A New Reagent for the Determination of the Optical Purity of Primary, Secondary, and Tertiary Chiral Alcohols and of Thiols

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A new reagent is described for the determination of the enantiomeric excess of chiral alcohols. This derivatizing agent (**22**) is a diazaphospholidine, easily prepared from hexamethylphosphorous triamide (HMPT) and a chiral diamine having a C_2 axis of symmetry: (*R,R*)-*N,N'*-dimethylcyclohexane-1,2-diamine. A large array of primary, secondary, and tertiary alcohols, functionalized or not, as well as thiols were successfully tested. The derivatization is fast at room temperature, proceeds without kinetic discrimination, does not need any added cosolvent or coreagent, and may be run directly in an NMR tube. This new reagent allows an accurate analysis by ^{31}P NMR spectroscopy, and after conversion of the trivalent phosphorus derivative to the corresponding P-sulfide in the NMR tube, a new ^{31}P NMR spectrum may be recorded. In addition, most of the P-sulfide derivatives when submitted to GC or HPLC analyses exhibit base line separation.

Introduction

The determination of the optical purity of a chiral alcohol is a constant need. This measure can be performed by numerous analytical procedures.[1,2] Polarimetry is usually used for comparative purposes with literature data, but is not usually considered sufficiently accurate or reliable.[1] Chromatographic analyses may be done on chiral phases[3] or, alternatively, after derivatization with an optically pure reagent to form a pair of diastereoisomers which can be analyzed on achiral phases.[3b,4] However, one of the most popular techniques uses NMR spectra of various nuclei.[1,5]

NMR analyses may be performed with chiral complexing reagents,[6] chiral lanthanide shift reagents,[7] or after derivatization with optically pure reagents.[8] Among the various chiral derivatizing agents (CDA), Mosher's reagent **1** enjoys a strong preference.[9] The so called MTPA derivatives **2** can be analyzed by ^1H, ^{13}C, and ^{19}F NMR spectroscopy as well as by gas or liquid chromatography (Chart I). Quite often, MTPA derivatives are used in combination with a lanthanide shift reagent, particularly when the absolute configuration has to be determined.[10] Despite these advantages, the formation[11] and the analysis of these derivatives are often troublesome and new CDA's have been, recently, developed. Noteworthy are the ones based on ^{31}P NMR analysis such as **3**, **3S**, **4**, **5**, and **6** (Chart II). The sensitivity of this nucleus is quite high, and the spectra are not plagued by extra signals other than the signals of the diastereomeric pair.

The achiral reagents **3**, and **3S**, introduced by Feringa,[12] react twice with 2 equiv of the chiral alcohol to produce diastereomeric O,O-dialkyl phosphonates. Thus, three signals are obtained with a racemic alcohol, two for the meso form and one for the *d,l* pair. Reagent **4**, although described as unstable by Johnson,[13] was recently reintroduced by Kato.[14] This reagent as well as reagent **5**, de-

Chart I

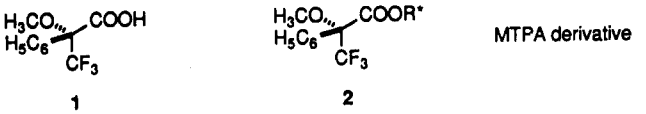

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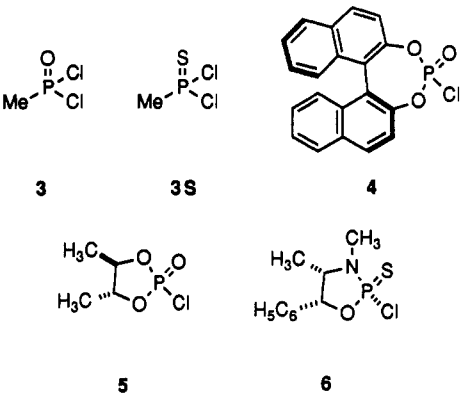
Chart II



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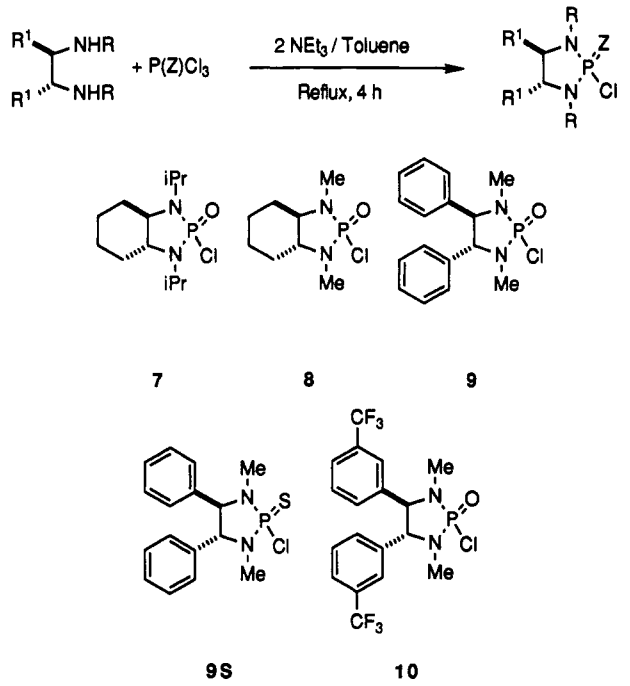
Scheme I



scribed by Shapiro,[15] are unique in that the phosphorus atom is not chiral, owing to the C_2 axis of symmetry of the chiral glycol. Therefore, either retention or inversion at phosphorus during derivatization of an enantiomerically pure alcohol yields a single diastereoisomer. This is not the case with reagent **6**, introduced by Johnson,[13] where the phosphorus atom is chiral. Although it usually reacts with retention of configuration,[16] a recent paper warns against some stereochemical scrambling.[17]

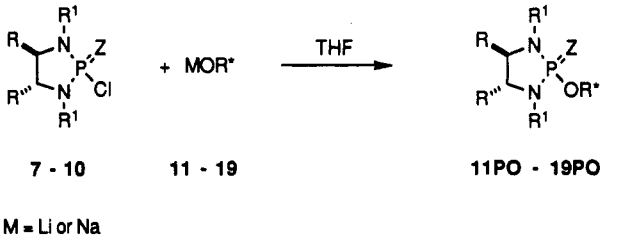
Our recent work on chiral diamines[18] having also a C_2 axis of symmetry taught us that much higher stereodifferentiations are usually attained whenever they can replace a diol. We have therefore prepared various phosphorylated reagents in the hope that they would be much more efficient than the previous ones. This article describes in detail our work in this area.[19]

Pentavalent Phosphorus Derivatives

Scheme I summarizes the five derivatives we have prepared. According to known procedures,[20] phosphorus oxychloride or phosphorus thiochloride were allowed to react with the diamine in refluxing toluene in the presence of 2 equiv of triethylamine. Phosphoramides **7** and **8** were obtained in 75% and 90% yield, respectively, after distillation, and **9** could be purified by column chromatography in 92% yield. However, **9S** and **10** were unstable to purification; **9S** was pure enough in crude form to be further used, whereas **10** could be recrystallized in 56% yield.

These derivatives were evaluated by their reactions with 2-butanol (**11**) for which much comparative data is

Scheme II



available. However, the reactivity of derivatives **7–10** proved to be very poor. 2-Butanol did not react in THF in the presence of 2 equiv of triethylamine, but gave several byproducts probably arising from the opening of the diazaphospholane ring. Such an anomalous reaction was also observed by Shapiro[15] and Johnson.[13] The use of other bases (DMAP, DBU, or DABCO) or other solvents (CH_2Cl_2, DMF) did not affect decisively this result. However, when we turned to the lithium or sodium alcoholate,[13] we did solve this problem.

Thus, the lithium alcoholate was formed with nBuLi and the sodium one with NaH. The chiral derivatizing agent **7–10** was then added, and the mixture was refluxed in THF for 2–6 h. (Scheme II). Problems were encountered with nBuLi which always contains traces of nBuOLi, and the NaH procedure was preferred. Under these conditions, the reaction is clean and quantitative, and the desired diasteromeric pairs of derivatives **11PO** and **11'PO** could be analyzed by ^{31}P NMR. The results are reported in Table I along with the ones obtained with alcohols **12–19**.

Reagent **7** did not react with 2-butanol (**11**, entry 1), even after prolonged heating. Steric crowding around the phosphorus atom may account for this lack of reactivity. The diastereoisomeric pairs obtained with reagents **8–10** (entries 2–5) all gave significant differences in ^{31}P chemical shifts ($\Delta\delta$). All these values compare very favorably with literature data and fulfill our expectations. Moreover, an interesting solvent effect was observed: in C_6D_6, the $\Delta\delta$ are higher than in $CDCl_3$ (entries 3, 5, and 6). It should, also, be observed that **9S**, the thio analogue of **9**, displays smaller differences in $\Delta\delta$ (compare entries 3 and 4 and also entry 2 in Table I with entry 1 in Table III), in contrast to Johnson's report with **6**[13] and Feringa's result with **3S**.[12c] In addition, reagent **9S** is much less reactive than its oxygenated analogue **9**, probably because of the lesser polarization of the P=S bond, as compared to the P=O bond.[21] Finally, although reagent **10** seems the most effective (entry 5) by ^{31}P NMR analysis, we did not observe as we hoped, any significant $\Delta\delta$ by ^{19}F NMR. The corresponding diamine was described by us to be an efficient reagent for the determination of the optical purity of chiral aldehydes by ^{19}F NMR.[18c]

Among the other secondary alcohols examined (entries 6–10), only the unhindered ones reacted cleanly and quantitatively, and the observed differences in chemical shift ($\Delta\delta$) are much larger than the literature data. As shown below, propargylic secondary alcohols **14** and **16** are particularly interesting cases and reagent **8** is very well suited for these alcohols. Such alcohols display the largest $\Delta\delta$ values, an observation also made by Shapiro.[15] C-Silylated propargylic alcohols, such as **17**, are not suited since they are partly desilylated, owing to the strongly basic conditions (NaH) during the derivatization. Finally, no reaction was observed with the very hindered 2-*tert*-bu-

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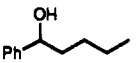
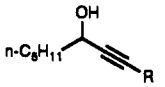
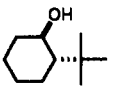
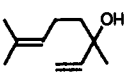
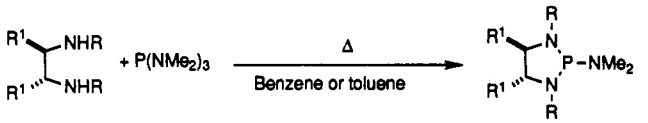
Table I. Evaluation of CDA's 7-11 with Various Chiral Alcohols (See Scheme II)

entry	phosphorus reagent	structure: alcohol	structure: R	structure: no.	δ (ppm) ^{31}P of the diastereomers	pair of derivatives	Δδ (ppm)	lit. data Δδ	observations
1	7		Et	11		11POa			no reaction
2	8				24.393 and 24.056	11POb	0.337[b]	0.0056[c,d] 0.200[b,e]	
3	9				24.701 and 24.226	11POc	0.475[c] 0.404[b]	0.350[f] 0.296[g]	
4	9S				82.448 and 82.111	11PSc	0.337[b]	0.531[h]	
5	10				24.230 and 24.691	11POd	0.539[c] 0.471[b]		
6	9		nC_6H_{13}	12	24.768 and 24.282	12PO	0.486[c] 0.471[b]	0.307[b,e] 0.383[f]	
7	9		iPr	13	24.634 and 23.998	13PO	0.636[b]	0.167[b,e]	
8	8		C≡CH	14	23.422 and 22.749	14PO	0.673		
9	9			15	24.903 and 24.338	15PO	0.565[c] 0.455[b]		
10	8		H	16	24.373 and 23.437	16PO	0.936		
11	8		$SiMe_3$	17	24.162 and 22.827	17PO	1.335		see text
12	9			18					no reaction
13	9			19					no reaction

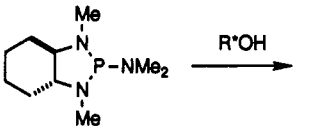
[a] All the alcohols are racemic mixtures. [b] Taken in $CDCl_3$. [c] Taken in C_6D_6. [d] Reference 15. [e] Reference 13. [f] Reference 12a. [g] Reference 12b. [h] Reference 12c.

Scheme III

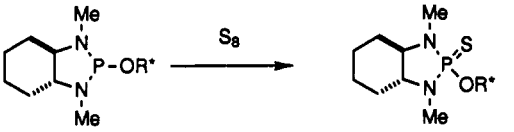


20 **21** **22**

Scheme IV



22



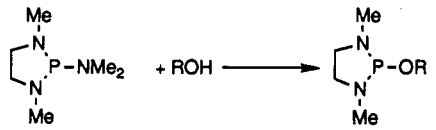
11P - 53P **11PS - 53PS**

tylcyclohexan-1-ol (18) or with tertiary alcohols, such as linalool (19).

Thus, although quite efficient, the methodology based on pentavalent phosphorus derivatives cannot be of general use. Our studies on the corresponding trivalent phosphorus reagents were much more successful in the discovery of a reagent of wide applicability and high reactivity.

Trivalent Phosphorus Derivatives

It is well-known that the P–N bond of aminophosphines is very easily cleaved by alcohols,[22] and Burgada has shown that the exocyclic P–N bond is preferentially cleaved in diazaphospholidines[23] (eq 1): It is easy to understand that



eq. 1

a chiral diamine fits ideally into this scheme. Thus, reagents **20**, **21**, and **22** were prepared by amine exchange with $P(NMe_2)_3$[23] (Scheme III). The reaction is complete after 2–5 days of reflux in benzene or toluene. Reagent **20** could not be purified either by chromatography or by distillation and was used crude. Reagents **21** and **22** were obtained in 86% and 85% yield, respectively, after distillation.

Reagents **20–22** are stable for months under inert atmosphere but are very sensitive to moisture. The exocyclic P–N bond is readily cleaved[24] as shown for reagent **22** (eq 2) which gave product **23**: For this reason, reagents **20–22** were conveniently stored as ~0.2 M solution in toluene and taken by syringe when needed. The derivatizing procedure involves the alcoholysis of the exocyclic P–N bond in analogy to the hydrolysis shown above. Thus, the optically active alcohol (**11–53**) is added to a slight excess

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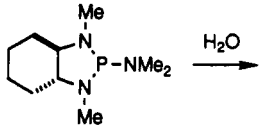
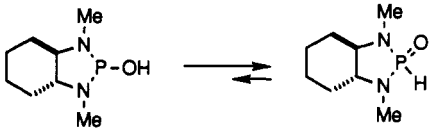


22



23

eq. 2

(1.1 equiv) of CDA in toluene and stirred (2–15 h) until no dimethylamine is evolved (checked with pH paper). Since the diastereomeric pair of derivatives **11P–53P** and **11'P–53'P** is not stable to TLC or GC analysis, a more reliable way was sought to check the completion of the reaction. This task was accomplished by conversion to the thiophosphoramidate with sulfur (S_8) powder[25] (Scheme IV). This reaction is quantitative and instantaneous, and the thio derivatives **11PS–53PS** were, this time, air stable compounds easily analyzable by TLC or GC.

