.7.

A Diastereomeric Mixture of 3-R$_P$ and 3-S$_P$ from a Mixture of 2-S$_P$ and 2-R$_P$. Similiarly, **2** (R:S=26:74, 87.5 mg, 0.17 mmol) in CH_3CN (20 mL), DBU (0.04 mL, 0.27 mmol), and (-)-menthyl chloroacetate (30.8 mg, 0.133 mmol) in THF (2 mL) gave **3** (106 mg, 87 %) slightly contaminated with (-)-menthyl chloroacetate.

Kinetic Measurements. Solutions enriched with **3-R$_P$** (ca. 50 mg in 0.6 ml of solvent) were sealed in NMR tubes. Temperatures for the kinetic runs were maintained at 100°C (±2°C). Since the composition of the diastereomers was monitored by integration of ^{31}P NMR signals. The data was analyzed assuming first order kinetics using the equation, $\ln\{(x_e-x_o)/(x_e-x)\}=k(K+1)t$, in which x_e=ratio at equilibrium, x_o=ratio observed at t=0, x=observed ratio at arbitrary intervals, k=rate constant to be determined, and K=equilibrium ratio. The equilibrium ratio K was determined to be 1.0.

Crystallographic Studies. Crystal data and numerical details of the structural determinations are given in Table 2. Crystals were mounted on a Mac Science MXC3 diffractometer and irradiated with graphite-monochromated Mo Kα radiation (λ=0.71073 Å) for data collection. Lattice parameters were determined by least-squares fitting of 27 reflections in the range of 23°<2θ<32° for **3-R$_P$**, 31 reflections in the range of 26°<2θ<30° for **6-R$_P$**, and 31 reflections in the range of 31°<2θ<35° for **10-R$_P$**. Data were collected with the 2θ/ω scan mode. Data for **6-R$_P$** and **10-R$_P$** were corrected for absorption.[20] Compound **3-R$_P$** was solved by a direct method with the Monte Carlo-Multan program[21] whereas Shelx86 was used for **6-R$_P$** and **10-R$_P$**.

Refinement on F was carried out by the full-matrix least squares method. All computations were carried out on a Titan 750 computer.

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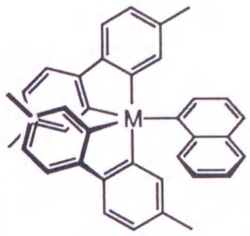
Chapter 3

The First Stereochemical Characterization of Configurationally Stable Diastereomers of Hypervalent 10-Sb-5 Stiboranes and Acceleration of Intramolecular Permutation by Donor Solvents

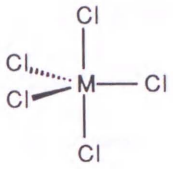
1. Introduction

The permutation process of pentacoordinate species has been well documented, especially for compounds with phosphorus as the central atom.[1] In the case of phosphorus the barrier of permutation has been successfully altered to allow the isolation of configurationally stable diastereomers[1] or optically active species[2] with phosphorus as a center of asymmetry. Assuming that the Berry pseudorotation mechanism,[3] which has its foundation upon vibrational bending motions, is operative the strength of the bonds about the pentacoordinate atom would reflect the barrier to permutation. Thus, pentacoordinate compounds of elements of lower rows on the periodic table having weaker bonds would naturally be expected to have smaller permutation barriers compared with phosphorus, therefore making it difficult to obtain configurationally stable diastereomers. In fact, there is experimental evidence that is in good accordance with this assumption. For example, for compound **1** with M=P, As, Sb the barriers for a multi-step permutation process between rapidly interconverting enantiomers have been determined by variable temperature NMR techniques to be 15.8, 15.4, 11.6 kcal/mol,[4] respectively. On the other hand, for compound **2** both measurements (3.6, 2.8, 1.6 kcal/mol, respectively)[5] and theoretical calculations (4.78, 2.80, 1.98 kcal/mol, respectively)[6] for a single step permutation process which exchange the apical and equatorial substituents support this tendency. In the case of antimony, Doak et al. have reported that compound **3** could be observed as two separate diastereomeric species by NMR,[7] but to our knowledge there have been no reports on the isolation of such compounds as configurationally stable species. Martin et al. have successfully prepared a number of hypervalent compounds of extraordinary thermal and kinetic stability by incorporating bidentate ligands derived from hexafluorocumyl alcohol.[8] With pentavalent phosphoranes,[2a,8c,d] and silicates[8d] it has also been found that the barrier to permutation was very high. By utilizing this bidentate ligand and a modified ligand with a methyl group instead of

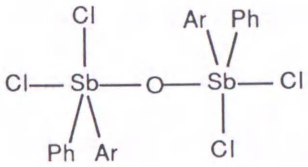
one of the trifluoromethyl groups, we have succeeded in preparing and stereochemically characterizing the first configurationally stable diastereomeric 10-Sb-5[9] stiborane, and herein we report the details. Kinetics of the interconversion process of the diastereomers have also been examined and it has been found that the process was very sensitive to the nature of the solvent and additives.



1 (M=P, As, Sb)



2 (M=P, As, Sb)



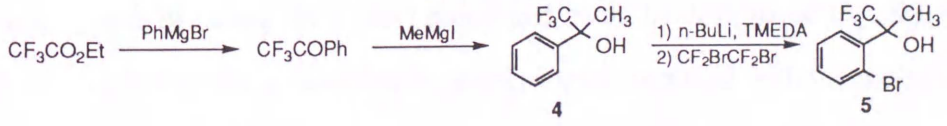
3

2. Results and Discussion

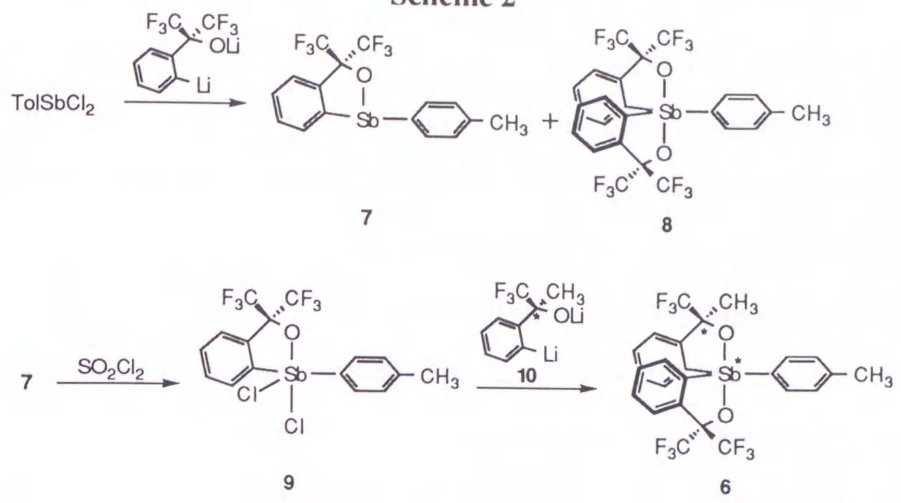
Preparation of Stiborane 6.

The ligand possessing the asymmetric carbon was prepared according to scheme 1. Trifluoromethyl phenyl ketone was prepared in 60 % yield from ethyl trifluoroacetate and phenyl Grignard reagent according to a reported procedure.[10] Treating the ketone with methyl Grignard reagent gave alcohol **4**. Treatment of **4** with n-BuLi in the presence of tetramethylethylenediamine in THF followed by the addition of 1,2-dibromo-1,1,2,2-tetrafluoroethane gave bromide **5** in 62% yield. The diastereomeric stiborane **6** was synthesized according to scheme 2. 2-Phenyl-1,1,1,3,3,3-hexafluoro-2-propanol dilithiated by the procedure reported by Martin et al.[8b] was added to a THF solution of (4-methylphenyl)antimony dichloride[11] to give monocyclic compound **7** in 78 % yield along with a small amount of spiro compound **8** (7 %). The tricoordinate compound **7** was oxidized with sulfuryl chloride in dichloromethane to yield moisture sensitive pentacoordinate compound **9**. Compound **9** was treated with dilithiated 2-phenyl-1,1,1-trifluoro-2-propanol **10** generated from the bromide **5** in ether to furnish compound **6** as a 6:4 diastereomeric mixture. Attempts to prepare **6** by the direct use of **4** met with failure and gave only trace amounts of the desired product.

Scheme1



Scheme 2



Determination of Stereochemistry by NOE.

In order to determine the relative stereochemistry of the diastereomers differential NOE spectra were taken with a mixture of diastereomers **6** in C_6D_6. Proton irradiation of the major methyl group (δ 1.73) of the bidentate ligand resulted in intensity enhancement of signals of the ortho protons of the p-tolyl group (δ 8.17) and of the proton ortho to the 2-propoxy group (δ 7.31) of the bidentate ligand **10** (**6a**: drawing on the left), whereas proton irradiation of the minor methyl group (δ 1.59) led to the intensity enhancement of the proton ortho (δ 8.21) to the antimony of the symmetric bidentate ligand and to the proton ortho to the 2-propoxy group (δ 7.32) of the bidentate ligand **10** (**6b**: drawing on the right). Thus, as shown in Fig. 1 the major diastereomer could be assigned as the compound with the methyl group of the bidentate ligand **10** facing the p-tolyl group and could be designated (S_C, S_{Sb})[12] and (R_C, R_{Sb}), while the minor could be assigned as the compound with the methyl group of the bidentate ligand **10** facing the other bidentate and designated (R_C, S_{Sb}) and (S_C, R_{Sb}).

As with other spiro compounds containing Martin's ligand, a significant low field shift for the protons (6-H) of the bidentate ligand benzene ring ortho to antimony and opposite to the 2-propoxy substituent could be observed at δ 8.38 and 8.32 for **6a**,

and δ 8.33 and 8.21 for **6b**. From the NOE measurements the signal at δ 8.21 could be assigned to the sole proton facing a methyl group while the other three all face trifluoromethyl groups. Thus in this case besides the low field shift caused by electrostatic repulsion by the polarized apical bond a secondary differentiation has occurred by the change from a trifluoromethyl group to a methyl group. The fact that the chemical shift of the proton facing the trifluoromethyl group of ligand **10** in the major diastereomer is slightly shifted more downfield (δ 8.38) than the other two protons (δ 8.33 and 8.32) is in accord with the fact that the ^{19}F NMR of this trifluoromethyl group is more upfield (δ -80.0 in C_6D_6) than those of the symmetric Martin's ligand (δ -76.5 and -75.1 in C_6D_6), corresponding to larger electron density upon the fluorines in ligand **10**.

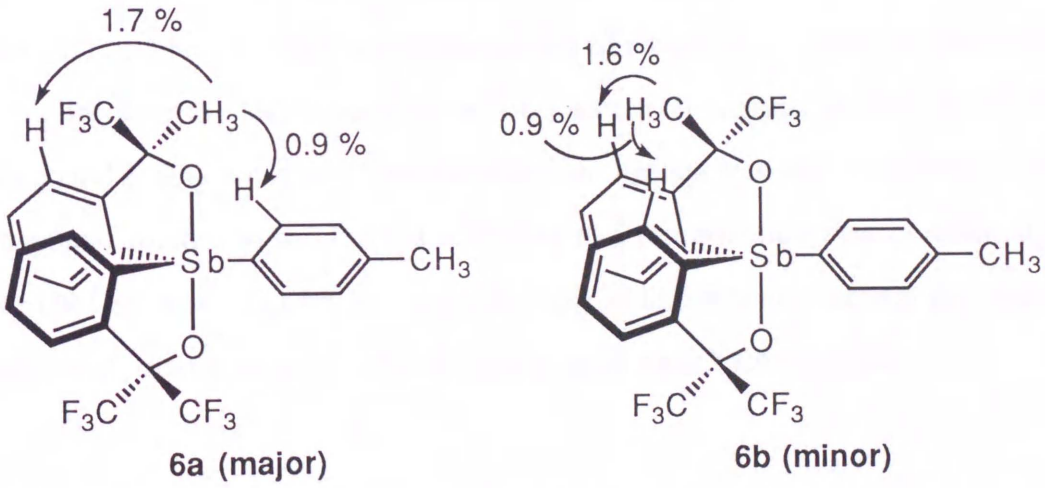


Figure 1. ^1H NMR NOE of diastereomers **6a** and **6b** by irradiation of the methyl group of bidentate ligand **10**.

X-ray Structural Analysis of 6a and 8.

Separation of the diastereomers was initially carried out by preparative TLC (hexane:CH_2Cl_2=3:1/SiO_2; major: R_f 0.24, minor: R_f 0.26). However, due to the closeness of the R_f value and facile permutation of the compounds under the separation conditions, workup usually afforded samples enriched up to only about 4:1 of either diastereomer. Other sources of gel (alumina and florisil) and gel permeation chromatography were even less effective. Fortunately, it was later found that careful recrystallization of the diastereomeric mixture from acetonitrile afforded the major diastereomer **6a** as the sole product in crystals sufficient for x-ray structural analysis. Examination of the filtrate showed the presence of the diastereomers as a near equilibrium mixture, thus implying that isomerization of the diastereomers had occurred to give the more crystallizable major diastereomer during the recrystallization. The ORTEP drawings of **6a** are depicted in Fig. 2, and selected structural parameters and crystal parameters are listed in Tables 1 and 2, respectively.

In order to make a comparison x-ray structural analysis of pentacoordinate compound **8** which has two identical bidentate ligands was also carried out. The compound could also be obtained according to a procedure previously reported.[13] The ORTEP drawings of **8** are shown in Fig.3 while selected structural parameters and crystal parameters are listed along side those of **6a** in Tables 1 and 2.

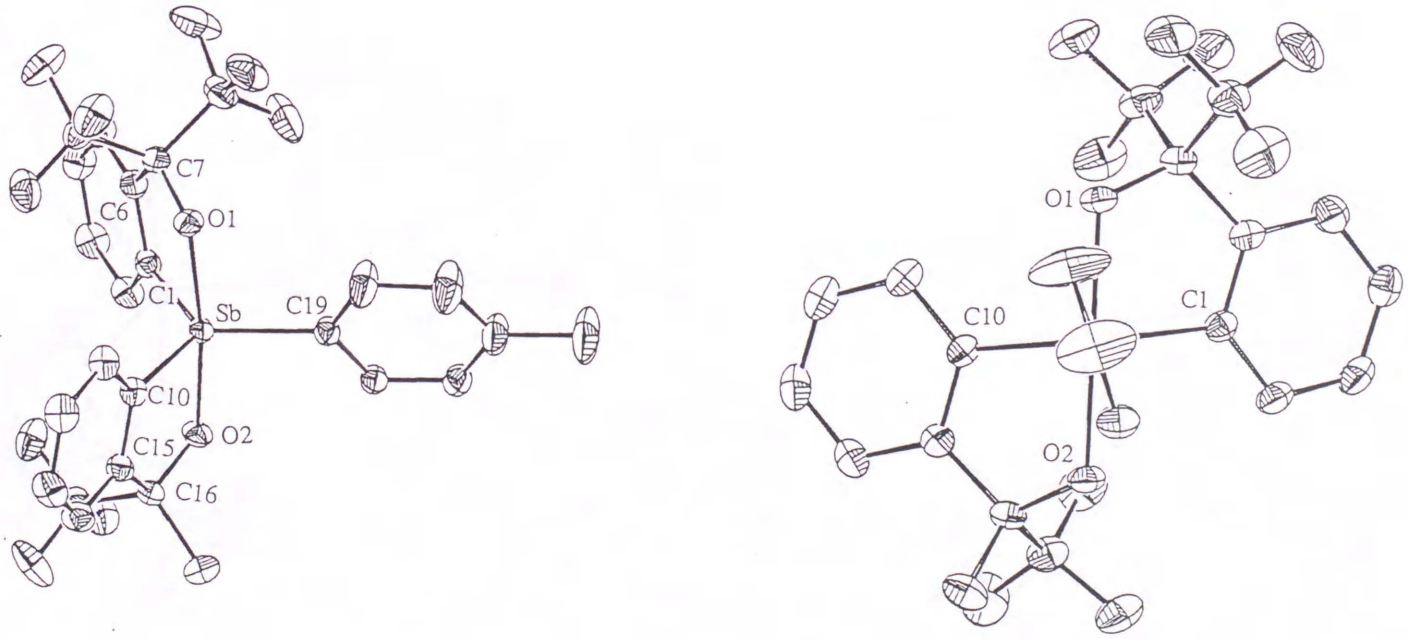


Figure 2. ORTEP drawing of **6a** showing the thermal ellipsoids at the 30 % probability level. The figure on the right is a view from the direction along the axis between Sb and the methyl group of the p-tolyl group.