The effectiveness of reagents **20–22** was again evaluated with 2-butanol (**11**), and the results are quoted in Table II. It is clear that trivalent phosphorus CDA's **20** and **22** are incomparably more efficient than the pentavalent ones **7–10**. The largest value of the difference of chemical shift ($\Delta\delta$), 3.7 ppm, obtained with **22** (entry 3), should also be compared with the values previously obtained by Shapiro with **5** (0.0056 ppm),[15] by Johnson with **6** (0.200 ppm),[13] or by Feringa with **3** (0.350 ppm)![12b] Thus, reagent **22** was chosen as our standard new CDA and evaluated with a variety of chiral alcohols in order to explore the scope of its effectiveness.

Evaluation of Reagent 22

Reagent **22** was easily prepared from $P(NMe_2)_3$ and (*R,R*)-*N,N'*-dimethylcyclohexane-1,2-diamine, itself obtained from commercially available (*R,R*)-cyclohexane-1,2-diamine. It reacted with all of the chiral alcohols (**11–53**) tested thus far, regardless of their steric bulk, in toluene solution, at room temperature within a few hours, to give the derivatives **11P–53P** (see Scheme IV). No other cosolvent or coreagent are needed, and the reaction may be run in an NMR tube. A small amount of C_6D_6 was added in the NMR tube for locking, and the spectrum was recorded. The ^{31}P NMR spectrum shows a small singlet of the starting reagent **22** (δ 122.5 ppm), sometimes a small singlet for the hydrolysis product **23** (δ 19.5 ppm), and two equal singlets (for racemic alcohols) (δ 130–145 ppm) for the diastereomeric pair **11P–53P**. Integration of these singlets can be done very accurately. Once this first ^{31}P NMR spectrum was recorded, S_8 was added into the NMR tube and the spectrum of the new thio derivatives **11PS–53PS** (see Scheme IV) was recorded. In many other cases optically enriched alcohols were tested, and the accuracy of our method could be compared with ee values obtained by other means. Excellent agreement was obtained in all cases. The excess of reagent **22** is also converted to **22PS**, but its NMR singlet does not interfere (δ 83.5 ppm). Neither do those of other byproducts interfere, such as the hydrolysis product **23**. Derivatives **11PS–53PS** display

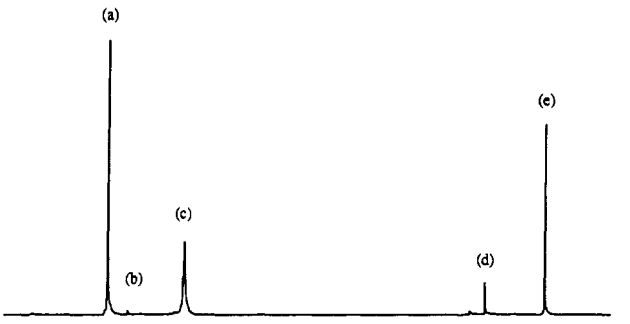


Figure 1. ^{31}P NMR (36.22 MHz) spectrum of a 99:1 mixture of menthol derivatives **26P** (a and b); (c) signal of CDA **22**; (d) signal of hydrolyzed CDA **23**; (e) reference H_3PO_4.

singlets in the range δ 79–89 ppm.

The variety of the tested chiral alcohols is shown in Tables III (secondary alcohols), IV (tertiary alcohols), and V (primary alcohols). In all cases optically pure reagent **22** was used (from (*R,R*)-*N,N'*-dimethylcyclohexane-1,2-diamine), except when the chiral alcohol was available only in optically pure form, in which case racemic **22** was used instead. Thus, the diastereomeric pair of derivatives was always observed. It is important to note that we never observed any kinetic resolution[26] when the reactions were followed from the begining up to the end, even with the most hindered alcohols tested (see for example, 2-*tert*-butylcyclohexan-1-ol (**18**), or borneol (**28**) in Table III or tertiary alcohols in Table V). The integration of the signals for these racemic mixtures always corresponds to 50:50 (±2%).

Simple secondary alcohols (Table III, entries 1–5) are clearly distinguished, and their purity could be accurately measured. More hindered ones such as (–)-menthol (**26**), (+)-neomenthol (**27**), and (–)-borneol (**28**) (Table III, entries 6–9) display very large $\Delta\delta$ values. In the case of menthol (**26**), we purposely prepared a 99:1 mixture of the two enantiomers in order to determine the precision of our method. As shown in Figure 1 the minor enantiomer is easily distinguished. A variety of functionalized alcohols were also tested. In contrast to allylic alcohol **25** (Table III, entry 4), which reacts normally, propargylic alcohol **17** undergoes rapid [2,3] rearrangement.[27] Nevertheless, it is possible to observe the signals corresponding to **17P** which display a very high $\Delta\delta$. However, the non-C-silylated alcohols **14** and **16** rearrange too fast (see Scheme V). Such rearrangements are known to occur with complete stereocontrol. Thus, we hoped to be able to determine the optical purity on the chiral phosphoallene **49**. However, dimethylamine, produced by cleavage of the exocyclic P–N bond, reacted with the allene to give ultimately the enamine **50**. Such a process was already described a few years ago by Sturtz[28a] and Altenbach.[28b,c] Thus, the determination of the optical purity of propargylic alcohols is better performed with our previous reagent **8** which cannot give rise to such a rearrangement (see above).

Another drawback was encountered with diols, such as 1,3-butanediol (**30**) (entry 12) which cyclizes into a diox-

(25) Gerrard, W.; Hudson, H. R. *Organic Phosphorus Compounds*; Kosolapoff, G. M.; Maier, L., Eds.; Wiley-Interscience: New York, 1973; Vol. 5.

(26) See, for example: Dutcher, J. S.; Mc Millan, J. G.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 2663.

(27) (a) Landor, S. R. In *The Chemistry of the Allenes*; Academic Press: London, 1982. (b) Schuster, H. F.; Coppola, G. M. In *Allenes in Organic Synthesis*; John Wiley: New York, 1984. (c) Kitano, Y.; Matsumoto, T.; Sato, F. *Tetrahedron* **1988**, *44*, 4073. (d) Curtin, M. L.; Okamura, W. H. *J. Org. Chem.* **1990**, *55*, 5278.

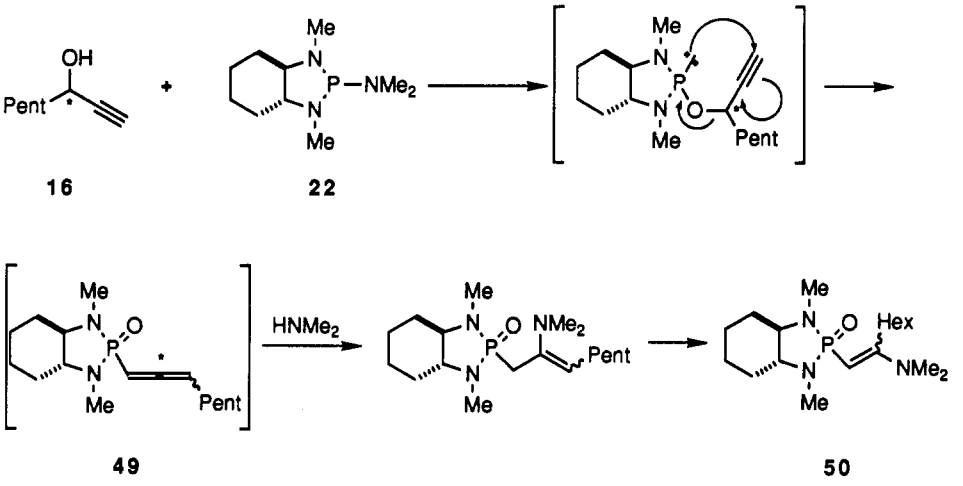
(28) (a) Sturtz, G. *Bull. Soc. Chim. Fr.* **1967**, 1345. (b) Altenbach, H. J.; Korff, R. *Tetrahedron Lett.* **1981**, *22*, 5175. (c) Altenbach, H. J.; Korff, R. *Ang. Chem. Suppl.* **1982**, 777. (d) Denmark, S. E.; Marlin, J. E. *J. Org. Chem.* **1991**, *56*, 1003.

Table II. Evaluation of Reagents 20, 21, and 22 with 2-Butanol (11)

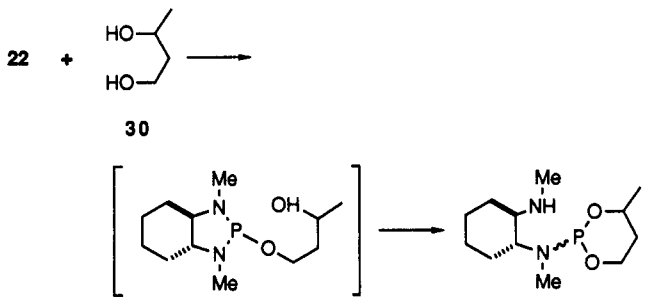
entry	phosphorus reagent	δ (ppm) ^{31}P of the diastereomers[a]	product no.	Δδ (ppm)	δ (ppm) ^{31}P of the sulfurated diastereomers[a]	product no.	Δδ (ppm)
1	**20**	142.295 and 140.478	**11Pc**	1.817	82.448 and 82.111	**11PSc**	0.337
2	**21**	124.109	**11Pa**	0.0	76.726 and 76.592	**11PSa**	0.134
3	**22**	139.387 and 135.685	**11Pb**	3.702	86.474 and 86.205	**11PSb**	0.269

[a] Taken in C_6D_6.

Scheme V



Scheme VI



aphospholane derivative with cleavage of the diazaphospholane ring (Scheme VI). The phosphorus atom becomes chiral, and many signals appear in the ^{31}P NMR spectrum. For such alcohols, camphanyl boronic acid was recently proposed as CDA.[29]

(*S*)-(−)-Ethyl lactate (**31**) and (*S*)-(+)benzoin (**32**)[30] are easily enolizable alcohols. Indeed, an aged bottle of **31** exhibited only 35% ee whereas a freshly purchased one was enantiomerically pure. No enolization was observed during the derivatization procedure. In this case, we have also checked the ee via the MTPA derivative (entry 13). Alcohol **34**[31] (Table III, entry 17) was chosen because of the possibility of β-elimination of the derivatives **34P** or **34PS** to give the corresponding enone–chalcone. However, this reaction did not take place. Finally we should note that β-chloro- **33** or β-amino- (from (+)-ephedrine (**35**)) alcohols (Table III, entries 15 and 17) also behave normally.

Thus, reagent **22** shows excellent reactivity toward hindered alcohols, and yet it is very mild toward sensitive functionalities. Tertiary alcohols are known to be among the most difficult cases, giving rise to elimination products

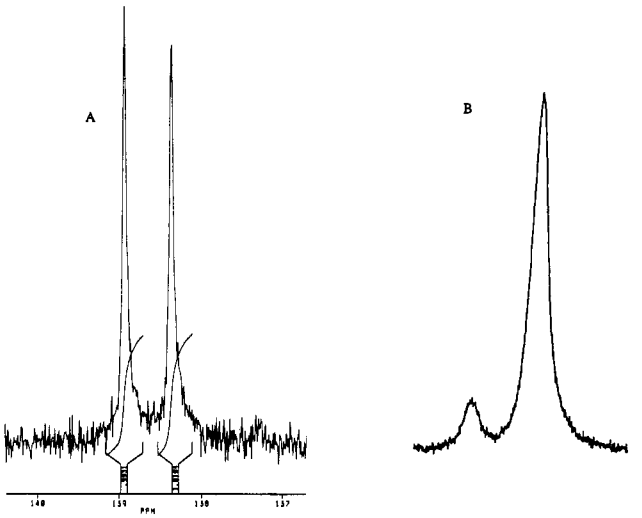


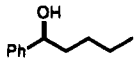
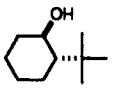
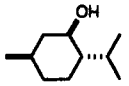
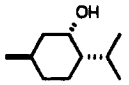
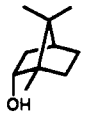
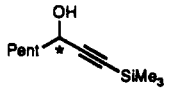
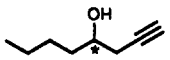
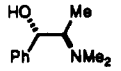
Figure 2. (A) ^{31}P NMR (100.61 MHz) spectrum of racemic linalool (**19P**). (B) ^{31}P NMR (36.22 MHz) spectrum of (*S*)-isopropylidene glycerol **44P** (ee 76.4%).

or displaying strong kinetic resolution.[1] In our hands, linalool (**19**) (Table IV, entry 1) reacted very well, but gave only a small difference in chemical shift of derivatives **19P** and none for the thio derivative **19PS**. Nevertheless, as shown in Figure 2A, the ^{31}P NMR peaks for diastereomeric derivatives **19P** show base line separation. The determination of the optical purity of linalool was previously determined with a chiral shift reagent.[32] Two other tertiary alcohols, **36** and **37**, were tested. Only the benzylic alcohol **37** could be clearly resolved, whereas alcohol **36** was not. Thus, it seems that the difference in chemical shift is sensitive not only to steric factors but also to stereoelectronic effects as well.

Another aspect of the behavior of **22** was tested with primary alcohols (Table V). We wished to determine how

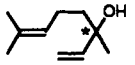
(29) Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1988**, *29*, 6063.
(30) The purity of benzoin has always been measured by polarimetry.
(31) The purity of this keto alcohol was previously analyzed through its MTPA derivative: Mashraqui, S. H.; Kellog, R. M. *J. Org. Chem.* **1984**, *49*, 2513.
(32) Ohwa, M.; Kogure, T.; Eliel, E. L. *J. Org. Chem.* **1986**, *51*, 2599.