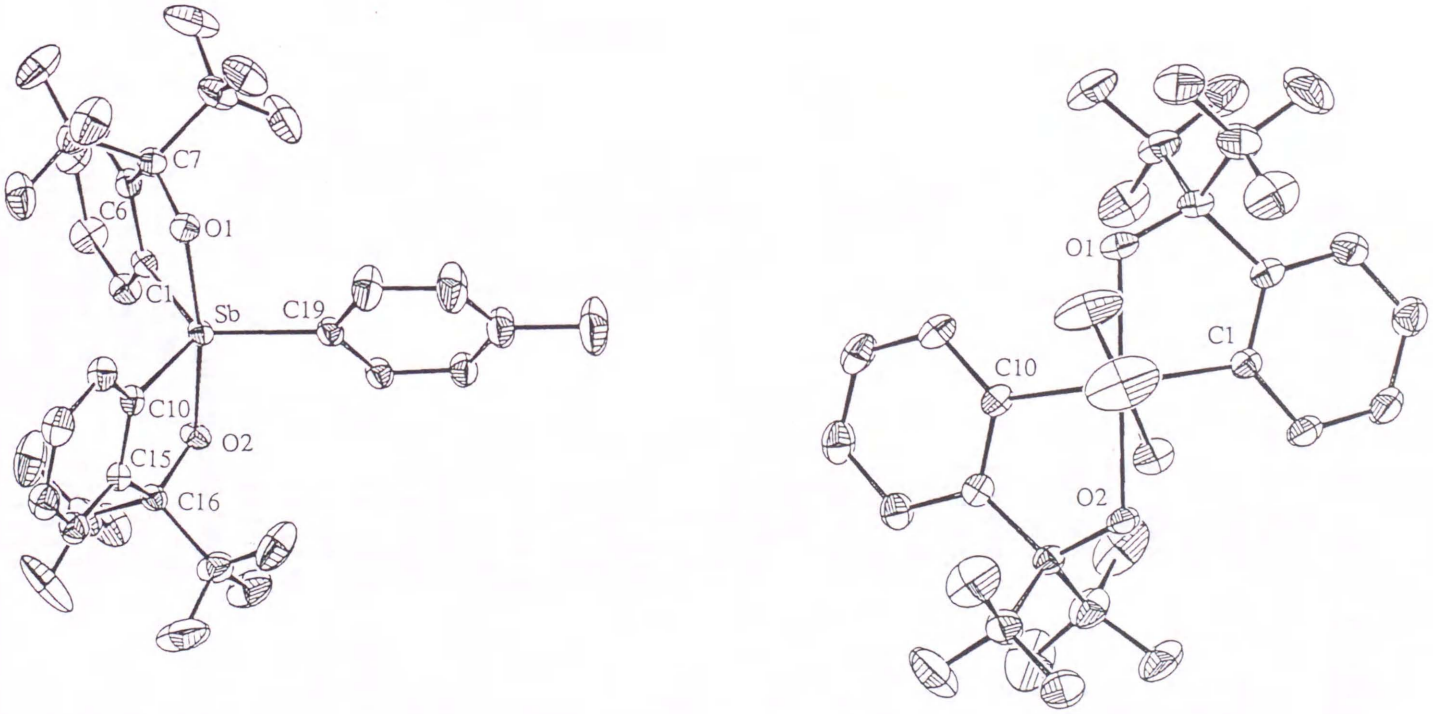


Figure 3. ORTEP drawing of **8** showing the thermal ellipsoids at the 30 % probability level. The figure on the right is a view from the direction along the axis between Sb and the methyl group of the p-tolyl group.

Table 1. Selected Crystallographic Data for **6a** and **8**.

	6a	**8**
	Bond length/Å	
Sb-O1	2.053(2)	2.042(3)
Sb-O2	2.019(2)	2.035(2)
Sb-C1	2.090(3)	2.094(4)
Sb-C10	2.083(3)	2.089(4)
Sb-C19	2.098(3)	2.094(4)
O1-C7	1.379(4)	1.377(5)
O2-C16	1.409(3)	1.384(4)
C1-C6	1.380(4)	1.385(6)
C10-C15	1.385(4)	1.382(5)
C6-C7	1.540(4)	1.546(6)
C15-C16	1.538(4)	1.533(6)
	Bond angle/deg	
O1-Sb-O2	172.43(8)	170.6(1)
C1-Sb-C10	123.0(1)	121.5(1)
C1-Sb-C19	119.2(1)	118.7(2)
C10-Sb-C19	117.7(1)	119.8(2)
O1-Sb-C1	80.9(1)	81.2(1)
O2-Sb-C10	82.4(1)	81.5(1)
O1-C7-C6	112.6(2)	112.8(3)
O2-C16-C15	111.4(2)	112.8(3)
Sb-O1-C7	116.6(2)	116.8(2)
Sb-O2-C16	116.3(2)	116.4(2)
Sb-C1-C6	113.1(2)	112.8(3)
Sb-C10-C15	111.7(2)	112.4(3)
C1-C6-C7	116.6(2)	116.3(4)
C10-C15-C16	117.7(2)	116.8(3)
	Torsion angle/deg	
O1-Sb-C19-C20	19.19	21.60
O1-Sb-C19-C24	18.39	21.39
O2-Sb-C19-C20	18.94	21.84
O2-Sb-C19-C24	18.14	21.64
avg	18.89	21.62

Table 2. Crystal Data for **6a**, **8**, and **11**.

	6a	**8**	**11**
formula	C25H18F9O2Sb	C25H15F12O2Sb	C33H35F13N1O2Sb
mol wt	643.2	697.1	846.40
cryst syst	monoclinic	monoclinic	orthorhombic
space group	$P2_1/n$	$P2_1/n$	$Pn2_1a$
cryst dimens, mm	0.60 x 0.50 x 0.30	0.60 x 0.60 x 0.40	0.50 x 0.40 x 0.25
a, Å	17.700(3)	18.064(2)	17.323(5)
b, Å	9.272(2)	9.238(1)	19.928(5)
c, Å	15.219(2)	15.514(2)	10.054(3)
α, deg	90	90	90
β, deg	93.99(1)	96.32(1)	90
γ, deg	90	90	90
V, Å^3	2491.7(7)	2573.3(6)	3471(2)
Z	4	4	4
D_{calc}, g cm^{-3}	1.71	1.80	1.62
abs coeff (ν), cm^{-1}	10.84	10.69	8.04
$F(000)$	1264	1360	1696
radiation; λ, Å	Mo Kα, 0.71073	Mo Kα, 0.71073	Mo Kα, 0.71073
temp, °C	23±1	23±1	23±1
$2\theta_{max}$, deg	55.0	50.0	55.0
scan rate, deg/min	10.0	10.0	6.0
linear decay,%	-	-	-
data collected	$+h, -k, \pm l$	$\pm h, +k, +l$	$+h, -k, +l$
total no. of data collcd, unique,obsd	6331, 5719, 4806 ($I>3\sigma(I)$)	6583, 5921, 5193 ($I>3\sigma(I)$)	4532, 4092, 3545 ($I>3\sigma(I)$)
R_{int}	0.03	0.01	0.00
no of params refined	394	407	456
R, R_w, S	0.028, 0.046, 0.95	0.036, 0.045, 3.23	0.036, 0.044, 1.45
max shift in final cycle	0.35	0.24	0.44
final diff map, max, e/Å^3	0.59	2.03	0.99

Both molecules have pseudotrigonal bipyramidal structures with the two oxygen atoms in the apical positions and three carbon atoms in the equatorial positions. The average dihedral angle between the plane of the p-tolyl group and the apical axis was found to be ca. 19° for compound **6a** and ca. 22° for compound **8** in the direction of the open space between the two bidentate ligands as shown on the right side drawing in Figs. 2 and 3. From the electronic viewpoint, this conformation corresponds to one in which the apical bonds and the p-orbitals of the aromatic ring have aligned nearly perpendicularly to avoid unfavorable orbital overlap. This observation implies that the apical bonds upon the antimony atom are of energy levels rather close to the highest occupied π energy level in the benzene ring and are not effectively stabilized by the benzene π^* orbital. The deviation of the angle from 0° is probably due to steric repulsion between the ortho H of the p-tolyl group and the oxygens of the bidentate ligands. The only notable difference between the two compounds is the bond length between the two apical bonds. In compound **6a** the bond of ligand **10** (Sb-O2: 2.019 Å) was observed to be shorter than that of the symmetric ligand (Sb-O1: 2.053 Å) by 0.034 Å, whereas little difference (0.007 Å) was observed in compound **8** (2.035 and 2.042 Å), while the sum of the two Sb-O bond lengths remains to be the same for **6a** and **8** (4.072 and 4.077 Å, respectively). This implies that the bond strength is nearly equal in the symmetric compound while it has been perturbed in compound **6a** to give a slightly stronger Sb-O bond for the ligand **10** moiety. The methyl group of ligand **10** in compound **6a** was found to be facing toward the p-tolyl group, thus confirming the relative stereochemistry established by NMR techniques. It is also evident from the acute bond angles (ca. 81°) of the rings that ring strain already exists in the ground state structure.

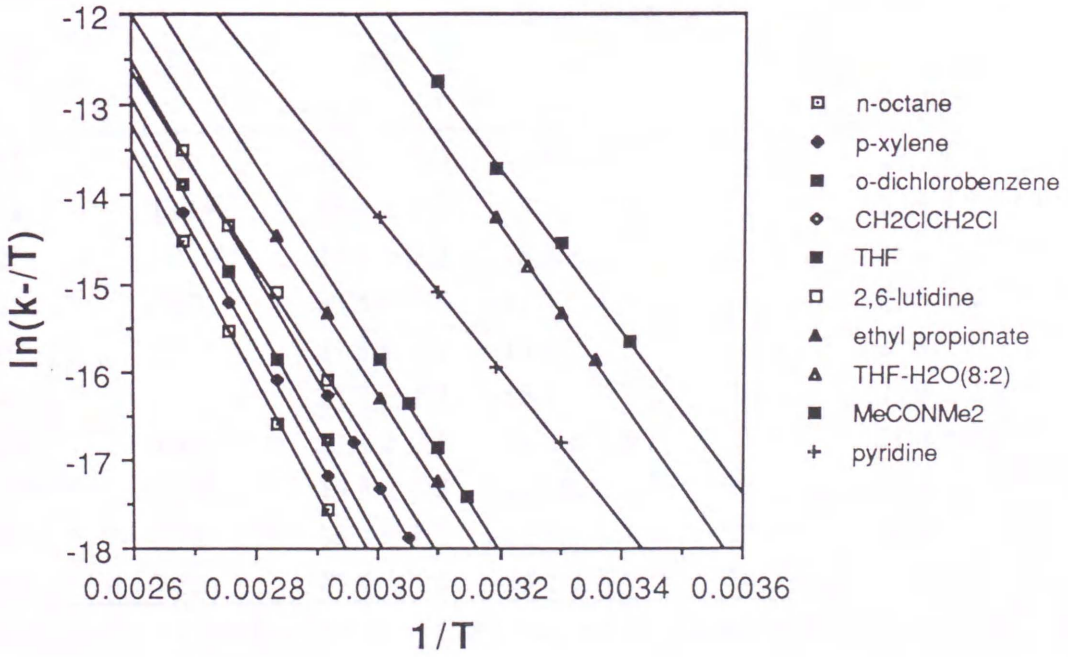


Figure 4. Eyring plot of the rates of conversion of minor **6b** to major **6a** determined in various solvents.

Table.3 Activation Parameters in Various Solvents[a]

solvent	E_T^N[b]	DN[c]	minor **6b** to major **6a**			major **6a** to minor **6b**		
			$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta S^{\neq}$ (eu)	$\Delta G^{\neq}_{298}$ (kcal mol^{-1})	$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta S^{\neq}$ (eu)	$\Delta G^{\neq}_{298}$ (kcal mol^{-1})
n-octane	0.012	0.00	26.0 ± 2.0	-6.3 ± 5.6	27.9	26.1 ± 2.1	-6.9 ± 5.9	28.2
p-xylene	0.074	(0.13)[d]	25.0 ± 1.0	-8.3 ± 2.9	27.7	25.1 ± 0.9	-8.9 ± 2.6	27.8
o-dichlorobenzene	0.225	(0.08)[d]	24.7 ± 2.2	-8.8 ± 6.2	27.3	25.0 ± 2.2	-8.8 ± 6.3	27.6
1,2-dichloroethane	0.327	0.00	23.5 ± 0.5	-11.1 ± 1.5	26.8	23.5 ± 0.6	-11.9 ± 1.8	27.1
THF	0.207	0.52	21.8 ± 0.9	-13.4 ± 2.8	25.7	21.9 ± 0.7	-13.8 ± 2.2	26.0
2,6-lutidine	0.191	-	21.7 ± 1.7	-15.8 ± 4.8	26.4	21.9 ± 1.7	-16.1 ± 4.6	26.7
ethyl propionate	0.228	0.44	21.1 ± 0.6	-16.2 ± 1.6	25.9	21.4 ± 0.6	-16.4 ± 1.8	26.2
THF-H_2O (8:2)	0.563[e]	0.51[f]	19.8 ± 0.8	-12.4 ± 2.6	23.5	19.8 ± 0.8	-13.5 ± 2.5	23.8
dimethylacetamide	0.401	0.72	18.1 ± 1.3	-16.4 ± 4.1	23.0	18.4 ± 1.3	-16.9 ± 4.3	23.4
pyridine	0.302	0.85	17.1 ± 1.0	-24.1 ± 3.1	24.3	17.4 ± 1.1	-24.3 ± 3.5	24.6

[a] Error estimated at 90 % confidence level. [b] Cited from ref 15. [c] Cited from ref 16. [d] Estimated values in ref 16. [e] Measured by us. [f] Weighted value between THF (0.52) and H_2O (0.46).

Permutation in Solvents of Various Donor Abilities.

Initially, it was found that permutation took place rather rapidly at room temperature in deuterated solvents, especially in $CDCl_3$ with equilibrium attained within a few hours or much less with no reproducibility in rates. However, by using freshly purified benzene, it was found that the rate could be reduced dramatically. Therefore in order to determine the magnitude of the permutation barrier and also deduce solvent effects on the rates we performed measurements in various solvents freshly distilled.

Kinetic measurements of the permutation process were carried out by using samples highly enriched with the major diastereomer **6a** and monitoring the relative amount of the ^{19}F NMR signals due to the trifluoromethyl group of ligand **10** of **6a** (δ -80) and **6b** (δ -79). Ten different solvents having varying polarities and donor abilities were utilized, and the rates were measured at four different temperatures each (Table 6). A THF-H_2O (8:2 by weight) mixture prepared from freshly distilled THF and deionized water was also included in the ten solvents as a substitute for pure water, which could serve not only as a highly polar and donating solvent but also as a proton source. By assuming that the process follows reversible pseudo-first-order kinetics, $\ln\{(x_e-x_o)/(x_e-x)\}$ (x=percentage of minor diastereomer, x_o=initial percentage, x_e=percentage at equilibrium) was plotted against time. In all cases, the plots showed good linear relationship. (See supplemental material for rate constants and equilibrium ratios.) In the case of p-xylene, in which we measured first of all, a sample with a concentration about five fold that of other samples was also measured at 343K, since there existed the slight possibility that the process might include some intermolecular process. If a second-order intermolecular process were operative a rate increase of up to five times could have occurred. However, the rates measured at this temperature (for minor **6b** to major **6a**: $(1.17 \pm 0.01) \times 10^{-5}$ and $(1.19 \pm 0.02) \times 10^{-5}$; for major **6a** to minor **6b**: $(7.70 \pm 0.07) \times 10^{-6}$ and $(7.84 \pm 0.13) \times 10^{-6}$) turned out to be essentially the same. Therefore it could be concluded that the process was

intramolecular and thereafter the measurements were primarily made with only one concentration. Since the observed rates of samples using dimethylacetamide (DMA) distilled from CaH_2 turned out to be unexpectedly large (for minor **6b** to major **6a**: $(1.47 \pm 0.04) \times 10^{-4}$; for major **6a** to minor **6b**: $(7.48 \pm 0.18) \times 10^{-5}$ at 303K), we suspected that there could be the presence of liberated amine generated during the distillation process. A measurement at 303K using DMA distilled from $CaSO_4$ gave a similar result (for minor **6b** to major **6a**: $(1.41 \pm 0.02) \times 10^{-4}$; for major **6a** to minor **6b**: $(7.21 \pm 0.12) \times 10^{-5}$) and thus this concern was dismissed.

The Eyring plot of these rate constants shown in Fig. 4 also showed good correlation, and from it activation parameters were calculated as tabulated in Table 3 along with reported values of E_T^N (polarity)[14] and DN^N (normalized donor number)[15]. The reported estimated donor numbers for p-xylene and o-dichlorobenzene are shown in the parenthesis, however, since aromatic π electrons do not coordinate to the antimony of **6**, we can regard the DN^N values to be 0 for these solvents. The E_T^N for the THF-H_2O mixture, of which we used a mixture by weight, was measured to be 0.563. Since enthalpy would be the basis of determining the stability of the transition state, the solvents have been listed in the order of activation enthalpy. A comparison of the activation enthalpies in solvents of no donor ability clearly show that as the E_T^N value of the solvent increases, i.e., 0.012 (n-octane), 0.074 (p-xylene), 0.225 (o-dichlorobenzene), 0.327 (1,2-dichloroethane), the enthalpies decrease accordingly, i.e., 26.1, 25.1, 24.9, 23.5 kcal mol^{-1}, respectively. THF (E_T^N=0.207) and THF-H_2O (E_T^N=0.563), which have about the same donor ability show a similar trend, with the $\Delta H^{\neq}$ values being 21.9 and 19.8 kcal mol^{-1}, respectively. Thus it is quite evident that the polarity of the solvent serves to stabilize the transition state. This implies that the transition state is more polarized than the ground state. When we compare pairs of solvents of similar polarity and of differing donor ability such as o-dichlorobenzene (E_T^N=0.225, DN^N=0.00) and ethyl propionate (E_T^N=0.228, DN^N=0.44), and pyridine (E_T^N=0.302, DN^N=0.85) and 1,2-dichloroethane (E_T^N=0.327, DN^N=0.00), it is quite

clear that the solvent with the larger donor number stabilizes the transition state to a much larger extent. The reduction of donor ability by virtue of steric hindrance in 2,6-lutidine brought about by the methyl groups in the vicinity of the nucleophilic center clearly led to quite significant decrease in rates compared with pyridine, and the activation parameters showed a consistent trend, i.e., the average activation enthalpy and activation entropy were 21.8 kcal mol^{-1} and -16.0 eu for 2,6-lutidine, and 17.3 kcal mol^{-1} and -24.2 eu for pyridine. The role of THF-H_2O as a proton source turned out to be insignificant.

The value of activation entropy was found to be negative for all the solvents measured, even for those solvents that do not possess donative character. Since n-octane also gave a negative value of significance, the value cannot be attributed to the realignment of solvent such that could be supposed for aromatic or polar solvents. We are not sure of the origin, but it could be due to the structural change on going from the trigonal bipyramidal structure in the ground state to the unfavorable trigonal bipyramidal structure where the p-tolyl group should be at an apical position or square pyramidal structure in the transition state, which is more congested. Solvents having donor abilities showed larger negative values, and the values corresponded well with the nature of the coordinating group, i.e., THF (-13.6) and THF-H_2O (-13.0) having single-bonded oxygen atoms, and ethyl propionate (-16.3) and dimethylacetamide (-16.7) having carbonyl oxygens. This probably indicates that these pairs share similar degrees of freedom or in other words similar structure in the transition state. The large negative value for pyridine compared with the others suggests a highly congested hexacoordinate transition state compared with the pentacoordinate ground state.