Table III. Evaluation of Reagent 22 with Various Secondary Alcohols

entry	alcohol structure	R	no.	δ (ppm) of PIII derivative[a]	no.	Δδ (ppm)	δ (ppm) of thio derivative[a]	no.	Δδ (ppm)	enantiomeric excess % by 22	enantiomeric excess % by other means
1		Et	11	139.387 and 135.685	11Pb	3.702[b]	86.474 and 86.205	11PSb	0.269		
2		nHex	(*S*)-12	139.724 and 135.551	12P	4.173[b]	86.205 and 85.936	12PS	0.269	91.4 ≥98	89.0,[c] 92.4,[d] 93.0,[e] 98.0[c]
3		Ph	24	136.695 and 134.945	24P	1.750[f-h]	87.167 and 86.763	24PS	0.404		
4		CH=CH$_2$	25	137.435 and 136.897	25P	0.538[m]	86.542 and 86.272	25PS	0.270		
5			(*S*)-15	144.234 and 135.282	15P	8.952	86.904 and 85.948	15PS	0.956	44.8	42.0,[i] 44.2[e]
6			18[j]	139.070 and 136.224	18P	4.846	84.590 and 83.719	18PS	0.871		
7			(−)-26	142.954 and 136.995	26P	6.259[k,l]	86.107 and 85.703	26PS	0.404	81.2 96.6	82.3,[c] 79.04,[d] 98.0[c]
8			(+)-27	142.349 and 136.157	27P	6.192	86.206 and 85.600	27PS	0.606	100	100 (commercial product)
9			(−)-28	139.993 and 130.301	28P	9.692	87.753 and 87.100	28PS	0.673	≥98	100 (commercial product)
10			17	147.061 and 130.840	17P	16.221	see text	17PS			
11			29	140.397 and 137.301	29P	3.096	86.676 and 86.272	29PS	0.404		
12		CH_2CH_2-OH	30	see text							
13		COOEt	(*S*)-31	137.368 and 134.003	31P	3.365	87.686 and 87.349	31PS	0.337	35 100	34.9,[i] 37.6,[d] 100 (commercial product)
14		CO-Ph	(*S*)-32	135.272 and 131.513	32P	2.759	87.484 and 87.147	32PS	0.337	≥96	100 (commercial product)
15		$CHCl_2$	33	143.964 and 131.782	33P	12.182	87.686 and 86.676	33PS	1.010		
16		CH_2CO-Ph	34	139.657 and 134.071	34P	5.586	86.004 and 85.600	34PS	0.404		
17			(+)-35	143.089 and 131.647	35P	11.442	87.551 and 86.205	35PS	1.346	100	100 (commercial product)

[a] Taken in C_6D_6; the underlined values are those of the major enantiomer. [b] See Table I for comparative data with literature reports. [c] Artificial mixture made by weighting each enantiomer or a pure enantiomer with the racemic material. [d] Determined from MTPA derivative. [e] Determined by GC analysis of the sulfurated deriv. PS (see text). [f] Reference 12b: 0.432 ppm. [g] Reference 12c: 0.938 ppm. [h] Reference 12a: 0.321 ppm. [i] Determined by polarimetry. [j] Racemic material; relative stereochemistry shown. [k] Reference 15: 0.137 ppm. [l] Reference 12a: 0.568 ppm. [m] Reference 12a: 0.247 ppm.

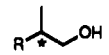
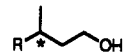
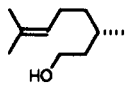
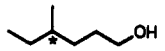
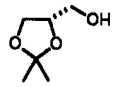
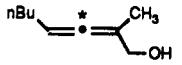
Table IV. Evaluation of Reagent 22 with Various Tertiary Alcohols

entry	alcohol structure	R	no.	δ (ppm) of the P^{III} derivative[a]	no.	Δδ (ppm)	δ (ppm) of the sulfurated derivative[a]	no.	Δδ (ppm)
1			19	133.330 and 132.724	19P	0.606	79.744	19PS	0
2		*n*-Pent	36	136.427	36P	0	79.352	36PS	0
3		Ph	37	138.446 and 136.718	37P	1.728	80.141 and 80.025	37PS	0.118

[a] Taken in C_6D_6.

far the stereogenic center could be from the chiral derivative and still give rise to chemical shift differentiation. Thus, primary alcohols with an α stereogenic center, such as **38** and **39**, could be easily differentiated (Table V, en-

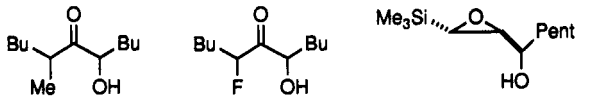
Table V. Evaluation of Reagent 22 with Various Primary Alcohols

entry	alcohol structure	R	no.	δ (ppm) of the P^{III} derivative[a]	no.	Δδ (ppm)	δ (ppm) of the thio derivative[a]	no.	Δδ (ppm)	enantiomers excess % by 22	enantiomers excess % by other means
1		Et	38	133.262 and 133.060	38P	0.202	87.349	38PS	0.019		
2		Ph	39	134.137 and 133.464	39P	0.673	87.282	39PS	0.065		
3		nBu	40	136.830 and 136.291	40P	0.539	87.686	40PS	0.016		
4		Ph	41	132.522 and 131.782	41P	0.740	87.215	41PS	0.054		
5			(S)-42	133.599 and 133.061	42P	0.538	87.417	42PS	0.032		
6			43	138.446	43P	0	87.429	43PS	0		
7			(+)-44	134.003 and 133.666	44P	0.337[c]	87.722	44PS	0.004	76.4	75.1,[b] 76.2[d]
8			45[e]	136.830 and 135.080	45P	1.750	88.427	45PS	0.024		
9			46	136.292 and 135.619	46P	0.673	88.898 and 88.809	46PS	0.089	78.2	80
10			47	134.205 and 133.869	47P	0.336	87.013 and 86.888	47PS	0.125		
11			48	138.849	48P[f]	0	88.009	48PS[g]	0		

[a] Taken in C_6D_6; the underlined values are those of the major enantiomer. [b] Artificial mixture made by weighting each enantiomer or a pure enantiomer with the racemic material. [c] Reference 15:0.000 ppm. [d] Determined by polarimetry. [e] Racemic material; relative stereochemistry shown. [f] Excellent separation of the diastereotopic benzylic hydrogen by ^1H NMR (C_6D_6): 4.86 ppm (d, $^3J_{PH}$ = 8.8 Hz), 4.58 ppm (d, $^3J_{PH}$ = 6.6 Hz). [g] Very good separation of the diastereotopic benzylic hydrogen by ^1H NMR ($CDCl_3$): 5.04 ppm (d, $^3J_{PH}$ = 12.7 Hz), 4.99 ppm (d, $^3J_{PH}$ = 11 Hz).

tries 1 and 2). An example, analogous to alcohol **39**, was also resolved with phosphorus CDA's **3**[12] and **5**.[15] Such alcohols can also be resolved by MTPA derivatives *with* a lanthanide shift reagent.[10b] More interestingly, a stereogenic center β to the hydroxy group (alcohols **40**, **41**, and **42**) still gives a notable Δδ value (Table V, entries 3–5). (*S*)-(−)-Citronellol (**42**) (Table V, entry 5) could, thus, be conveniently evaluated. Its optical purity was previously measured after oxidation to citronellic acid and derivatization with chiral ethyl naphtylamine by high-resolution liquid chromatographic analysis on microparticulate silica column.[33] Another possibility is the oxidation to the corresponding aldehyde whose ee was conveniently measured through chiral aminal formation.[18c] An α-allenic alcohols such as **47** (Table IV, entry 10), with axial chirality, was also cleanly evaluated with our reagent. Such alcohols usually need a lanthanide shift reagent *and* a chiral derivatizing agent to be distinguished![34] However, alcohols with a γ stereogenic center, such as alcohol **43** (entry 6), were no longer distinguished. (*S*)-(+)-Isopropylideneglycerol (**44**) (Table V, entry 7) is known to be an extremely difficult case.[35] Although thio derivative **44PS** could not be very clearly resolved, the simple derivative **44P** was well separated (see Figure 2B). Finally, α-epoxy alcohols **45** and **46** (Table V, entries 8 and 9), are also distinguished, and the ee of **46**,[36] obtained through

Chart III

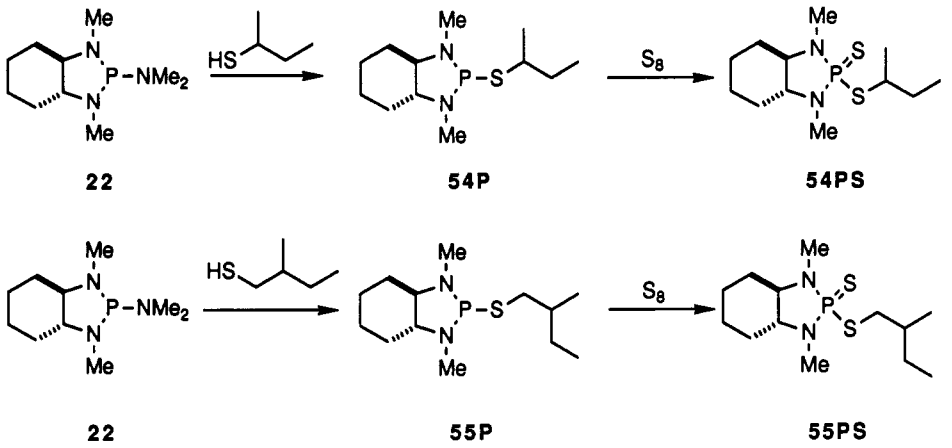


51 **52** **53**

Sharpless' asymmetric epoxidation, could be accurately measured. The MTPA derivative of epoxide **46** did not give a base line separation. Epoxy alcohols, obtained through Sharpless' asymmetric epoxidation, were usually estimated through either the MTPA derivative or with $Eu(hfc)_3$ shift on the acetate.[37] The last example shown in Table V concerns the α-deuterioalcohol **48**. The ee of such alcohols could previously be determined with lanthanide shift[38] or combination of MTPA derivative *and* lanthanide shift[39] on the α-diastereotopic protons. By ^{31}P NMR, it was not possible to observe two differentiated signals. However, by ^1H NMR, the two α-hydrogens of the phosphorus derivative of Ph–CH_2–OH (as they also are on **48**) are diastereotopic and very well resolved. As shown in Figure 3, integration of these protons on the deuterated derivatives **48P** or **48PS** would allow an accurate deter-

(33) Bergot, B. J.; Anderson, R. J.; Schooley, D. A.; Henrick, C. A. *J. Chromatogr.* **1978**, *155*, 97.
(34) (a) Claesson, A.; Olsson, L.; Sullivan, G. R.; Mosher, H. S. *J. Am. Chem. Soc.* **1975**, *97*, 2919. (b) Olsson, L.; Claesson, A. *Acta Chem. Scand.* **1977**, *B31*, 614. (c) Gooding, O. W.; Beard, C. C.; Jackson, D. Y.; Wren, D. L.; Cooper, G. F. *J. Org. Chem.* **1991**, *56*, 1083.
(35) See, for example: Mukaiyama, T.; Tanabe, Y.; Shimizu, M. *Chem. Lett.* **1984**, 401.
(36) Gosmini, C.; Dubuffet, T.; Sauvêtre, R.; Normant, J. F. *Tetrahedron: Asymmetry* **1991**, *2*, 223.
(37) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. (c) Pelter, A.; Ward, R. S.; Little, G. M. *J. Chem. Soc., Perkin Trans 1* **1990**, 2775.
(38) (a) Gerlach, H.; Zagalak, B. *J. Chem. Soc., Chem. Commun.* **1973**, 274. (b) Schwab, J. M. *J. Am. Chem. Soc.* **1981**, *103*, 1876. (c) Parker, D. J. *J. Chem. Soc., Perkin Trans. 2* **1983**, 83.
(39) Reich, C. J.; Sullivan, G. R.; Mosher, H. S. *Tetrahedron Lett.* **1973**, 1505.

Scheme VII



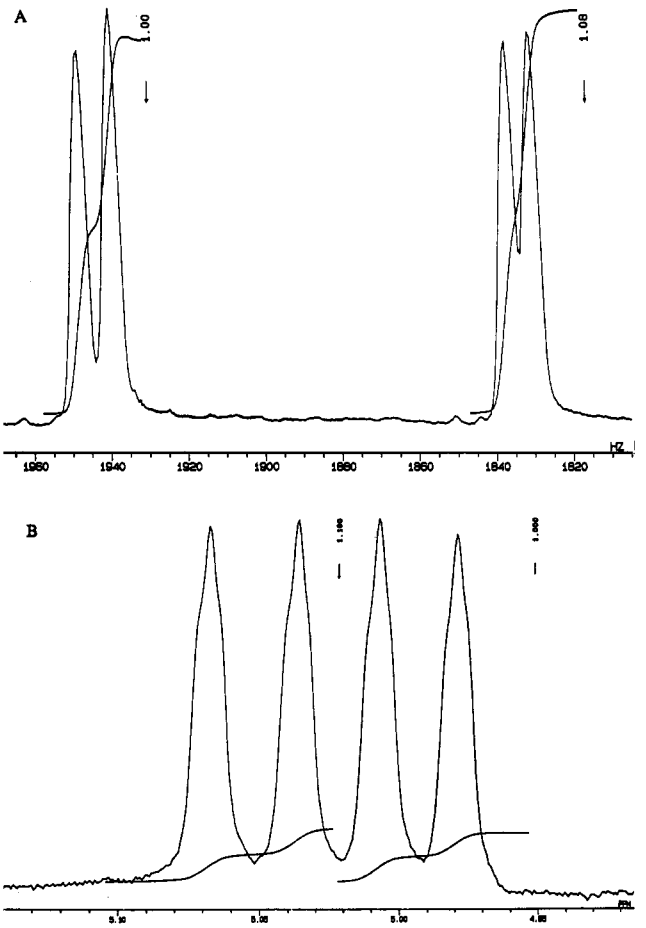


Figure 3. ^{1}H NMR (400 MHz) spectra of the benzylic protons of **48P** (A) and **48PS** (B).

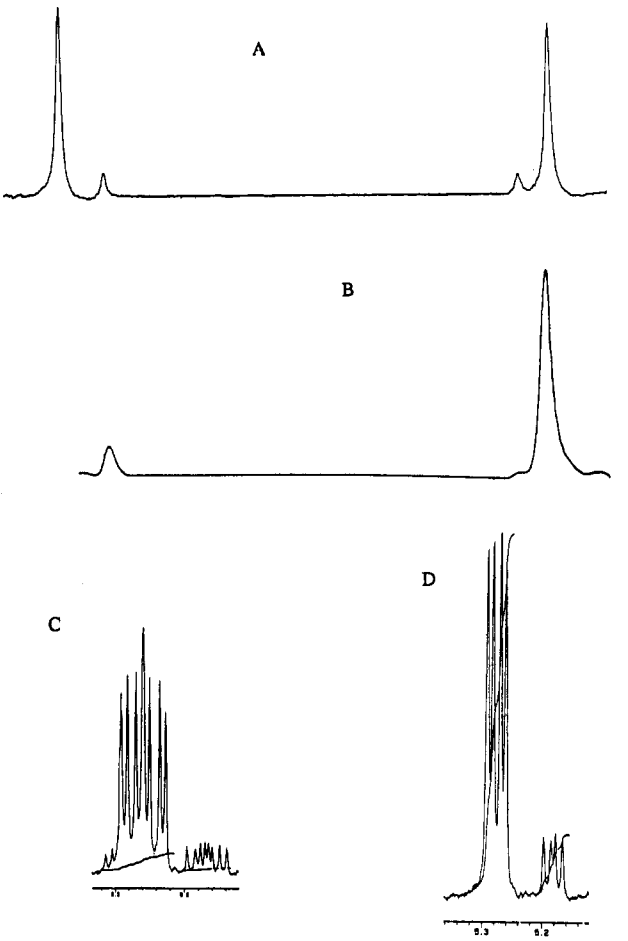


Figure 4. (A) ^{31}P NMR (36.22 MHz) spectrum of racemic **51P**. (B) Same spectrum of optically pure **51P**. (C) Part of the ^{1}H NMR (400 MHz) spectrum of MTPA derivative of racemic **51**. (D) Same ^{1}H NMR (400 MHz) spectrum of optically pure **51**.

mination of the optical purity of such alcohols.