Although the data clearly show that the effect of donor ability is more significant than the polarity, we decided to evaluate the two in quantitative terms by applying multi-regression analysis, using the normalized E_T^N and DN^N as variants of the nine solvents (2,6-lutidine was omitted) of which both values have been determined.[16] The following equation was thus derived.

$$\Delta H^{\neq} = 25.83 - 5.00 E_T^N - 7.42 DN^N \quad (1)$$

The equation showed a very good fit of R=0.984. The fact that coefficient of DN^N turned out to be larger than that of E_T^N implies that it has a larger role in stabilizing the transition state.

Although there was a strong dependence of the rate upon the solvent, there was no appreciable change in relative difference of ^{19}F NMR chemical shifts among the three trifluoromethyl groups in either diastereomer no matter which solvent was used, thus implying that there was little if any stabilization by coordination of solvent in the ground state even when pyridine was used as solvent, whereas solvent effect was substantial in chemical shift difference in stiboranes in which the p-tolyl group in **8** was replaced with halogen atoms.[17] The temperature dependence of the chemical shift was also examined in the temperature range of 20°C to 100°C, and the shift showed practically no change in this case either. Therefore it could be concluded that there is little perturbation if any in the ground state and its contribution need not be considered for the observed solvent effects.

Our observations lead us to the following mechanistic interpretation of the permutation. In solvents of no donor ability the pentacoordinate compounds probably undergo a permutation that can be illustrated by the usual Berry pseudorotation mechanism, having a transition state of high ring strain brought about by the five membered bidentate in an unfavorable and inevitable equatorial-equatorial disposition whereas the least ring strain is expected in the ground state structure in which the bidentate occupies apical-equatorial positions in a nearly ideal 90° angle. Whether or not the transition state of highest energy in this multi-step transformation is actually the trigonal bipyramid shown in Fig. 5 is not known for certain, and it could be that the transition state is more of a square pyramidal structure. Whichever it may be the presence of large ring strain does not diminish to a large extent and does not change

the essence of the transition state. However, when solvents of donating nature are used it can relieve the ring strain by interacting with the antimony atom and thus creating a pseudooctahedral species in which the bond angles upon antimony become close to the ideal value of 90°, thereby lowering the energy of the transition state. This explanation is consistent with the fact that solvents with small donor numbers would give a weakly coordinate species resembling more of a pentacoordinate species, while those of larger donor numbers would give tighter coordination to form pseudooctahedral species, leading to larger stabilization in the transition state. This stabilization effect was absent in the case of corresponding pentacoordinate phosphorus compounds.[18]

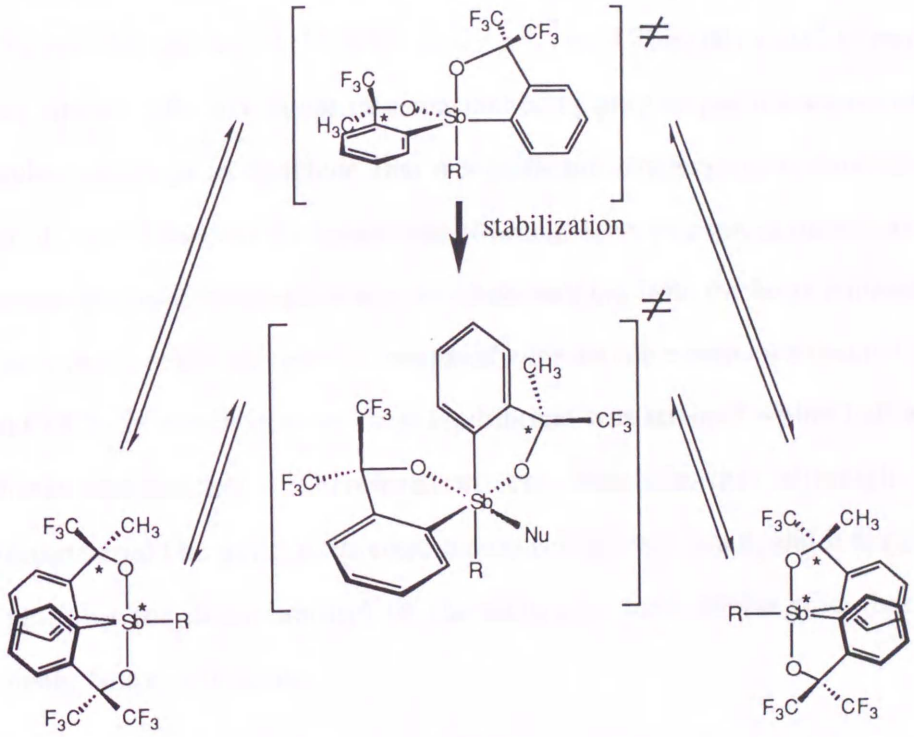


Figure 5. Possible transition state structures in the absence and presence of donative species.

Permutation in the Presence of Acid.

In order to look into other possible factors, we next carried out measurements in the presence of acid, to see whether protonation of the pentacoordinate antimony

compound could be the key factor for the rapid permutation observed in unpurified $CDCl_3$.

The THF-H_2O mixture can be considered a weakly acidic solvent, however, we found no effect (vide supra). Therefore we considered examination with a strong acid, namely trifluoroacetic acid. The results of measurements of THF solutions with 0.35 and 7.4 equiv of trifluoroacetic acid (TFA) at 293K are shown in Table 4 along with the rate in THF without the presence of TFA at this temperature derived by extrapolating the plotted data in Fig. 4. Assuming that the observed data follow reversible pseudo-first order kinetics as before, the observed rate could be analyzed according to equation $k_{obs}=k_1+k_2[TFA]$ (k_{obs}=observed rate, k_1=rate constant first order on **6**, k_2=rate constant first order on both **6** and TFA, and second order overall). From this we obtained $k_1=(4.99\pm0.44) \times 10^{-7}\ s^{-1}$, $k_2=(9.21\pm0.60) \times 10^{-5}\ s^{-1}mol^{-1}L$.[19] When k_1 and the effective molar rate constant of k_2 are compared even the order of magnitude is enough to conclude that a significant acceleration is caused by the addition of acid. However the magnitude of acceleration was not as drastic as would have been expected if protonation was the cause judging from the large amount of the strong acid in the acidic samples as compared with the trace amount expected in non-purified $CDCl_3$ in which in some cases equilibrium was attained within half an hour at ambient temperature. Therefore, we can conclude that although proton concentration could be a factor, its contribution is relatively small, and it is rather the nucleophilicity (or donor ability) of the conjugate base of the acid that is the predominant factor in this case.

Table 4. Rates of Equilibration in the Presence of Trifluoroacetic Acid at 293K[a]

	rates (s^{-1})[b]	
concn (mol L^{-1})	minor to major	major to minor
none	$(4.0 \pm 0.2) \times 10^{-7}$[c]	$(2.0 \pm 0.1) \times 10^{-7}$[c]
8.33×10^{-3}	$(1.25 \pm 0.13) \times 10^{-6}$	$(7.54 \pm 0.80) \times 10^{-7}$
1.90×10^{-1}	$(1.78 \pm 0.06) \times 10^{-5}$	$(1.07 \pm 0.03) \times 10^{-5}$

[a] THF was used as solvent. [b] Error estimated at 90 % confidence level.

[c] Extrapolated from data in Table 3.

Permutation in the Presence of Anionic Nucleophiles.

In order to make the role of nucleophiles clear, we next attempted to examine the rates in the presence of very strong nucleophiles. NMR samples with less than ca. 0.1 eq ("less than" meaning that 0.1 eq of the nucleophile was mixed but most of it was left undissolved) of Et_4NF or MeONa present in THF were measured within ten minutes of their preparation. The spectra indicated that equilibration had already taken place in both cases. Therefore, we can conclude that there is a strong influence of nucleophiles on the rate. Thus, the great acceleration observed in unpurified $CDCl_3$ could be explained according to these results. That is, the nucleophilic nature of the trace amount of liberated chloride anion should be the cause of the acceleration, and the varying rates can be attributed to the actual amount of the chloride anion present in the solvent. We attempted to examine rates in the presence of Bu_4NCl to verify this assumption. As a whole the rates were in measurable range and acceleration was obvious. However the rate values were not reproducible.

Formation and Structure of Hexacoordinate Species.

Close examination of the ^{19}F NMR spectra of the mixture with a small amount of Et_4NF revealed the presence of small peaks other than those of the pentacoordinate diastereomers. Since there were no broad peaks that could be assigned to a free fluoride anion it could be assumed that the peaks were those of hexacoordinate ate complexes formed by the coordination of the fluoride anion. Since it was possible that these ate complexes could be intermediates or catalysts for the acceleration, we next attempted the isolation of the hexacoordinate adduct. To simplify matters, we utilized compound **8** instead of **6**, because a less number of configurational diastereomers are possible for the adduct derived from **8**. By dissolving compound **8** and an excess amount of tetraethylammonium fluoride in acetone and allowing the solution to stand, the desired compound could be obtained as cubic crystals. ^1H and ^{19}F NMR spectra of the compound in acetone-d_6 measured at rt were complex with mostly broad signals, however a measurement at -40°C revealed the presence of three sets of signals, none of which could be assigned to pentacoordinate **8**. Thus, at least three different configurational isomers out of the six geometrically possible, as shown in Fig. 6, are present in solution. When this solution was treated with water the pentacoordinate starting material **8** could be recovered, quantitatively. This implies that an equilibrium between the pentacoordinate and the hexacoordinate species exists, in which the hexacoordinate species is highly favored thermodynamically. The presence of a fast equilibration process between the penta and hexacoordinate species implies that the interconversion among the hexacoordinate isomers is a very rapid process. However, assignment of the isomers could not be carried out because of the complexity of the spectra and lack of data with which to compare . Among the three compounds we believe that two are **A** and **C** on the basis of the solid state structure of **11** which had an oxygen and the fluorine in an anti relationship (vide infra).

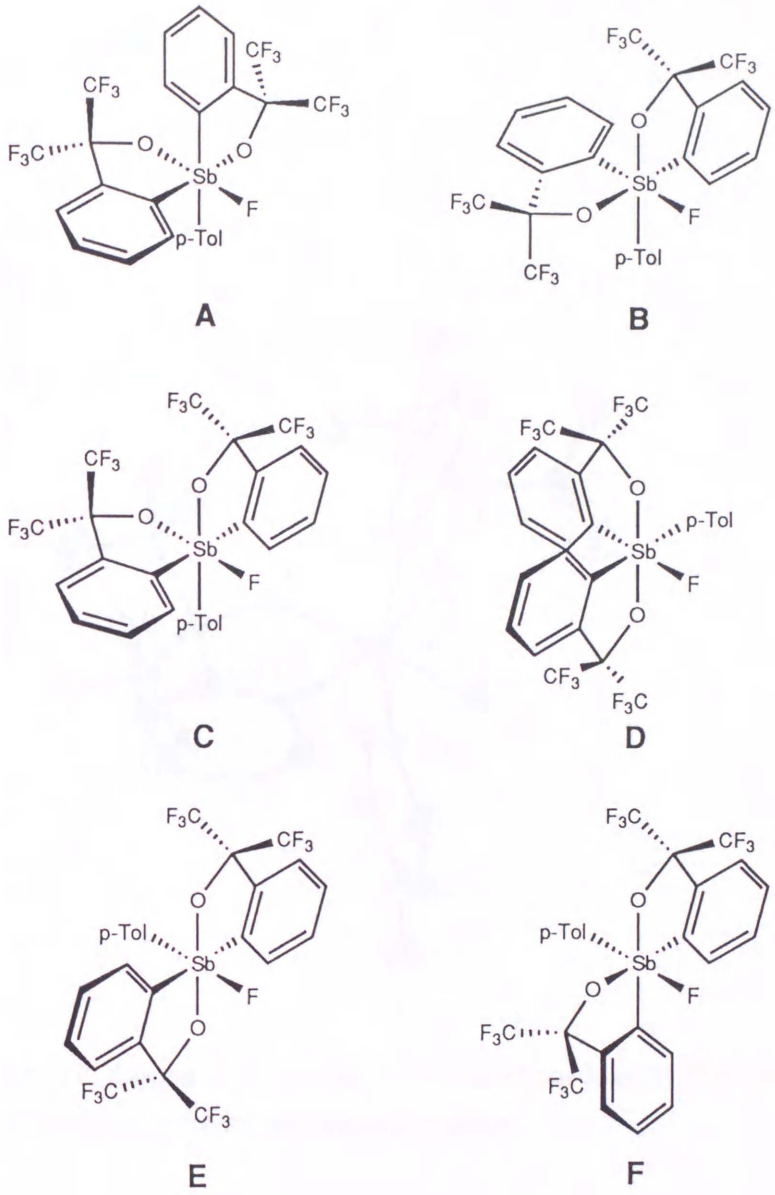


Figure 6. Probable configurational isomers of **11**.

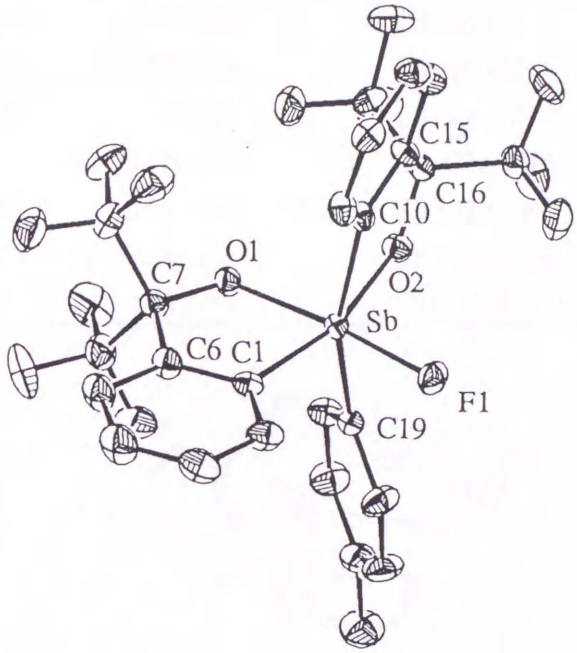
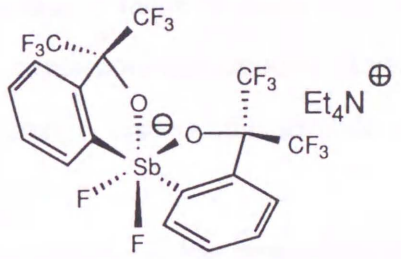


Figure 7. ORTEP drawing of **11** showing the thermal ellipsoids at the 30 % probability level. The tetraethylammonium cation has been omitted for clarity.

Table 5. Selected Crystallographic Data for **11**

	Bond length/Å		
Sb-O1	2.066(4)	Sb-O2	2.107(4)
Sb-C1	2.148(7)	Sb-C10	2.116(7)
Sb-C19	2.124(6)	Sb-F1	1.999(4)
O1-C7	1.360(8)	O2-C16	1.378(7)
C1-C6	1.36(1)	C10-C15	1.368(9)
C6-C7	1.56(1)	C15-C16	1.543(9)
	Bond angle/deg		
O1-Sb-F1	172.0(2)	O2-Sb-C1	164.8(2)
C10-Sb-C19	159.6(2)	O1-Sb-C1	79.2(2)
O2-Sb-C10	77.5(2)	O1-Sb-O2	86.5(2)
C1-Sb-C10	98.7(3)	C1-Sb-C19	100.6(2)
O1-C7-C6	112.6(5)	O2-C16-C15	111.9(5)
Sb-O1-C7	118.5(4)	Sb-O2-C16	118.4(4)
Sb-C1-C6	113.5(5)	Sb-C10-C15	116.7(5)
C1-C6-C7	116.2(6)	C10-C15-C16	115.1(6)



12

X-Ray structural analysis on **11** was carried out and the ORTEP drawing is depicted in Fig. 7, with structural parameters in Table 5, and crystal parameters listed along with those of **6a** and **8** in Table 2. The fluoride was found to be attached anti to one of the oxygen atoms of the bidentate. All the bonds in the original pentacoordinate compound are elongated because of the incoming fluoride. The ring angles about the antimony atom are very close to those of **6a** and **8**, with a slight contraction in line with the elongation of the Sb-element bonds. Thus the ring strain in **11** should not be too different from that in **6a** and **8**. The configuration about the

antimony atom turned out to be that of **A** and not **C** which can be considered an analog of **12**[17] having a fluorine in the place of the p-tolyl group. The main reason for adopting this configuration can be explained on steric grounds. Configuration **A** seems to be less structurally hindered than **C** because the two sets of trifluoromethyl groups are further apart. The distance between the two CF_3 carbons facing each other is 5.018 Å in **11** while it is 4.561 Å in ate complex **12**. Since **12** turned out to assume a structure like **C** with two pairings of anti fluorine and oxygen atoms, it seems that the electronic preference for fluorine and oxygen to assume an anti relationship prevails over repulsion of the trifluoromethyl groups. A point to note is that the anti relationship of one oxygen and the fluorine of the x-ray structure resembles the stereochemical relationship of one oxygen and the nucleophilic species in the transition state structure we proposed for the permutation in the presence of nucleophilic species (Fig. 5 and **A** in Fig. 6). Thus, this x-ray structure is highly indicative that hexacoordination is facile to attain especially with coordination of a nucleophilic species to the pentacoordinate compound anti to an oxygen atom. The same should apply for the strongly nucleophilic alkoxide anion, and also nucleophilic solvents.

In conclusion, we have succeeded in stereochemically characterizing the first configurationally stable 10-Sb-5 stiborane and through kinetic investigations we have found that the permutation of the compound was strongly accelerated by electron donating species, assumingly by the formation of transient or stable hexacoordinate compounds. To gain further insight to this process we are currently examining substituent effects from the steric and electronic standpoints by introducing other groups in the place of the p-tolyl group. The results will be reported in due course.