Our reagent **22** distinguishes diastereomers as well as enantiomers. Thus, α-keto alcohol **51**[36] (Chart III) has two stereogenic centers and could be obtained as a racemic mixture (erythro:threo = 85:15) or as enantiomerically pure material. ^{31}P NMR clearly shows four singlets corresponding to the racemic material (Figure 4A); the enantiomerically pure product gives one singlet for each diastereoisomer (Figure 4B). Compound **51** was also analyzed through its MTPA derivative; only ^{1}H NMR (400 MHz) could distinguish partially the four signals of the -CH(OH)- (Figure 4C and D). In a similar manner, it was possible to analyze the even more sensitive alcohol **52**[36] (Chart III).

Epoxy alcohol **53** also possesses several stereogenic centers (Chart III). Epoxidation of the corresponding racemic (*E*)-allylic alcohol with *m*-CPBA gave a 2:1 mixture of erythro and threo diastereoisomers. Analysis of this material with reagent **22** gave the racemic mixture **53P**, which displays fours distinct signals (Figure 5). The optically and diastereomerically pure material could be obtained through Sharpless' epoxidation.[40] The ^{31}P NMR spectrum of its derivative **53P** shows only one singlet. The

(40) Kitano, Y.; Matsumoto, T.; Sato, F. *J. Chem. Soc., Chem. Commun.* **1986**, 1323.

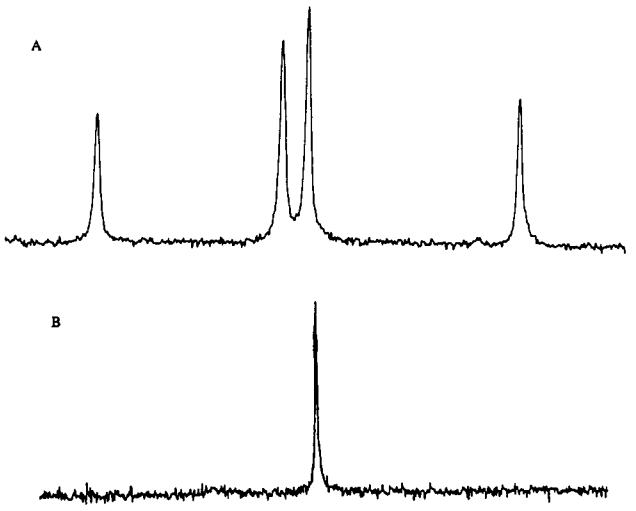


Figure 5. (A) ^{31}P NMR (36.22 MHz) spectrum of racemic erythro and threo **53P**. (B) Same spectrum of optically pure erythro **53P**.

optical purity of this epoxy alcohol was previously analyzed as the corresponding acetate with $Eu(dppm)_3$.[41]

Reagent **22** is not restricted to the analysis of the optical purity of alcohols. We have also briefly examined its applicability to *thiols*.[42] Thus, secondary thiol **54** (Scheme VII) reacted easily under the usual conditions to afford derivatives **54P**. Again, the spectrum displays an excellent separation of the signals ($\Delta\delta$ = 1.817 ppm). This derivative could also be converted to derivative **54PS** and, again, the two signals are very well separated ($\Delta\delta$ = 0.740 ppm). The primary chiral thiol **55** was also clearly resolved ($\Delta\delta$ = 0.468 ppm for **55P** and $\Delta\delta$ = 0.0646 ppm for **55PS**).

In most of the examples shown up to now, we have also done the ^1H and ^{13}C NMR spectra. In almost every case it was possible to find signals allowing clean integration of the diastereomeric pair and thus to confirm the values of ee measured by ^{31}P NMR spectroscopy. Quite often, the phosphorus moiety induces strong differences in the diastereotopic protons in the molecule. However, care should be taken on the duplication of signals owing to the strong coupling with the phosphorus atom.

One of the attractive features of the MTPA derivatives is the possibility of complementary analyses by GC or HPLC.[1] In our case, the thio derivatives **12PS–54PS** are stable enough to be also analyzed by these analytical techniques. Thus, derivatives **11PS**, **12PS**, **14PO**, **15PS**, **16PO**, **17PO**, **18PS**, **24PS**, **25PS**, **27PS**, **28PS**, **29PS**, **33PS**, **41PS**, **42PS**, **44PS**, and **47PS** were subjected to GC analysis on a capillary glass column (SE 30, 25 m). Among the thio derivatives tested, **11PS**, **12PS**, **14PO**, **15PS**, **16PO**, **18PS**, **24PS**, **25PS**, **28PS**, and **33PS** gave clean base line separation (see Figure 6); **27PS**, **29PS** and **42PS** were partially resolved; **17PO**, **41PS**, and **44PS** were not separated at all; and **47PS** decomposed. Perhaps different kinds of stationary phases could be more efficient, but no attempt was made to check this point. Some other derivatives were of too high molecular weight for GC analysis. HPLC is not subject to such restrictions, and compounds **27PS**, **28PS**, and **33PS** were also analyzed by this technique (Prolabo SIL 1 S5 W, 15 cm × 4.6 mm column). Clean base line separation was obtained with the two first

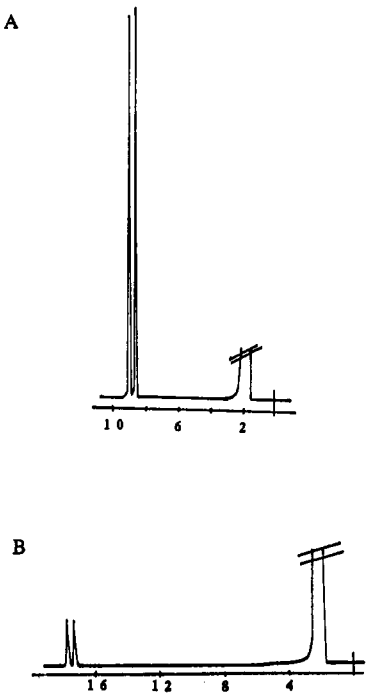


Figure 6. GC analyses of racemic **12PS** (A) and **25PS** (B).

derivatives. Although we were less successful with HPLC than with GC, these analytical methods are complementary. They offer, in fact, one more confirmation of the NMR measurements.

Conclusions

This survey of various CDAs' based on phosphorus derivatives of our previously described chiral diamines, with a C_2 axis of symmetry, shows that the trivalent phosphorous heterocycle **22** is an extremely powerful reagent for the determination of the enantiomeric purity of alcohols and thiols. After derivatization with this reagent two different measurements may be performed by ^{31}P NMR spectroscopy. Complementary analyses may be done by ^1H and ^{13}C NMR spectroscopy and also by chromatographic techniques.

Thus, various secondary alcohols have been analyzed successfully. Hindered secondary and tertiary alcohols react normally with reagent **22** without any kinetic discrimination. On the other hand, many functionalities are tolerated (epoxides, halides, amines, esters, ketones); neither epimerization of enolizable positions nor β-elimination have been observed thus far. The only limitations encountered to date concern propargylic alcohols (however, reagent **8** allows such an analysis) and 1,2- or 1,3-diols which cyclize with opening of the diazaphospholidine ring. Various chiral primary alcohols having an α or β stereogenic center, and even axial chirality in all allenic alcohol, could be efficiently distinguished. Extension of this study to other functional groups, as well as to the determination of absolute configuration of chiral alcohols are presently under way.

Experimental Section

^{31}P NMR spectra were recorded at 36.22 MHz on a JEOL FX 90 instrument and ^1H and ^{13}C NMR spectra on a Brucker AC 200 or Jeol GSX 400 instruments. Chemical shifts are expressed with TMS as internal standard or H_3PO_4 as external standard. Values in italic correspond to the second diastereomer (or the minor one) when it is clearly distinct. GC analyses were performed on a capillary quartz column (SE 20, 25 m, ∅ 0.32 mm) and H_2 as gas vector. HPLC analyses were performed using a UV (λ = 220 mm)

(41) Kitano, Y.; Matsumoto, T.; Sato, F. *Tetrahedron* **1988**, *44*, 4073.
(42) For the determination of the optical purity of thiols, see: Strijtveen, B.; Feringa, B. L.; Kellog, R. M. *Tetrahedron* **1987**, *43*, 123 and references cited therein.
(43) We thank Dr. F. Marcinac (Rhône-Poulenc, Centre de Recherche des Carrières, Lyon) for the HPLC analyses.

detector and Prolabo SIL 1 S5 W (15 cm × 4.6 mm) column; flow rate 0.8 mL/min; eluent, heptane/diisopropyl ether = 95/5.

Synthesis of Chiral Diamines. The preparation of *N,N'*-dimethyl-1,2-diphenylethylene-1,2-diamine,[44,45] *N,N'*-dimethyl-1,2-[bis(*m*-trifluoromethyl)phenyl]ethylene-1,2-diamine,[18c] and *N,N'*-diisopropyl-1,2-diphenylethylene-1,2-diamine[44] was already described by us.

(*R,R*)-*N,N'*-Dimethylcyclohexane-1,2-diamine.[46] A solution of commercial (Fluka) (*R,R*)-(−)-cyclohexane-1,2-diamine (34.2 g, 0.3 mmol) in toluene (450 mL) is stirred and cooled at 0 °C, as ethyl chloroformate (71 g, 0.72 mol) and NaOH (28.8 g, 0.72 mol) dissolved in water (30 mL) are added simultaneously through different addition funnels. The addition rate is adjusted to maintain the reaction temperature between 0 and 10 °C. When this addition is over, the mixture is stirred at rt for 3 h, then the heavy precipitate is filtered off and rinsed once with CH_2Cl_2 (250 mL). The filtrate is dried on $MgSO_4$ and concentrated in vacuo. The residue is recrystallized in CH_2Cl_2 containing the minimum amount of pentane. The dicarbamate is obtained as white crystals in 87% yield. To a solution of $LiAlH_4$ (16.7 g, 0.44 mol) in THF (700 mL) is slowly added, at rt, the above dicarbamate (28.2 g, 0.11 mol). After the addition is over, the mixture is heated at reflux for 36 h. This mixture is cooled, ethylenediamine (40 mL) is slowly added, then, a 15% aqueous solution of NaOH (19 mL), and finally water (39 mL) are added. The precipitate is removed through Celite, and the filtrate is concentrated in vacuo. The residue is diluted with 250 mL of Et_2O, filtered again if needed, dried over Na_2SO_4, and concentrated. After vacuum distillation, through a 10-cm Vigreux column, the colorless diamine is obtained in 84% yield: bp 78–80 °C (18 mm); $[\alpha]^{20}_D$ −145.7° (*c* 4.47; $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 25.2 ($NHCH_3$), 31.0 ($NCHCH_2CH_2CH_2CH_2CHN$), 33.7 ($NCHCH_2CH_2CH_2CH_2CHN$), 63.4 (NHCH).

(*R,R*)-*N,N'*-Diisopropylcyclohexane-1,2-diamine.[47] A solution of commercial (Fluka) (*R,R*)-(−)-cyclohexane-1,2-diamine (2 g, 17.6 mmol) and acetone (5.1 g, 88 mmol) in EtOH (60 mL) are hydrogenated, at atmospheric pressure, in the presence of PtO_2 (100 mg) as catalyst. After the absorption of the theoretical amount of H_2, the catalyst is separated by filtration on Celite and the solvent is removed in vacuo. Distillation of the residue affords the pure diamine in 98% yield: bp 116 °C (18 mm); $[\alpha]^{20}_D$ −125.2° (*c* 9.64; $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.95 (d, 6 H, $^2J_{HH}$ = 6.1 Hz, $NCH(CH_3)_2$), 1.05 (d, 6 H, $^2J_{HH}$ = 6.2 Hz, $NCH(CH_3)_2$), 1.1–1.25 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.5–1.8 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.9–2.2 (m, 2 H, $NCH(CH_3)_2$), 2.8 (m, 2 H, $NCHCH_2$).

Synthesis of Phosphorus CDA's 7, 8, 9, 9S, and 10. To a solution of the appropriate chiral diamine (26.8 mmol) in toluene (50 mL) is added NEt_3 (5.5 g, 53.6 mmol). To this ice-cooled solution is slowly added $POCl_3$ (4.1 g, 26.8 mmol) or $PSCl_3$ (4.53 g, 26.8 mmol). The mixture is refluxed for 4 h, and then the salts are filtered off and the solvent evaporated under vacuum. The residue is purified; **7** and **8** are distilled, **9** is flash chromatographied on silica gel, **10** is recrystallized in cold Et_2O, and **9S** was used crude. CDA's **9**, **9S**, and **10** were not used in optically pure form.

Phosphoramide 7: Yield = 74.6%; bp 180 °C (0.5 mm); $[\alpha]^{20}_D$ −45.6° (*c* 5.7; CH_2Cl_2); ^{31}P NMR ($CDCl_3$) δ 27.7; ^1H NMR ($CDCl_3$) δ 1.24 (d, 3 H, $^3J_{HH}$ = 4.4 Hz, $PNCHCH_3$), 1.28 (d, 3 H, $^3J_{HH}$ = 4.4 Hz, $PNCHCH_3$), 1.3–1.48 (m, 8 H, $PNCHCH_3$), 1.75–2.18 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 2.85–3.12 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 3.4–3.75 (m, 2 H, PNCH).

Phosphoramide 8: yield = 90%; bp 125–135 °C (0.2 mm); mp 70 °C; $[\alpha]^{20}_D$ −57.5° (*c* 5.7; CH_2Cl_2); IR (KBr) 1280 cm^{-1}; ^{31}P NMR (C_6D_6) δ 26.9; ^{31}P NMR ($CDCl_3$) δ 30.3; ^1H NMR ($CDCl_3$) δ 1.08–1.52 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.77–2.15 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 2.45–2.77 (m, 7 H, $PNCH_3$ and PNCH), 2.87 (m, 1 H, PNCH); ^{13}C NMR ($CDCl_3$) δ 12.23, 14.21 ($NCHCH_2CH_2CH_2CH_2CHN$), 27.00 (d, $^3J_{PC}$ = 12.7 Hz, $NCHCH_2CH_2CH_2CHN$), 27.69 (s, $NCHCH_2CH_2CH_2CH_2CHN$), 27.86 (s, $PNCH_3$), 28.25 (s, $PNCH_3$), 62.24 (d, $^2J_{PC}$ = 10.0 Hz, PNCH), 63.80 (d, $^2J_{PC}$ = 10.1 Hz, PNCH). Anal. Calcd for $C_8H_{16}ClN_2OP$: C, 43.15; H, 7.19; N, 12.58; P, 13.93; Cl, 15.96. Found: C, 43.21; H, 7.10; N, 12.58; P, 13.50; Cl, 16.11.

Phosphoramide 9: eluent, cyclohexane/Et_2O = 90/10; yield = 92%; ^{31}P NMR ($CDCl_3$) δ 29.3; ^1H NMR ($CDCl_3$) δ 2.45 (d, 3 H, $^3J_{HP}$ = 14.3 Hz, $PNCH_3$), 2.6 (d, 3 H, $^3J_{HP}$ = 10.5 Hz, $PNCH_3$), 3.85 (dd, 1 H, $^2J_{HH}$ = 8.5 Hz, $^3J_{HP}$ = 4.3 Hz, PNCH), 4.15 (d, 1 H, $^2J_{HH}$ = 8.5 Hz, PNCH), 7.2–7.38 (m, 10 H, H Ar); ^{13}C NMR ($CDCl_3$) δ 29.5 (d, $^2J_{CP}$ = 5.3 Hz, $PNCH_3$), 30.2 (d, $^2J_{CP}$ = 2.6 Hz, $PNCH_3$), 70.2 (d, $^2J_{CP}$ = 12 Hz, PNCH), 71 (d, $^2J_{CP}$ = 12 Hz, PNCH), 127.9, 128, 128.8, 128.9, 129 (C Ar), 136 (d, $^3J_{CP}$ = 12.8 Hz, C quat), and 137 (d, $^3J_{CP}$ = 5.5 Hz, C quat).

Thiophosphoramide 9S: yield = 100%; ^{31}P NMR ($CDCl_3$) δ 85.2; ^1H NMR ($CDCl_3$) δ 2.48 (d, 3 H, $^3J_{HP}$ = 17.5 Hz, $PNCH_3$), 2.62 (d, 3 H, $^3J_{HP}$ = 13.1 Hz, $PNCH_3$), 3.93 (dd, 1 H, $^3J_{HH}$ = 9 Hz, $^3J_{HP}$ = 2.1 Hz, PNCH), 4.16 (dd, 1 H, $^3J_{HH}$ = 9 Hz, $^3J_{HP}$ = 5.2 Hz, PNCH), 6.95–7.35 (m, 10 H, H Ar); ^{13}C NMR ($CDCl_3$) δ 30.95 (d, $^2J_{CP}$ = 4.8 Hz, $PNCH_3$), 31.28 (s, $PNCH_3$), 72.95 (d, $^2J_{CP}$ = 5.7 Hz, $PNCH_3$), 73.95 (d, $^2J_{CP}$ = 6.3 Hz, PNCH), 128.95, 129.28, 129.62, 129.72, 129.95, 130.01 (C Ar), 135.95 (d, $^3J_{CP}$ = 13.6 Hz, C quat), 136.95 (d, $^3J_{CP}$ = 4.3 Hz, C quat).

Phosphoramide 10: yield = 56%; ^{31}P NMR ($CDCl_3$) δ 29.6; ^{19}F NMR ($CDCl_3$) δ −63.35 (s, CF_3), −63.46 (s, CF_3); ^1H NMR ($CDCl_3$) δ 2.48 (d, 3 H, $^3J_{HP}$ = 14.3 Hz, $PNCH_3$), 2.63 (d, 3 H, $^3J_{HP}$ = 10.3 Hz, $PNCH_3$), 3.86 (d, 1 H, $^3J_{HH}$ = 10.5 Hz, PNCH), 4.17 (dd, 1 H, $^3J_{HH}$ = 8.5 Hz, $^3J_{HP}$ = 3.9 Hz, PNCH), 7.15–7.7 (m, 8 H, H Ar).

Synthesis of Phosphorus CDA's 20, 21, and 22. The appropriate chiral diamine (28.35 mmol) and hexamethylphosphorous triamide (5.78 g, 35.43 mmol) are heated neat at 150 °C for 96 h. A slow stream of N_2 is passed through the flask in order to remove the formed dimethylamine. The reaction may be followed by ^{31}P NMR or by checking that no more dimethylamine is evolved. Excess of $P(NMe_2)_3$ is removed under pump vacuum (0.05 mm), and the desired product is directly distilled (**21** and **22**) at the same pressure. However, CDA **20** could not be distilled or chromatographed and was used crude. These compounds are very sensitive to moisture. They are stored in benzene (or C_6D_6) or toluene solution under Ar at 4 °C and kept unalterated at least for 3–6 months. Only CDA **22** was prepared in optically pure form.

Diazaphospholidine 20: yield = 100%; ^{31}P NMR ($CDCl_3$) δ 124.5; ^1H NMR ($CDCl_3$) δ 2.24 (d, 3 H, $^3J_{HP}$ = 12.4 Hz, NCH_3), 2.43 (d, 3 H, $^3J_{HP}$ = 7.7 Hz, NCH_3), 2.85 (d, 6 H, $^3J_{HP}$ = 7.6 Hz, $N(CH_3)_2$), 3.69 (d, 1 H, $^3J_{HH}$ = 8.5 Hz, CHC_6H_5), 4.14 (dd, 1 H, $^3J_{HH}$ = 9.1 Hz, $^3J_{HP}$ = 2.5 Hz, CHC_6H_5), 7.03–7.25 (m, 10 H, H Ar); ^{13}C NMR ($CDCl_3$) δ 30.89 (d, $^2J_{CP}$ = 9.9 Hz, NCH_3), 34.37 (d, $^2J_{CP}$ = 34.6 Hz, NCH_3), 37.88 (d, $^2J_{CP}$ = 17.7 Hz, $N(CH_3)_2$), 76.07 (d, $^2J_{CP}$ = 10 Hz, CHN), 76.84 (d, $^2J_{CP}$ = 4.9 Hz, CHN), 128.43, 128.22, 128.17, 127.94, 127.55, 127.44 (C Ar), 139.98 (s, C quat), 140.37 (d, $^3J_{CP}$ = 6.4 Hz, C quat).

Diazaphospholidine 21: yield = 86%; bp 95–100 °C (0.4 mm); ^{31}P NMR ($CDCl_3$) δ 99.1; ^1H NMR ($CDCl_3$) δ 0.85–1.45 (m, 16 H, $(CH_3)_2CH$ and CH_2CH_2CH), 1.64–1.88 (m, 2 H, CH_2CHN), 1.93–2.18 (m, 2 H, CH_2CHN), 2.4 and 2.75 (m, 7 H, $N(CH_3)_2$ and $CH(CH_3)_2$), 2.85–3 (m, 1 H, $CH(CH_3)_2$), 3.2–3.5 (m, 2 H, CHNP).

Diazaphospholidine 22:[46b] yield = 85%; bp 59–61 °C (0.5 mm); $[\alpha]^{25}_D$ −100.4° (*c* 2.7; C_6H_6); ^{31}P NMR (C_6D_6) δ 122.5; ^1H NMR (C_6D_6) δ 0.95–1.15 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.55–1.65 (m, 2 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.83–1.93 (m, 2 H, $NCHCH_2CH_2CH_2CH_2CHN$), 2.2–2.72 (m, 14 H, $NCHCH_2CH_2CH_2CHN$, $PNCH_3$, and $PN(CH_3)_2$); ^{13}C NMR (C_6D_6) δ 25.16, 25.32, 30.32, 30.58 ($NCHCH_2CH_2CH_2CH_2CHN$), 33.82 (s, $PNCH_3$), 34.54 (s, $PNCH_3$), 38.60 (d, $^2J_{CP}$ = 17.6 Hz, $PN(CH_3)_2$), 67.34 (d, $^2J_{CP}$ = 8.9 Hz, PNCH), 69.43 (d, $^2J_{CP}$ = 3.5 Hz, PNCH). Elemental analysis could not be performed on compound **22**, neither could high-resolution mass spectroscopy. CDA **22** was therefore sulfurated to **22S**, and high-resolution spectrum could be obtained: for $C_{10}H_{22}N_3PS$ calcd 247.1272, found 247.1265.[48]

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(48) We thank Dr. P.-H. Lambert (Institut de Recherche Servier, Paris) for the high-resolution mass spectrum.

This thio derivative **22S** discloses the following data: bp 130–135 °C (0.05 mm); yield = 92%; ^{31}P NMR (C_6D_6) δ 83.5; ^{1}H NMR (C_6D_6) δ 0.82–1.12 (m, 4 H, NCHCH$_2$*CH$_2$CH$_2$*CH$_2$CHN), 1.44–1.72 (m, 4 H, NCHC*H$_2$*CH$_2$CH$_2$C*H$_2$*CHN), 2.25–2.47 (m, 8 H, NC*H*-CH$_2$CH$_2$CH$_2$CH$_2$*CH*N and PNC*H$_3$*), 2.65 (d, 6 H, $^3J_{HP}$ = 10.8 Hz, PN(C*H$_3$*)$_2$); ^{13}C NMR (C_6D_6) δ 24.96 (s, NCHCH$_2$*CH$_2$*CH$_2$CH$_2$CHN), 27.75 (d, $^2J_{CP}$ = 4.7 Hz, PNC*H$_3$*), 28.75, 29.19, 29.55 (NCH*CH$_2$*CH$_2$CH$_2$CH$_2$CHN), 30.40 (d, $^2J_{CP}$ = 3.4 Hz, PNC*H$_3$*), 38.28 (d, $^2J_{CP}$ = 4.0 Hz, PN(C*H$_3$*)$_2$), 64.87 (d, $^2J_{CP}$ = 7.4 Hz, PNCH), 65.41 (d, $^2J_{CP}$ = 6.0 Hz, C*H*NP).

Procedure for Derivatization with Pentavalent Phosphorus CDA's 8, 9, 9S, and 10. The required alcohol (0.3 mmol) is added to a suspension of NaH (0.33 mmol) in THF (5 mL). The mixture is stirred for 0.5 h at rt, then the selected CDA **7**, **8**, **9**, **9S**, or **10** (0.33 mmol) is added, and refluxing is started. After 2 h, aqueous NH_4Cl (5 mL) is added, the water phase is extracted (2 × 10 mL), and the organic extracts are dried over Na_2SO_4. The solvents are evaporated in vacuo, and the residue is transferred into the NMR tube. For GC and HPLC analyses, the contents of the NMR tube are used directly. In some cases, elemental analyses were performed, although such analyses were not systematically done, due to the analytical nature of this study.

Procedure for Derivatization with Trivalent Phosphorus CDA 22. Into a flame-dried small (5-mL) flask, under a stream of Ar, is placed CDA **22** (550 μL of a 0.2 M solution in C_6H_6; 0.11 mmol). The alcohol to be analyzed (0.1 mmol) is added and stirring is continued (2–15 h) until no more Me_2NH is evolved (check with humid pH paper). A more careful control may be done by taking an aliquot and adding it to a suspension of sulfur (S_8) in Et_2O (1 mL). A GC or TLC analysis indicates if any starting alcohol is left. When the reaction is over, the contents of the flask are transferred into an NMR tube and 100 μL of C_6D_6 is added for locking. Once the first ^{31}P NMR analysis is done, sulfur (S_8, 10 mg, 0.04 mmol) is added at once. The thio derivative is formed instantaneously, and a new ^{31}P NMR analysis is done. ^{1}H and ^{13}C NMR spectra could also be recorded, although this was not done on all the alcohols. For GC and HPLC analyses, the contents of the NMR tube (after reaction with sulfur) is purified on a preparative TLC, mainly to remove excess sulfur. In most cases the eluent is cyclohexane/EtOAc = 95/5.

Derivatives of Table I. Derivative 11POb: ^{31}P NMR ($CDCl_3$) δ 24.393 and *24.056* ($\Delta\delta$ = 0.337).

Derivative 11POc: eluent, cyclohexane/Et_2O = 50/50; yield = 92%; ^{31}P NMR (C_6D_6) δ 24.701 and *24.226* ($\Delta\delta$ = 0.475); ^{1}H NMR ($CDCl_3$) δ 1.05 (m, 3 H, CH$_2$C*H$_3$*), 1.4 (m, 3 H, CHC*H$_3$*), 1.72 (m, 2 H, CHC*H$_2$*CH$_3$), 2.48 (m, 6 H, PNC*H$_3$*), 3.85 (2 H, PNC*H*), 4.55 (m, 1 H, POC*H*), 6.9–7.2 (m, 10 H, H Ar); ^{13}C NMR ($CDCl_3$) δ 9.70, 9.80 (CH$_2$*CH$_3$*), 21.58, 21.66, 21.75, 21.80 (CH*CH$_3$*), 29.97, 30.02, 30.10, 30.15, 30.63, 30.76, 30.82, 30.88 (CH*CH$_2$*CH$_3$ and PNC*H$_3$*), 70.62, 70.66, 70.85, 70.89, 71.43, 71.45, 71.68 (PN*C*H), 75.10, 75.25, 75.56, 75.72 (PO*C*H), 127.63, 127.66, 127.99, 128.07, 128.21, 128.46, 128.51 (C Ar), 137.90, 138.10, 138.82, 138.85, 138.96 (C Ar).

Derivative 11PSc: eluent, cyclohexane/AcOEt = 95/5; yield = 80%; bp 170 °C (0.1 mm); ^{31}P NMR (C_6D_6) δ 82.448 and *82.111* ($\Delta\delta$ = 0.337); ^{1}H NMR ($CDCl_3$) δ 1.01 (t, 3 H, $^3J_{HH}$ = 7.5 Hz, CH$_2$C*H$_3$*), and *1.03* (t, 3 H, $^3J_{HH}$ = 7.5 Hz, CH$_2$C*H$_3$*), 1.36 (m, 3 H, CHC*H$_3$*), 1.72 (m, 2 H, CHC*H$_2$*CH$_3$), 2.45 (m, 6 H, PNC*H$_3$*), 3.9–4.06 (m, 2 H, PNC*H*), 4.62 (m, 1 H, POC*H*), 7.06–7.30 (m, 10 H, H Ar); ^{13}C NMR ($CDCl_3$) δ 9.78 (s, CH$_2$*CH$_3$*), 21.17, 21.28, 21.48 (CH*CH$_3$*), 29.49, 29.55, 29.72, 29.77 (PNC*H$_3$*), 30.30, 30.42, 30.49 (OCHC*H$_2$*), 31.54, 31.65, 31.74 (PNC*H$_3$*), 71.32, 71.46, 73.00, 73.12, 73.26 (PN*C*H), 76.16, 76.32, 76.84, 76.99 (PO*C*H), 127.62, 128.04, 128.09, 128.22, 128.50, 137.72, 137.92, 138.67, 138.81 (C Ar). Anal. Calcd for $C_{20}H_{27}N_2OPS$: C, 64.17; H, 7.22; N, 7.49. Found: C, 63.98; H, 7.27; N, 7.43.

Derivative 11POd: eluent, cyclohexane/Et_2O = 50/50; yield = 85%; ^{31}P NMR (C_6D_6) δ 24.230 and *23.691* ($\Delta\delta$ = 0.539); ^{19}F NMR (C_6D_6) δ –62.54 (s, C*F$_3$*) and –62.66 (s, C*F$_3$*); ^{1}H NMR (C_6D_6) δ 0.7 (m, 3 H, CH$_2$C*H$_3$*), 1.05 (m, 3 H, CHC*H$_3$*), 1.3 (m, 2 H, C*H$_2$*CH$_3$), 1.93 (m, 6 H, PNC*H$_3$*), 3.35 (m, 2 H, PNC*H*), 4.4 (m, 1 H, POC*H*), 6.5–7.15 (m, 8 H, H Ar).

Derivative 12PO: eluent, cyclohexane/Et_2O = 50/50; yield = 87%; ^{31}P NMR (C_6D_6) δ 24.768 and *24.282* ($\Delta\delta$ = 0.486).

Derivative 13PO: ^{31}P NMR ($CDCl_3$) δ 24.634 and *23.998* ($\Delta\delta$ = 0.636).