Table 6. Rates of Equilibration in Various Solvents

		equilibrium ratio	rates (s^{-1})[a]	
solvent	temp (K)	**6a** : **6b**	minor **6b** to major **6a**	major **6a** to minor **6b**
n-octane	343	61.0:39.0	$(8.00 \pm 0.10) \times 10^{-6}$	$(5.11 \pm 0.07) \times 10^{-6}$
	353	61.1:38.9	$(2.20 \pm 0.01) \times 10^{-5}$	$(1.40 \pm 0.01) \times 10^{-5}$
	363	60.8:39.2	$(6.47 \pm 0.06) \times 10^{-4}$	$(4.17 \pm 0.04) \times 10^{-4}$
	373	60.8:39.2	$(1.87 \pm 0.02) \times 10^{-4}$	$(1.20 \pm 0.01) \times 10^{-4}$
p-xylene	343	60.3:39.7	$(1.17 \pm 0.01) \times 10^{-5}$	$(7.70 \pm 0.07) \times 10^{-6}$
	343[b]	60.3:39.7	$(1.19 \pm 0.02) \times 10^{-5}$	$(7.84 \pm 0.13) \times 10^{-6}$
	353	60.3:39.7	$(3.61 \pm 0.04) \times 10^{-5}$	$(2.37 \pm 0.03) \times 10^{-5}$
	363	60.0:40.0	$(8.98 \pm 0.09) \times 10^{-5}$	$(5.99 \pm 0.06) \times 10^{-5}$
	373	60.1:39.9	$(2.54 \pm 0.08) \times 10^{-4}$	$(1.68 \pm 0.05) \times 10^{-4}$
o-dichlorobenzene	343	62.6:37.4	$(1.76 \pm 0.02) \times 10^{-5}$	$(1.05 \pm 0.01) \times 10^{-5}$
	353	62.3:37.7	$(4.53 \pm 0.06) \times 10^{-5}$	$(2.74 \pm 0.04) \times 10^{-5}$
	363	62.0:38.0	$(1.26 \pm 0.02) \times 10^{-4}$	$(7.73 \pm 0.11) \times 10^{-5}$
	373	61.7:38.3	$(3.50 \pm 0.14) \times 10^{-4}$	$(2.17 \pm 0.09) \times 10^{-4}$
1,2-dichloroethane	328	61.7:38.3	$(5.76 \pm 0.08) \times 10^{-6}$	$(3.57 \pm 0.05) \times 10^{-6}$
	333	61.7:38.3	$(9.91 \pm 0.24) \times 10^{-6}$	$(6.15 \pm 0.15) \times 10^{-6}$
	338	61.7:38.3	$(1.70 \pm 0.03) \times 10^{-5}$	$(1.06 \pm 0.02) \times 10^{-5}$
	343	61.6:38.4	$(2.91 \pm 0.07) \times 10^{-5}$	$(1.81 \pm 0.04) \times 10^{-5}$
2,6-lutidine	343	61.5:38.5	$(3.49 \pm 0.04) \times 10^{-5}$	$(2.19 \pm 0.02) \times 10^{-5}$
	353	61.4:38.6	$(9.70 \pm 0.09) \times 10^{-5}$	$(6.10 \pm 0.06) \times 10^{-5}$
	363	61.2:38.8	$(2.14 \pm 0.02) \times 10^{-4}$	$(1.36 \pm 0.01) \times 10^{-4}$
	373	60.9:39.1	$(5.02 \pm 0.11) \times 10^{-4}$	$(3.22 \pm 0.07) \times 10^{-4}$

ethyl propionate	323	62.2:37.8	$(1.04 \pm 0.02) \times 10^{-5}$	$(6.31 \pm 0.14) \times 10^{-6}$
	333	62.0:38.0	$(2.78 \pm 0.03) \times 10^{-5}$	$(1.70 \pm 0.02) \times 10^{-5}$
	343	61.7:38.3	$(7.39 \pm 0.04) \times 10^{-5}$	$(4.58 \pm 0.02) \times 10^{-5}$
	353	61.4:38.6	$(1.85 \pm 0.02) \times 10^{-4}$	$(1.16 \pm 0.01) \times 10^{-4}$
THF	318	62.2:37.8	$(8.73 \pm 0.34) \times 10^{-6}$	$(5.31 \pm 0.21) \times 10^{-6}$
	323	62.4:37.6	$(1.56 \pm 0.06) \times 10^{-5}$	$(9.37 \pm 0.35) \times 10^{-6}$
	328	62.2:37.8	$(2.57 \pm 0.13) \times 10^{-5}$	$(1.56 \pm 0.08) \times 10^{-5}$
	333	61.9:38.1	$(4.35 \pm 0.09) \times 10^{-5}$	$(2.68 \pm 0.05) \times 10^{-5}$
pyridine	303	63.5:36.5	$(1.53 \pm 0.03) \times 10^{-5}$	$(8.76 \pm 0.15) \times 10^{-6}$
	313	63.3:36.7	$(3.70 \pm 0.07) \times 10^{-5}$	$(2.15 \pm 0.04) \times 10^{-5}$
	323	63.0:37.0	$(8.99 \pm 0.15) \times 10^{-5}$	$(5.28 \pm 0.09) \times 10^{-5}$
	333	62.5:37.5	$(2.17 \pm 0.03) \times 10^{-4}$	$(1.30 \pm 0.02) \times 10^{-4}$
THF-H_2O (8:2)	298	63.5:36.5	$(3.86 \pm 0.09) \times 10^{-5}$	$(2.22 \pm 0.05) \times 10^{-5}$
	303	63.5:36.5	$(6.59 \pm 0.11) \times 10^{-5}$	$(3.79 \pm 0.06) \times 10^{-5}$
	303[c]	63.5:36.5	$(6.62 \pm 0.23) \times 10^{-5}$	$(3.81 \pm 0.13) \times 10^{-5}$
	308[c]	63.4:36.6	$(1.14 \pm 0.02) \times 10^{-4}$	$(6.56 \pm 0.09) \times 10^{-5}$
	313[c]	63.5:36.5	$(2.01 \pm 0.02) \times 10^{-4}$	$(1.15 \pm 0.01) \times 10^{-4}$
dimethylacetamide	293	66.7:33.3	$(4.60 \pm 0.11) \times 10^{-5}$	$(2.30 \pm 0.06) \times 10^{-5}$
	303	66.2:33.8	$(1.47 \pm 0.04) \times 10^{-4}$	$(7.48 \pm 0.18) \times 10^{-5}$
	303[d]	66.2:33.8	$(1.41 \pm 0.02) \times 10^{-4}$	$(7.21 \pm 0.12) \times 10^{-5}$
	313	66.0:34.0	$(3.43 \pm 0.11) \times 10^{-4}$	$(1.77 \pm 0.05) \times 10^{-4}$
	323	65.7:34.3	$(9.68 \pm 0.36) \times 10^{-4}$	$(5.05 \pm 0.16) \times 10^{-4}$

[a] Error estimated at 90 % confidence level. [b] Concentration was fivefold of usual samples. [c] Measured with a seperately prepared mixture. [d] Distilled from $CaSO_4$, while others were distilled from CaH_2.

3. Experimental

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. ^1H NMR (400 MHz) and ^{19}F (376 MHz), spectra were recorded on a JEOL EX-400 spectrometer or routinely on a Hitachi R-90H spectrometer. ^1H NMR chemical shifts (δ) are given in ppm downfield from internal Me_4Si, or from residual chloroform (δ = 7.26) or benzene (δ = 7.2). ^{19}F NMR chemical shifts (δ) are given in ppm downfield from internal $CFCl_3$. Elemental analyses were performed on a Perkin Elmer 2400CHN elemental analyzer.

All reactions were carried out under N_2 except where noted otherwise. THF and Et_2O were freshly distilled from Na-benzophenone. Dimethylacetamide was distilled from either CaH_2 or $CaSO_4$. All other solvents and liquid reagents were distilled from CaH_2. Trifluoromethyl phenyl ketone[10] and dichloro-(4-methylphenyl)stibine[11] were prepared according to published procedures. Column chromatography was carried out with Merck silica gel 60 (70-230 mesh). Preparative thin layer chromatography was carried out on plates of Merck silica gel 60 GF_{254}.

1,1,1-Trifluoro-2-phenyl-2-propanol (4). To an ether (130 mL) solution of MeMgI prepared from magnesium (10.4 g, 0.43 mol) and iodomethane (26.6 mL, 0.43 mol) was added trifluoromethyl phenyl ketone (40.0 mL, 0.29 mol) in ether (40 mL) at 0°C. After the mixture was stirred overnight at rt, the solution was quenched with aqNH_4Cl, extracted with ether, dried with $MgSO_4$, and concentrated in vacuo. Distillation under reduced pressure from CaH_2 gave the product (48.4 g, 89 %) as a colorless liquid. Bp 83-85 C°/15 mmHg; ^1H NMR ($CDCl_3$) δ 7.26-7.64 (m, 5 H), 2.47 (bs, 1 H), 1.79 (q, $J_{H\text{-}F}$ = 1.1 Hz, 3 H); ^{19}F NMR ($CDCl_3$) δ -81.5 (s).

1,1,1-Trifluoro-(2-bromophenyl)-2-propanol (5). To a THF (15 mL) solution of n-BuLi (*c* 1.65 M in hexane, 203 mL, 0.34 mol) and tetramethylethylenediamine (50.6 mL, 0.34 mol) was added alcohol **2** (28.98 g, 0.152 mol) at 0°C and solution was stirred for 2 hr. To this solution was added 1,2-dibromo-1,1,2,2-tetrafluoroethane

(23.7 mL, 0.20 mol) at -78°C. After allowing the solution to warm to room temperature, it was additionally stirred for 2 hr, and then quenched with aqNH_4Cl. Extraction with ether, drying with $MgSO_4$, removal of solvent, followed by distillation under reduced pressure yielded the product as a colorless liquid. (25.4 g, 62 %) Bp 84-85°C/0.9 mmHg; ^1H NMR ($CDCl_3$) δ 7.17-7.70 (m, 5 H), 4.04 (s, 1 H), 1.92 (q, J_{H-F} = 1.1 Hz, 3 H); ^{19}F NMR ($CDCl_3$) δ -79.3 (s).