Derivative 14PO: colorless oil; eluent, Et_2O/CH_2Cl_2 = 80/20; yield = 97%; ^{31}P NMR ($CDCl_3$) δ 23.422 and *22.749* ($\Delta\delta$ = 0.673); ^{1}H NMR ($CDCl_3$) δ 0.55–0.75 (m, 4 H, NCHCH$_2$*CH$_2$CH$_2$*CH$_2$CHN), 1.00–1.38 (m, 7 H, NCHC*H$_2$*CH$_2$C-H$_2$*CH$_2$*CHN and CHC*H$_3$*), 2.02–2.3 (m, 9 H, PNC*H$_3$*, PNC*H*, and C≡C*H*), 5.1 (m, 1 H, POC*H*); ^{13}C NMR (C_6D_6) δ 23.49 (d, $^3J_{CP}$ = 6.9 Hz, CHC*H$_3$*) and *24.10* (d, $^3J_{CP}$ = 3.8 Hz, CHC*H$_3$*), 24.44 (s, NCHCH$_2$*CH$_2$CH$_2$*CH$_2$CHN), 28.16, 28.28, 28.38, 28.50, 29.54, 30.12, 30.75 (NCHC*H$_2$*CH$_2$CH$_2$C*H$_2$*CHN and PNC*H$_3$*), 62.61, 62.74, 63.13, 63.25, 63.33, 64.48, 64.59, 64.68, 64.77 (PN*C*H and PO*C*H), 73.46 (C≡*C*H) and 84.26, 84.41 (*C*≡CH); GC analysis 160 °C, ret. time 30.0 and 30.6 min.

Derivative 15PO: eluent, cyclohexane/Et_2O = 50/50; yield = 85%; ^{31}P NMR (C_6D_6) δ 24.903 and *24.338* ($\Delta\delta$ = 0.565).

Derivative 16PO: colorless oil; eluent, CH_2Cl_2/Et_2O = 20/80; yield = 93%; IR (neat) 990, 1020, 1250, 2100 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ 23.373 and *23.437* ($\Delta\delta$ = 0.936); ^{1}H NMR ($CDCl_3$) δ 0.89 (t, $^3J_{HH}$ = 6.4 Hz, CH$_2$C*H$_3$*), 1.1–1.55 (m, 10 H), 1.7–2.05 (m, 6 H, NCHC*H$_2$*CH$_2$CH$_2$C*H$_2$*CHN and POCHC*H$_2$*), 2.4–2.7 (m, 9 H, PNC*H$_3$*, PNC*H*, and C≡C*H*), 5.05 (m, 1 H, POC*H*).

Derivatives of Table II. Derivative 11Pc: ^{31}P NMR (C_6D_6) δ 142.295 and *140.478* ($\Delta\delta$ = 1.81).

Derivative 11PSc: see above.

Derivative 11Pa: ^{31}P NMR (C_6D_6) δ 124.109 ($\Delta\delta$ = 0.000).

Derivative 11PSa: white crystals; eluent, cyclohexane/AcOEt = 95/5; yield = 70%; bp = 140 °C (0.1 mm); mp = 118.5 °C; ^{31}P NMR (C_6D_6) δ 76.726 and *76.592* ($\Delta\delta$ = 0.134); ^{1}H NMR (C_6D_6) δ 0.82–1.84 (m, 28 H), 2.85 (m, 2 H, PNC*H*), 3.88 (m, 2 H, PNC*H*(CH$_3$)$_2$), 4.78 (m, 1 H, POC*H*); ^{13}C NMR (C_6D_6) δ 10.07 (s, CH$_2$*CH$_3$*), 19.05, 19.70, 19.82, 21.35, 21.44, 21.56, 24.25, 24.40 (CH(*CH$_3$*)$_2$ and *C*H$_3$CHO), 24.79, 24.89, 25.00 (*CH$_2$*), 31.05, 31.19, 31.29 (*CH$_2$*), 32.25, 32.44, 32.60 (*CH$_2$*), 44.89, 44.99, 45.10 (N*C*H-(CH$_3$)$_2$), 46.21, 46.33 (N*C*H(CH$_3$)$_2$), 59.84, 59.97 (PN*C*HCH$_2$), 61.28, 61.33, 61.45, 61.49 (PN*C*HCH$_2$), 76.36, 76.47, 76.60 (PO*C*H).

Derivative 11Pb: ^{31}P NMR (C_6D_6) δ 139.387 and *135.685* ($\Delta\delta$ = 3.702).

Derivative 11PSb: eluent, cyclohexane/AcOEt = 95/5; yield = 78%; bp = 130 °C (0.2 mm); ^{31}P NMR (C_6D_6) δ 86.474 and *86.205* ($\Delta\delta$ = 0.269); ^{1}H NMR (C_6D_6) δ 0.78–1.05 (m, 7 H, NCH-CH$_2$*CH$_2$*CH$_2$CH$_2$CHN and CH$_2$C*H$_3$*), 1.16 (d, 3 H, $^3J_{HH}$ = 6.2 Hz, CHC*H$_3$*), and *1.19* (d, 3 H, $^3J_{HH}$ = 6.2 Hz, CHC*H$_3$*), 1.38–1.67 (m, 6 H, NCHC*H$_2$*CH$_2$CH$_2$C*H$_2$*CHN and POCHC*H$_2$*), 2.22–2.58 (m, 8 H, PNC*H$_3$* and PNC*H*), 4.7 (m, 1 H, POC*H*); ^{13}C NMR (C_6D_6) δ 10.39 (s, OCHCH$_2$*CH$_3$*), 21.85, 21.95 (OCHC*H$_3$*), 24.94 (s, NCHCH$_2$*CH$_2$CH$_2$*CH$_2$CHN), 28.11, 29.03, 29.60, 29.76 (NCHC-H$_2$CH$_2$*CH$_2$*CH$_2$CHN), 28.95 (PNC*H$_3$*), 31.07, 31.21, 31.26 (POC-HC*H$_2$*), 31.68, 31.77, 31.85 (PNC*H$_3$*), 63.51, 63.58, 63.64 (PN*C*H), 66.62, 66.73, 66.85 (PN*C*H), 75.99 (d, $^2J_{CP}$ = 7.4 Hz, *C*HOP) and *76.36* (d, $^2J_{CP}$ = 7.4 Hz, PO*C*H); GC analysis 180 °C, ret. time 14.0 and 14.4 min. Anal. Calcd for $C_{12}H_{25}N_2OPS$: C, 52.13; H, 9.11; N, 10.17; P, 11.20; S, 11.60. Found: C, 52.33; H, 9.41; N, 9.99; P, 11.08; S, 11.49.

Derivatives of Table III. Derivative 11Pb: see above.

Derivative 11PSb: see above.

Derivative 12P: ^{31}P NMR (C_6D_6) δ *139.724* (*R* enantiomer) and 135.551 (*S* enantiomer) ($\Delta\delta$ = 4.173).

Derivative 12PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 82%; ^{31}P NMR (C_6D_6) δ *86.205* (*R* enantiomer) and 85.936 (*S* enantiomer) ($\Delta\delta$ = 0.269); ^{1}H NMR (C_6D_6) 0.78–1.05 (m, 7 H, NCHCH$_2$*CH$_2$CH$_2$*CH$_2$CHN and CH$_2$CH$_2$C*H$_3$*), 1.15–1.73 (m, 17 H), 2.22–2.64 (m, 8 H, PNC*H$_3$* and PNC*H*), 4.62–4.9 (m, 1 H, POC*H*); ^{13}C NMR (C_6D_6) δ 14.76 (s, CH$_2$*CH$_3$*), 22.45, 22.57, 22.60 (CH*CH$_3$*), 23.45 (s, *CH$_2$*CH$_3$), 24.98 (s, NCHCH$_2$*CH$_2$CH$_2$*CH$_2$CHN), 26.17, 26.23 (OCHCH$_2$*CH$_2$CH$_2$*), 28.85, 29.07, 29.64, 29.80, 30.05 (NCHCH$_2$CH$_2$CH$_2$*CH$_2$*CHN and OCHCH$_2$CH$_2$*CH$_2$*), 29.00 (s, PNC*H$_3$*), 31.74, 31.85, 31.96 (PNC*H$_3$*), 32.68 (s, *CH$_2$*CH$_2$CH$_3$), 38.34, 38.40, 38.49 (OCHC*H$_2$*), 63.52, 63.60 (PN*C*H), 66.68, 66.80, 66.93 (PN*C*H), 74.78 (d, $^2J_{CP}$ = 7.8 Hz, PO*C*H), and *75.18* (d, $^2J_{CP}$ = 7.4 Hz, PO*C*H); GC analysis 240 °C, ret. time 8.7 and 9.1 min.

Derivative 24P: ^{31}P NMR (C_6D_6) 136.695 and *134.945* ($\Delta\delta$ = 1.750).

Derivative 24PS: slighly yellow oil; eluent, cyclohexane/AcOEt = 95/5; yield = 93%; ^{31}P NMR (C_6D_6) δ 87.167 and *86.763* ($\Delta\delta$ = 0.404); ^{1}H NMR (C_6D_6) δ 0.7–1.08 (m, 4 H, NCHCH$_2$*CH$_2$CH$_2$*CH$_2$CHN), 1.3–1.68 (m, 7 H, NCHC*H$_2$*CH$_2$C-

H_2CH_2CHN and $OCHCH_3$), 2.1–2.6 (m, 8 H, $PNCH_3$ and PNCH), 5.82 (m, 1 H, POCH), 7–7.4 (m, 5 H, H Ar), 144.37 (C quat); GC analysis 230 °C, ret. time 12.6 and 13.6 min.

Derivative 15P: ^{31}P NMR (C_6D_6) δ 144.234 (*S* enantiomer) and *135.282* (*R* enantiomer) (Δδ = 8.952).

Derivative 15PS: colorless oil; eluent, cyclohexane/AcOEt = 90/10; yield = 93%; IR (neat) 980, 1010, 1030, 1170 cm^{-1}; ^{31}P NMR (C_6D_6) δ 86.904 (*S* enantiomer) and 85.948 (*R* enantiomer) (Δδ = 0.956); ^1H NMR (C_6D_6) δ 0.7–1.1 (m, 7 H, CH_2CH_3 and $NCHCH_2CH_2CH_2CH_2CHN$), 1.2–2.6 (m, 18 H), 5.5 (m, 1 H, POCH), 6.9–7.45 (m, 5 H, H Ar); ^{13}C NMR (C_6D_6) δ 14.11 (s, CH_2CH_3), 22.78 (s, $CH_2CH_2CH_3$), 24.37, 24.46 ($NCHCH_2CH_2CH_2CH_2CHN$), 27.93 (s, $CH_2CH_2CH_3$), 28.16, 28.38, 28.96, 29.12 ($NCHCH_2CH_2CH_2CH_2CHN$), 28.27 ($PNCH_3$), 30.47 (d, $^2J_{CP}$ = 5.6 Hz, $PNCH_3$) and *30.85* (d, $^2J_{CP}$ = 5.6 Hz, $PNCH_3$), 38.19 (d, $^3J_{CP}$ = 5.4 Hz, $POCHCH_2$), and *38.53* (d, $^3J_{CP}$ = 8.7 Hz, $POCHCH_2$), 63.07, 63.19, 63.30 (PNCH), 65.93, 65.99, 66.13 (PNCH), 79.64 (d, $^2J_{CP}$ = 7.7 Hz, POCH) and *80.11* (d, $^2J_{CP}$ = 6.1 Hz, POCH), 127.41, 127.79, 127.97, 128.42, 128.62, 142.74, 142.83, 142.97 (C Ar); GC analysis 234 °C, ret. time 14 and 15 min.

Derivative 18P: ^{31}P NMR (C_6D_6) 139.070 and *136.224* (Δδ = 4.846).

Derivative 18PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 90%; ^{31}P NMR (C_6D_6) δ 84.590 and *83.719* (Δδ = 0.871); ^1H NMR (C_6D_6) δ 0.75–1.76 (m, 26 H), 2.15–2.75 (m, 8 H, $PNCH_3$ and PNCH), 4.5 (m, 1 H, POCH); ^{13}C NMR (C_6D_6) δ 24.91, 25.00 ($NCHCH_2CH_2CH_2CH_2CHN$), 25.48, 26.16, 26.82, 27.05, 27.69 ($POCHCH_2CH_2CH_2CH_2$), 28.79, 29.01, 29.59, 29.70 ($NCHCH_2CH_2CH_2CH_2CHN$), 28.91, 29.19 ($PNCH_3$), 29.78 ($C(CH_3)_3$) and *30.11* ($C(CH_3)_3$), 32.00 (d, $^2J_{CP}$ = 5.9 Hz, $PNCH_3$) and *32.47* (d, $^2J_{CP}$ = 4.6 Hz, $PNCH_3$), 33.52, 33.77 ($C(CH_3)_3$), 35.46, 37.13 ($POCHCH_2$), 52.29 (d, $^3J_{CP}$ = 8.7 Hz, POCHCH) and *52.70* (d, $^3J_{CP}$ = 7.4 Hz, POCHCH), 62.68 (d, $^2J_{CP}$ = 5.8 Hz, PNCH) and *63.15* (d, $^2J_{CP}$ = 5.4 Hz, PNCH), 66.99 (d, $^2J_{CP}$ = 5.9 Hz, PNCH) and *68.11* (d, $^2J_{CP}$ = 5.2 Hz, PNCH), 79.94 (d, $^2J_{CP}$ = 8.8 Hz, POCH) and *80.53* (d, $^2J_{CP}$ = 8.5 Hz, POCH); GC analysis 230 °C, ret. time 6.4 and 6.6 min.

Derivative 25P: ^{31}P NMR (C_6D_6) δ 137.435 and *136.897* (Δδ = 0.538).

Derivative 25PS: eluent, cyclohexane/AcOEt = 95/5; bp = 110–120 °C (0.1 mm); yield = 89%; ^{31}P NMR (C_6D_6) δ 86.542 and *86.272* (Δδ = 0.270); ^1H NMR (C_6D_6) δ 0.8–1.05 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.25 (t, 3 H, $CHCH_3$), 1.3–1.62 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 2.22–2.6 (m, 8 H, $PNCH_3$ and PNCH), 4.98 (m, 1 H, CH:CHH), 5.15–5.38 (m, POCH and CH:CHH); 5.8 (m, 1 H, CH:CH_2). GC analysis 180 °C, ret. time 17.0 and 17.4 min. Anal. Calcd for $C_{12}H_{23}N_2OPS$: C, 52.55; H, 8.39; N, 10.22; P, 11.31; S, 11.68. Found: C, 52.74; H, 8.57; N, 10.22; P, 11.39; S, 11.44.

Derivative 26P: ^{31}P NMR (C_6D_6) δ 142.954 (*l*-menthol) and *136.995* (*d*-menthol) (Δδ = 6.259).