3,3-Bis(trifluoromethyl)-1-(4-methylphenyl)-3*H*-2,1-benzoxastibole (7). To n-BuLi (*c* 1.6 M in hexane, 52 mL, 83 mmol) was added tetramethylethylenediamine (1.21 mL, 7.81 mmol) and the solution was stirred for a few minutes to allow the formation of a suspension. After THF (3 mL) was added to dissolve the precipitation, 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (6.68 mL, 40.0 mmol) was added dropwise at 0°C. After stirring the solution overnight at room temperature, THF (100 mL) was added to dissolve the newly formed precipitate followed by the dropwise addition of **3** (11.28 g, 40.0 mmol) in THF (100 mL) at -78°C. The solution was quenched with aqNH_4Cl after stirring overnight. Extraction was done with ether followed by usual workup. Chromatography (n-hexane-ethyl acetate=10:1 on SiO_2) furnished **7** (14.19 g, 78 %) as a colorless solid along with a small amount of spiro compound **8** (2.87 g, 7 %). Compound **7**: mp 113.5-115°C; ^1H NMR ($CDCl_3$) δ 7.05-7.54 (m, 4 H), 2.25 (s, 3 H); ^{19}F NMR ($CDCl_3$) δ -75.1 (q, *J*=9.3 Hz, 3F).-77.3 (q, *J*=9.3 Hz, 3F). Anal. Calcd for $C_{16}H_{11}F_6OSb$: C, 42.24; H, 2.44. Found: C, 42.39; H, 2.51. Compound **8**: mp 135.5-136°C; ^1H NMR ($CDCl_3$) δ 8.0-8.2 (m, 2H), 7.92 (d, *J*=7.9 Hz, 2H), 7.5-7.9 (m, 6H), 7.32 (d, *J*=7.9 Hz, 2H), 2.33 (s, 3H). ^{19}F NMR ($CDCl_3$) δ -74.2 (q, *J*=8.3 Hz, 3F).-73.0 (q, *J*=8.3 Hz, 3F).

1,1-Dichloro-3,3-bis(trifluoromethyl)-1-(4-methylphenyl)-3*H*-2,1-benzoxastibole (9), and 3,3,3'-Tris(trifluoromethyl)-3'-methyl-1-(4-methyl-phenyl)-1,1'-spirobis-3*H*-2,1-benzoxastibole (6). To compound **7** (0.553 g, 1.22 mmol) dissolved in CH_2Cl_2 (10 mL) was added SO_2Cl_2 (0.20 mL, 2.5 mmol) at 0°C. After stirring at room temperature for 1hr, the solvent and excess SO_2Cl_2 were removed under reduced

pressure, to give the dichloride quantitatively as a white solid sensitive to moisture. This product was subsequently used without further purification. ^{1}H NMR ($CDCl_3$) δ 7.05-7.54 (m, 4 H), 2.25 (s, 3 H); ^{19}F NMR ($CDCl_3$) δ -75.1 (q, *J*=9.3 Hz, 3 F).-77.3 (q, *J*=9.3 Hz, 3 F).

To 1,1,1-trifluoro-2-(2-bromophenyl)-2-propanol (0.352 g, 1.31 mmol) in ether (10 mL) was added n-BuLi (*c* 1.65 M, 1.7 mL, 2.80 mmol) at -78°C and the resulting solution was stirred overnight at rt, during which the gradual formation of a white mass was observed. THF (10 mL) was added to the mixture to make a homogeneous solution of lithium 1,1,1-trifluoro-2-(2-lithiophenyl)-2-propoxide **10**.

The solution of **10** was added dropwise to a THF (10 mL) solution of the dichloride **9** at -78°C. After stirring the solution at this low temperature for 1hr, the solution was allowed to warm to room temperature. The solution was treated with aqNH_4Cl followed by extraction with CH_2Cl_2. Usual workup and subsequent chromatography (n-hexane-CH_2Cl_2=2:1) yielded a diastereomeric mixture of **6** (0.182 g, 23 %) as a colorless oil. Slow recrystallization from CH_3CN gave the major diastereomer (0.141 g, 18 %) as colorless crystals. The filtrate was found to have an equilibrium mixture of the diastereomers. Separation by TLC could give the minor diastereomer in up to only 80 % purity due to the facile permutation under the separation procedure. **6a (major)**: mp 152-153°C; ^{1}H NMR (C_6D_6) δ 8.38 (d, J=7.3 Hz, 1 H), 8.32 (d, J=7.3 Hz, 1 H), 8.17 (d, J=6.8 Hz, 2 H), 7.81 (d, J=7.8 Hz, 1 H), 7.31 (d, J=6.3 Hz, 1H), 6.99-7.11 (m, 4 H), 6.93 (d, J=7.3 Hz, 2 H), 1.93 (s, 3 H), 1.73 (s, 3 H); ^{19}F NMR (C_6D_6) δ -74.0 (q, *J*=9.3 Hz, 3 F).-76.5 (q, *J*=9.3 Hz, 3 F), -80.0 (s, 3 F). Anal. Calcd for $C_{23}H_{18}F_9O_2Sb$: C, 46.69; H, 2.82. Found: C, 46.50; H, 2.71. **6b (minor)**: ^{1}H NMR (C_6D_6) δ 8.33 (d, J=6.8 Hz, 1 H), 8.28 (d, J=8.4 Hz, 2 H), 8.21 (d, J=8.0 Hz, 1 H), 7.84 (d, J=9.6 Hz, 1 H), 7.32 (d, J=10.8 Hz, 1H), 6.99-7.12 (m, 4 H), 6.93 (d, J=7.3 Hz, 2 H), 1.83 (s, 3 H), 1.59 (s, 3 H); ^{19}F NMR (C_6D_6) δ -74.2 (q, *J*=9.3 Hz, 3 F).-75.1 (q, *J*=9.3 Hz, 3 F), -78.7 (s, 3 F).

Tetraethylammonium Fluorobis[α,α-bis(trifluoromethyl)benzene-methanolato(2-)-*C*^{2},*O*](4-methylphenyl)antimonate(1-) (11). 3,3,3',3'-Tetrakis(trifluoromethyl)-1-(4-methylphenyl)spirobis-3*H*-2,1-benzoxastibole (105 mg, 0.150 mmol) and tetraethylammonium fluoride (64 mg, 0.43 mmol) were dissolved in acetone in the open air and the solution was left standing overnight. The resulting colorless crystals (92 mg, 73 %) were collected. They were found to be suitable crystals for X-ray analysis. Mp 226-228°C. Anal. Calcd for $C_{33}H_{35}F_{13N}O_2Sb$: C, 46.83; H, 4.17; N, 1.65. Found: C, 46.75; H, 4.08; N, 1.59.

Kinetic Measurements. Samples enriched with **6a** (ca. 8.5-10 mg in 0.5-0.6 mL of solvent unless noted otherwise) dissolved in freshly distilled solvents were sealed in NMR tubes under N_2. Measurements for the kinetic runs were carried out with a JEOL EX-400 spectrometer in a variable temperature mode and the specified temperatures were maintained throughout each set of measurements (error within ±1°C). The observed temperatures were calibrated with the ^{1}H NMR chemical shift difference of signals of neat MeOH (low temperature region) and neat 1,3-propanediol (high temperature region). The composition of the diastereomers was monitored by integration of ^{19}F NMR signals. The data was analyzed assuming reversible first order kinetics using the equation, $\ln\{(x_e-x_o)/(x_e-x)\}=k(K+1)t$, in which x_e=(ratio at equilibrium), x_o=(ratio observed at t=0), x=(ratio observed at arbitrary intervals), k=(rate constant to be determined), and K=(equilibrium ratio). The equilibrium ratios were determined by heating the measured sample in a silicon oil bath at the specified temperature (±2°C) for at least 5 lifetimes.

Crystallographic Studies. Crystal Structures of 6a, 8, and 11. Crystal data and numerical details of the structural determinations are given in Table 3. Crystals were mounted on a Mac Science MXC3 diffractometer and irradiated with graphite-monochromated Mo Kα radiation (λ=0.71073 Å) for data collection. Lattice parameters were determined by least-squares fitting of 24 reflections for **6a**, and 31 reflections for **8** and **11** in the range of $31°<2\theta<35°$. Data were collected with the

$2\theta/\omega$ scan mode. Data for **6a** were corrected for absorption.[20] The structures were solved by a direct method with the Shelx 86 program. Refinement of *F* was carried out by the full-matrix least squares method. All non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms in **11** were included in the refinement at calculated positions (C-H=1.0 Å) riding on their carrier atom with isotropic thermal parameters. All computations were carried out on a Titan 750 computer.

4. References

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List of Publications

* (1) The Wittig Rearrangement of Chiral Phosphinothioates Induced by the Tin-Lithium Transmetallation.
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