Derivative 26PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 96%; ^{31}P NMR (C_6D_6) δ 86.107 (*l*-menthol) and *85.703* (*d*-menthol) (Δδ = 0.404). *l*-Menthol derivative: ^1H NMR (C_6D_6) δ 0.6–1.85 (m, 24 H), 2.18–2.65 (m, 10 H, $PNCH_3$, PNCH, $POCHCHCH(CH_3)_2$, and $POCHCH_{ax}H$), 4.52 (dtd, 1 H, $^3J_{HP}$ = 12.4 Hz, $^3J_{HHax}$ = 10.6 Hz, $^3J_{HHeq}$ = 4.5 Hz, POCH); ^{13}C NMR (C_6D_6) δ 17.06 (s, $CHCH_3CH_3$), 21.71 (s, $CHCH_3CH_3$), 22.84 (s, $CHCH_3$), 23.90 (s, $(CH_3)_2CHCHCH_2CH_2CHCH_3$), 24.97 (s, $NCHCH_2CH_2CH_2CH_2CHN$), 26.51 (s, $CH(CH_3)_2$), 28.87, 29.08, 29.62, 29.79 ($PNCH_3$ and $NCHCH_2CH_2CH_2CH_2CHN$), 32.13 (d, $^2J_{CP}$ = 8.6 Hz, $PNCH_3$), 35.17 (s, $CH_2CHCH_2CH_3$), 44.48 (s, $OCHCH_2$), 49.35 (d, $^3J_{CP}$ = 6.1 Hz, $CHCH(CH_3)_2$), 63.40 (d, $^2J_{CP}$ = 5.1 Hz, PNCH), 66.93 (d, $^2J_{CP}$ = 6.0 Hz, CHNP), 78.90 (d, $^2J_{CP}$ = 7.5 Hz, POCH), 32.22 (s, CH_2CHCH_3).

d-Menthol derivative: ^1H NMR (C_6D_6) δ 0.64–1.64 (m, 24 H), 2.18–2.68 (m, 10 H, $PNCH_3$, PNCH, $POCHCHCH(CH_3)_2$, and $POCHCH_{ax}H$), 4.49 (dq, 1 H, $^3J_{HP}$ = $^3J_{HHax}$ = 10.4 Hz, $^3J_{HHeq}$ = 4.6 Hz, POCH); ^{13}C NMR (C_6D_6) δ 16.58 (s, $CHCH_3CH_3$), 21.76 (s, $CHCH_3CH_3$), 22.86 (s, $CHCH_3$), 23.61 (s, $(CH_3)_2CHCHCH_2CH_2CHCH_3$), 24.97 (s, $NCHCH_2CH_2CH_2CH_2CHN$), 26.13 (s, $CH(CH_3)_2$), 28.84, 29.72, 29.88 ($NCHCH_2CH_2CH_2CH_2CHN$), 29.02 ($PNCH_3$), 31.99 (d, $^2J_{CP}$ = 5.7 Hz, $PNCH_3$), 32.16 (s, CH_2CHCH_3), 35.08 (s, $CH_2CH_2CHCH_3$), 44.29 (s, $OCHCH_2$), 49.47 (d, $^3J_{CP}$ = 8.8 Hz, $CHCH(CH_3)_2$), 63.24 (d, $^2J_{CP}$ = 5.4 Hz, CHNP), 67.26 (d, $^2J_{CP}$ = 5.5 Hz, CHNP), 78.33 (d, $^2J_{CP}$ = 8.2 Hz, POCH).

Derivative 27P: ^{31}P NMR (C_6D_6) δ 142.349 (−)-neomenthol *136.157* (+)-neomenthol (Δδ = 6.192).

Derivative 27PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 87%; ^{31}P NMR (C_6D_6) δ 86.206 (−)-neomenthol and *85.600* (+)-neomenthol (Δδ = 0.606); ^1H NMR (C_6D_6) δ 0.7–1.9 (m, 25 H), 2.02–2.62 (m, 9 H, $PNCH_3$, PNCH, and $POCHCH_{ax}H$), 4.85–5.08 (m, 1 H, POCH); ^{13}C NMR (C_6D_6) δ 21.39, 21.60, 21.82, 22.22, 22.88, 23.04 ($CHCH_3$ and $CH(CH_3)_2$), 24.96 (s, $NCHCH_2CH_2CH_2CH_2CHN$), 25.67, 26.24 ($POCHCHCH_2CH_2$), 26.67, 27.07 ($CHCH(CH_3)_2$), 28.65, 29.27, 29.47, 29.65 ($PNCH_3$ and CH_2CHCH_3), 28.89, 29.13, 29.80, 29.95, 30.11 ($NCHCH_2CH_2CH_2CH_2CHN$), 32.05, 32.16, 32.27 ($PNCH_3$), 35.75 (s, $CH_2CH_2CHCH_3$), 42.01 (s, $POCHCH_2$), 48.68, 48.81, 48.92, 49.11 ($CHCH(CH_3)_2$), 63.38, 63.48, 63.59, 63.68 (PNCH), 66.96, 67.08, 67.25, 67.35 (PNCH), 74.75 (d, $^2J_{CP}$ = 8.1 Hz, POCH) and *75.83* (d, $^2J_{CP}$ = 7.5 Hz, POCH); HPLC analysis eluent, heptane/iPr_2O = 80/20, ret. time 10.11 and 10.65 min.

Derivative 28P: ^{31}P NMR (C_6D_6) δ 139.993 (*l*-borneol) and *130.301* (*d*-borneol) (Δδ = 9.692).

Derivative 28PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 86%; ^{31}P NMR (C_6D_6) δ 87.753 (*l*-borneol) and *87.100* (*d*-borneol) (Δδ = 0.673); ^1H NMR (C_6D_6) δ 0.77–1.8 (m, 22 H), 2.04–2.6 (m, 10 H, $PNCH_3$, PNCH, and $POCHCH_2$), 3.55 (m, 1 H, POCH); ^{13}C NMR (C_6D_6) δ 14.17 (s, $OCHCCH_3$), 19.45 (s, $CHCH_3CH_3$), 20.49 (s, $CHCH_3CH_3$), 24.95, 28.05, 28.84, 29.07, 29.69, 29.86 ($NCHCH_2CH_2CH_2CH_2CHN$ and $POCHCCH_2CH_2CHCH_2$), 28.86, 29.16 ($PNCH_3$), 31.79 (d, $^2J_{CP}$ = 5.9 Hz, $PNCH_3$) and *32.04* (d, $^2J_{CP}$ = 5.3 Hz, $PNCH_3$), 38.05, 38.66 ($POCHCH_2$), 45.83, 46.03 ($POCHCH_2CH$), 48.10, 48.37 ($CHC(CH_3)_2$), 50.18, 50.28 (POCHC), 63.89 (s, PNCH), 66.66, 66.78 (PNCH), 82.59 (d, $^2J_{CP}$ = 8.0 Hz, POCH) and *83.13* (d, $^2J_{CP}$ = 7.6 Hz, POCH); GC analysis 250 °C, ret. time 11.2 and 11.4 min.

Derivative 29P: ^{31}P NMR (C_6D_6) δ 140.397 and *137.301* (Δδ = 3.096).

Derivative 29PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 88%; ^{31}P NMR (C_6D_6) δ 86.676 and *86.272* (Δδ = 0.404).

Derivative 31P: ^{31}P NMR (C_6D_6) δ *137.368* (*R* enantiomer) and 134.003 (*S* enantiomer) (Δδ = 3.365).

Derivative 31PS: colorless oil; eluent, cyclohexane/AcOEt = 70/30; yield = 95%; ^{31}P NMR (C_6D_6) δ *87.686* (*R* enantiomer) and 87.349 (*S* enantiomer) (Δδ = 0.337); ^1H NMR (C_6D_6) δ 0.74–1.06 (m, 7 H, $NCHCH_2CH_2CH_2CH_2CHN$ and $COOCH_2CH_3$), 1.3–1.68 (m, 7 H, $NCHCH_2CH_2CH_2CH_2CHN$ and $OCHCH_3$), 2.2–2.74 (m, 8 H, $PNCH_3$ and PNCH), 3.93 (m, 2 H, $CO_2CH_2CH_3$), 5.3 (m, 1 H, POCH); ^{13}C NMR (C_6D_6) δ 14.60 (s, $COOCH_2CH_3$); 19.24 (d, $^3J_{CP}$ = 7.7 Hz, $POCHCH_3$) and *20.08* (d, $^3J_{CP}$ = 3.8 Hz, $POCHCH_3$), 24.85 (s, $NCHCH_2CH_2CH_2CH_2CHN$), 28.55 ($PNCH_3$), 28.67, 28.90, 29.30, 29.43 ($NCHCH_2CH_2CH_2CH_2CHN$), 31.12, 31.19 ($PNCH_3$), 61.34 (s, $COOCH_2CH_3$), 63.55, 63.65 (PNCH), 66.19 (d, $^2J_{CP}$ = 7.1 Hz, PNCH) and *66.47* (d, $^2J_{CP}$ = 6.4 Hz, PNCH), 72.51, 72.62, 72.76 (POCH), 171.89, 172.13 (CO).

Derivative 32P: ^{31}P NMR (C_6D_6) δ *135.272* (*R* enantiomer) and 131.513 (*S* enantiomer) (Δδ = 2.759).

Derivative 32PS: yellow oil; eluent, cyclohexane/AcOEt = 70/30; yield = 95%; ^{31}P NMR (C_6D_6) δ *87.484* (*R* enantiomer) and 87.147 (*S* enantiomer) (Δδ = 0.337); ^1H NMR (C_6D_6) δ 0.68–1.00 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.3–1.6 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 2–2.7 (m, 8 H, $PNCH_3$ and PNCH), 6.9–8.15 (m, 11 H, POCH and H Ar); ^{13}C NMR (C_6D_6) δ 24.80 ($NCHCH_2CH_2CH_2CH_2CHN$), 28.51, 28.75 ($PNCH_3$), 28.61, 28.84, 29.08, 29.24 ($NCHCH_2CH_2CH_2CH_2CHN$), 30.61 (d, $^2J_{CP}$ = 5.6 Hz, $PNCH_3$) and *31.00* (d, $^2J_{CP}$ = 5.5 Hz, $PNCH_3$), 63.58, 63.66 (PNCH), 66.23 (d, $^2J_{CP}$ = 7.2 Hz, PNCH), and *66.44* (d, $^2J_{CP}$ = 6.7 Hz, PNCH), 81.21 (d, $^2J_{CP}$ = 6.5 Hz, POCH) and *88.08* (d, $^2J_{CP}$ = 6.0 Hz, POCH), 129.10, 129.19, 129.26, 129.38, 129.57, 129.87, 133.39, 133.56 (C Ar), 136.31, 136.38, 136.91, 137.08, 137.30, 137.39 (C quat), 195.42 (d, $^3J_{CP}$ = 6.3 Hz, CO) and 196.17 (s, CO).

Derivative 33P: ^{31}P NMR (C_6D_6) δ 143.964 and *131.782* (Δδ = 12.182).

Derivative 33PS: slighly yellow oil; eluent, cyclohexane/AcOEt = 95/5; yield = 89%; ^{31}P NMR (C_6D_6) δ 87.686 and *86.676* (Δδ = 1.010); ^1H NMR (C_6D_6) δ 0.75–0.97 (m, 4 H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.38–1.59 (m, 4 H,

NCHCH_2CH$_2$CH$_2$CH_2CHN), 1.92 (d, 3 H, $^3J_{HP}$ = 6.0 Hz, PNCH_3) and *1.99* (d, 3 H, $^3J_{HP}$ = 5.5 Hz, PNCH_3), 2.18–2.35 (m, 1 H, C*H*NP), 2.49–2.71 (m, 4 H, C*H*NP and PNCH_3), 5.67 (d, 1 H, $^3J_{HH}$ = 4.6 Hz, C*H*Cl$_2$) and *5.78* (d, 1 H, $^3J_{HH}$ = 5.7 Hz, C*H*Cl$_2$), 5.96 (dd, 1 H, $^3J_{HP}$ = 11.7 Hz, $^3J_{HH}$ = 4.6 Hz, POC*H*) and *6.10* (dd, 1 H, $^3J_{HP}$ = 14.3 Hz, $^3J_{HH}$ = 5.7 Hz, POC*H*); ^{13}C NMR (C_6D_6) δ 24.30 (s, NCHCH$_2$CH_2CH$_2$CH$_2$CHN), 28.28, 29.16 (PN*C*H$_3$), 28.46, 28.63, 28.82, 29.39, 29.54 (NCH*C*H$_2$CH$_2$CH$_2$CH$_2$CHN), 30.77 (d, $^2J_{CP}$ = 5.0 Hz, PN*C*H$_3$) and *31.05* (d, $^2J_{CP}$ = 5.5 Hz, PN*C*H$_3$), 63.53, 63.66 (PN*C*H), 66.31, 66.45 (PN*C*H), 75.05, 75.22, 75.48 (CHCHCl$_2$), 82.66, 83.16 (PO*C*H), 137.20 (C quat); GC analysis 260 °C, ret. time 11.48 and 13.7 min; HPLC analysis eluent, hepatne/iPr$_2$O = 95/5, ret. time 11.48 and 13.70 min.

Derivative 34P: ^{31}P NMR (C_6D_6) δ 139.657 and *134.071* (Δδ = 5.586).

Derivative 34PS: slighly yellow oil; eluent, cyclohexane/AcOEt = 80/20; yield = 91%; ^{31}P NMR (C_6D_6) δ 86.004 and *85.600* (Δδ = 0.404).

Derivative 35P: ^{31}P NMR (C_6D_6) 143.089 and *131.647* (Δδ = 11.442).

Derivative 35PS: colorless oil; eluent, cyclohexane/AcOEt = 70/30; yield = 85%; ^{31}P NMR (C_6D_6) δ 87.551 and *86.205* (Δδ = 1.346); ^{1}H NMR (C_6D_6) δ 0.7–1.02 (m, 4 H, NCHCH$_2$CH_2CH_2CH$_2$CHN), 1.15 (d, 3 H, $^3J_{HH}$ = 6.7 Hz, CH_3CHN(CH$_3$)$_2$) and *1.17* (d, 3 H, $^3J_{HH}$ = 6.6 Hz, (CH$_3$)$_2$NCHCH_3), 1.28–1.17 (m, 4 H, NCHCH_2CH$_2$CH$_2$CH$_2$CH_2CHN), 1.9–3.0 (m, 15 H, PNCH_3, CHN(CH_3)$_2$, PNC*H*, and C*H*CH$_3$), 5.65 (dd, 1 H, $^3J_{HH}$ = 6.5 Hz, $^3J_{HP}$ = 11.3 Hz, POC*H*) and *5.78* (dd, 1 H, $^3J_{HH}$ = 7.8 Hz, $^3J_{HP}$ = 14.4 Hz, POC*H*), 7.0–7.5 (m, 5 H, H Ar); ^{13}C NMR (C_6D_6) δ 9.90, 10.28 (CH*C*H$_3$), 24.90 (s, NCHCH$_2$*C*H$_2$CH$_2$CH$_2$CHN), 28.39, 29.20 (PN*C*H$_3$), 28.67, 28.82, 29.01, 29.51, 29.68 (NCH*C*H$_2$CH$_2$-CH$_2$CH$_2$CHN), 31.04, 31.39 (PN*C*H$_3$), 41.92, 42.10 (CH(*C*H$_3$)$_2$), 63.58, 65.13, 65.28, 65.87, 66.07, 66.65 (PN*C*H and *C*HCH$_3$), 81.02 (d, $^2J_{CP}$ = 8.2 Hz, PO*C*H) and *82.16* (d, $^2J_{CP}$ = 7.7 Hz, PO*C*H), 142.75, 142.94 (C Ar).

Derivatives of Table IV. Derivative 19P: ^{31}P NMR (C_6D_6) δ 133.330 and *132.724* (Δδ = 0.606).

Derivative 19PS. This compound was not stable to silica gel chromatography: ^{31}P NMR (C_6D_6) δ 79.744 (Δδ = 0.000).

Derivative 36P: ^{31}P NMR (C_6D_6) δ 136.427 (Δδ = 0.000).

Derivative 36PS: ^{31}P NMR (C_6D_6) δ 79.352 (Δδ = 0.000).

Derivative 37P: ^{31}P NMR (C_6D_6) δ 138.446 and *136.718* (Δδ = 1.728).

Derivative 37PS: ^{31}P NMR (C_6D_6) 80.141 and *80.025* (Δδ = 0.118).

Derivatives of Table V. Derivative 38P: ^{31}P NMR (C_6D_6) δ 133.262 (*S* enantiomer) and *133.060* (*R* enantiomer) (Δδ = 0.202).

Derivative 38PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; bp = 140 °C (0.5 mm); yield = 89%; IR 980, 1010 cm^{-1}; ^{31}P NMR (C_6D_6) δ 87.349 (Δδ = 0.019).

Derivative 39P: ^{31}P NMR (C_6D_6) δ 134.137 and *133.464* (Δδ = 0.673).

Derivative 39PS: slighly yellow oil; eluent, cyclohexane/AcOEt = 95/5; yield = 87%; ^{31}P NMR (C_6D_6) δ 87.282 (Δδ = 0.065); ^{1}H NMR (C_6D_6) δ 0.88 (m, 4 H, NCHCH$_2$CH_2CH_2CH$_2$CHN), 1.19 (d, 3 H, $^3J_{HH}$ = 7 Hz, CHCH_3) and *1.20* (d, 3 H, $^3J_{HH}$ = 7 Hz, CHCH_3), 1.37–1.56 (m, 4 H, NCHCH_2CH$_2$CH$_2$CH_2CHN), 2.25–2.52 (m, 8 H, PNC*H* and PNCH_3), 3.00 (m, 1 H, OCH$_2$C*H*), 4.12 (m, 2 H, POCH_2), 7.05–7.17 (m, 5 H, H Ar); ^{13}C NMR (C_6D_6) 18.44 (s, CH*C*H$_3$) and *18.53* (s, CH*C*H$_3$), 24.90 (s, NCHCH$_2$*C*H$_2$CH$_2$CH$_2$CHN), 28.72, 28.95, 29.52, 29.68 (NCH*C*H$_2$CH$_2$CH$_2$*C*H$_2$CHN), 28.89 (s, PN*C*H$_3$), 31.85, 31.90, 31.96 (PN*C*H$_3$), 41.40, 41.53 (CH$_2$*C*HPh), 63.60, 63.69 (PN*C*H), 66.64, 66.78 (PN*C*H), 72.64, 72.77, 72.91 (POCH$_2$), 127.22, 128.10, 128.35, 128.58, 129.10 (C Ar), 144.27 (C quat).

Derivative 40P: ^{31}P NMR (C_6D_6) δ 136.830 and *135.080* (Δδ = 0.539).

Derivative 40PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 94%; ^{31}P NMR (C_6D_6) δ 87.686 (Δδ = 0.016).

Derivative 41P: ^{31}P NMR (C_6D_6) δ 132.522 and *131.782* (Δδ = 0.740).

Derivative 41PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 90%; ^{31}P NMR (C_6D_6) δ 87.215 (Δδ = 0.054); ^{1}H NMR (C_6D_6) δ 0.82–0.90 (m, 4 H, NCHCH$_2$CH_2CH_2CH$_2$CHN), 1.12 (d, 3 H, $^3J_{HH}$ = 6.9 Hz, CHCH_3) and *1.13* (d, 3 H, $^3J_{HH}$ = 6.9 Hz, CHCH_3), 1.3–1.6 (m, 4 H, NCHCH_2CH$_2$CH$_2$CH_2CHN), 1.79 (m, 2 H, CH_2CHC$_6$H$_5$), 2.22–2.53 (m, 8 H, PNCH_3 and PNC*H*), 2.79 (m, 1 H, C*H*C$_6$H$_5$), 3.91 (m, 2 H, CH_2OP), 7.00–7.19 (m, 5 H, H Ar); ^{13}C NMR (C_6D_6) 22.66 (s, CHCH_3) and *22.77* (s, CHCH_3), 24.90 (s, NCHCH$_2$CH_2CH$_2$CH$_2$CHN), 28.70, 29.93, 29.52, 29.69 (NCHCH_2CH$_2$CH$_2$CH_2CHN), 28.78 (s, PNCH_3), 31.89 (s, PNCH_3), 37.03 (s, CH$_2$*C*HC$_6$H$_5$), 39.60, 39.73 (POCH$_2$CH_2), 63.66, 63.76 (PN*C*H), 65.90, 66.03, 66.17 (POCH_2), 66.66, 66.77 (PN*C*H), 126.87, 127.80, 129.20 (C Ar), 147.38 (C quat).

Derivative 42P: ^{31}P NMR (C_6D_6) δ *133.599* (*R*) and 133.061 (*S*) (Δδ = 0.538).

Derivative 42PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 87%; ^{31}P NMR (C_6D_6) δ 87.417 (Δδ = 0.032).

Derivative 43P: ^{31}P NMR (C_6D_6) δ 138.446 (Δδ = 0.000).

Derivative 43PS: ^{31}P NMR (C_6D_6) δ 87.429 (Δδ = 0.000).

Derivative 44P: ^{31}P NMR (C_6D_6) δ *134.003* (*R*) and 133.666 (*S*) (Δδ = 0.337).

Derivative 44PS: colorless oil; eluent, cyclohexane/AcOEt = 70/30; yield = 94%; ^{31}P NMR (C_6D_6) δ 87.722 (Δδ = 0.004).

Derivative 45P: ^{31}P NMR (C_6D_6) δ 136.830 and *135.080* (Δδ = 1.750).

Derivative 45PS: colorless oil; eluent, cyclohexane/AcOEt = 85/15; yield = 92%; ^{31}P NMR (C_6D_6) δ 88.427 (Δδ = 0.024).

Derivative 46P: ^{31}P NMR (C_6D_6) δ 136.292 (d, $^4J_{PF}$ = 4.9 Hz) and *135.619* (d, $^4J_{PF}$ = 4.9 Hz) (Δδ = 0.673).

Derivative 46PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 92%; ^{31}P NMR (C_6D_6) δ 88.898 (d, $^4J_{PF}$ = 0.7 Hz) and *88.809* (d, $^4J_{PF}$ = 0.7 Hz) (Δδ = 0.089).

Derivative 47P: ^{31}P NMR (C_6D_6) δ 134.205 and *133.869* (Δδ = 0.336).

Derivative 47PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 91%; IR 910, 1010, 1970 cm^{-1}; ^{31}P NMR (C_6D_6) δ 87.013 and *86.888* (Δδ = 0.125).

Derivative 48P: ^{31}P NMR (C_6D_6) δ 138.849 (Δδ = 0.000); ^{1}H NMR (C_6D_6) δ 4.86 (d, 1 H, $^3J_{HP}$ = 8.8 Hz, POC*H*C$_6$H$_5$) and *4.58* (d, 1 H, $^3J_{HP}$ = 6.6 Hz, POC*H*C$_6$H$_5$) (Δδ = 0.275).

Derivative 48PS: colorless oil; eluent, cyclohexane/AcOEt = 95/5; yield = 93%; ^{31}P NMR (C_6D_6) δ 88.009 (Δδ = 0.000); ^{1}H NMR ($CDCl_3$) δ 1.01–1.4 (m, 4 H, NCHCH$_2$CH_2CH_2CH$_2$CHN), 1.8–2.05 (m, 4 H, NCHCH_2CH$_2$CH$_2$CH_2CHN), 2.4–2.6 (m, 7 H, PNC*H* and PNCH_3), 2.7 (m, 1 H, PNC*H*), 4.99 (d, 1 H, $^3J_{HP}$ = 11.0 Hz, POC*H*) and *5.04* (d, 1 H, $^3J_{HP}$ = 12.7 Hz, POC*H*), 7.2–7.5 (m, 5 H, H Ar); ^{13}C NMR ($CDCl_3$) δ 24.06 (NCHCH$_2$CH_2CH$_2$C-H$_2$CHN), 27.92, 27.95, 28.03, 28.60, 28.67 (NCHCH$_2$CH$_2$CH$_2$CH$_2$CHN and PNCH_3), 30.51, 30.57 (PN*C*H$_3$), 63.08, 63.14, 65.59, 65.64 (PN*C*H), 68.31, 68.37, 68.53, 68.59, 68.75, 68.82 (POCHD), 127.73, 127.84, 128.06, 128.20, 137.04, 137.11 (C Ar).

Derivatives of Chart III and Scheme VII. Derivative 51P: ^{31}P NMR (C_6D_6) δ 147.330 (erythro), 146.906 (threo), *143.003* (threo), *142.707* (erythro) (Δδ(threo) = 3.903 and Δδ (erythro) = 4.623).

Derivative 52P: ^{31}P NMR (C_6D_6) δ 146.389 (threo), 144.774 (erythro), *139.591* (erythro), *138.111* (threo) (Δδ(threo) = 8.278 and Δδ(erythro) = 5.183).

Derivative 53P: ^{31}P NMR (C_6D_6) δ 148.235 (threo), 146.387 (erythro), *146.070* (erythro), *143.898* (threo) (Δδ(threo) = 4.337 and Δδ(erythro) = 0.317).

Derivative 53PS: ^{31}P NMR (C_6D_6) δ 87.430 (erythro), *87.400* (erythro), *87.093* (threo), *86.945* (threo) (Δδ(erythro) = 0.030 and Δδ(threo) = 0.148).

Derivative 54P: ^{31}P NMR (C_6D_6) δ 170.348 and *168.531* (Δδ = 1.817).

Derivative 54PS: slightly yellow oil; eluent, cyclohexane/AcOEt = 90/10; yield = 92%; ^{31}P NMR (C_6D_6) δ 95.438 and *94.698* (Δδ = 0.740); ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 3 H, CH$_2$CH_3), 1.1–1.4 (m, 7 H, CHCH_3 and NCHCH$_2$CH_2CH_2CH$_2$CHN), 1.54–1.72 (m, 2 H, CHCH_2CH$_3$), 1.78–2.07 (m, 4 H, NCHCH_2CH$_2$CH$_2$CH_2CHN), 2.48–2.76 (m, 8 H, PNC*H* and PNCH_3), 3.12 (m, 1 H, PCH_3); ^{13}C NMR ($CDCl_3$) 11.61, 11.67 (CH$_2$CH$_3$), 22.65, 22.75, 23.05, 23.10 (CH*C*H$_3$), 24.37, 24.38 (NCHCH$_2$*C*H$_2$CH$_2$CH$_2$CHN), 28.37, 28.42, 28.80, 28.85 (PN*C*H$_3$), 28.17, 28.39, 28.71, 28.99 (NCH*C*H$_2$CH$_2$-CH$_2$CH$_2$CHN), 31.33, 31.43 (PSCHCH$_2$), 47.17, 47.25, 47.48, 47.56 (PSCH), 64.51, 64.58 (PN*C*H).

Derivative 55P: ^{31}P NMR (C_6D_6) δ 174.925 and *174.457* (Δδ = 0.468).

Derivative 55PS: slighly yellow oil; eluent, cyclohexane/AcOEt = 95/5; yield = 91%; ^{31}P NMR (C_6D_6) δ 97.457 ($\Delta\delta$ = 0.065); ^{1}H NMR ($CDCl_3$) δ 0.8–1.00 (m, 6 H, $CH_3CH_2CHCH_3$), 1.1–2.15 (m, 11 H, $NCHCH_2CH_2CH_2CH_2CHN$ and $CH_3CH_2CHCH_3$), 2.5–2.9 (m, 10 H, $PNCH_3$, PNCH, and $PSCH_2$); ^{13}C NMR ($CDCl_3$) δ 11.43 (CH_2CH_3), 19.01, 19.09 ($CHCH_3$), 24.34, 24.41 ($NCHCH_2CH_2CH_2CH_2CHN$), 28.13, 28.33 (CH_2CH_3), 28.39 ($PNCH_3$), 28.68, 28.77, 28.85, 28.94 ($NCHCH_2CH_2CH_2CH_2CHN$), 29.08 ($PNCH_3$), 35.85, 35.93, 36.04 ($CHCH_3$), 41.36, 41.43 ($PSCH_2$), 64.55, 64.63, 64.69 (PNCH).

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Registry No. 7, 137943-76-1; 8, 137943-77-2; 9, 137943-78-3; 9S, 137943-79-4; 10, 137943-80-7; (±)-11, 15892-23-6; 11Pa, 137943-81-8; 11Pb, 138051-22-6; 11'Pb, 138051-23-7; 11Pc, 137943-82-9; 11'Pc, 138051-24-8; 11POb, 137943-83-0; 11'POb, 138051-25-9; 11POc, 137943-84-1; 11'POc, 138051-26-0; 11POd, 137943-85-2; 11'POd, 138124-49-9; 11PSa, 137943-86-3; 11'PSa, 138051-27-1; 11PSb, 138051-28-2; 11'PSb, 138051-29-3; 11PSc, 137943-87-4; 11'PSc, 138051-30-6; (±)-12, 4128-31-8; (S)-12, 6169-06-8; 12P, 131897-19-3; 12'P, 131780-03-5; 12PO, 137943-88-5; 12'PO, 138051-31-7; 12PS, 131780-20-6; 12'PS, 131898-25-4; (±)-13, 70116-68-6; 13PO, 137943-89-6; 13'PO, 138051-32-8; (±)-14, 65337-13-5; 14PO, 137943-90-9; 14'PO, 138051-33-9; (±)-15, 21632-19-9; (S)-15, 33652-83-4; 15P, 137943-91-0; 15'P, 138051-34-0; 15PO, 137943-92-1; 15'PO, 138051-35-1; 15PS, 137943-93-2; 15'PS, 138051-36-2; (±)-16, 37911-28-7; 16PO, 137943-94-3; 16'PO, 138051-37-3; (±)-17, 119046-43-4; 17P, 137943-95-4; 17'P, 138124-50-2; 17PO, 137943-96-5; 17'PO, 138124-51-3; (±)-18, 67738-25-4; 18P, 137943-97-6; 18'P, 138051-38-4; 18PS, 137943-98-7; 18-PS, 138051-39-5; (±)-19, 22564-99-4; 19P, 138124-52-4; 19'P, 138125-58-3; 19PS, 138124-53-5; 20, 137943-99-8; 21, 137944-00-4; 22, 91633-80-6; (±)-22, 138051-40-8; 22S, 137944-01-5; (±)-24, 13323-81-4; 24P, 137944-02-6; 24'P, 138051-41-9; 24PS, 138125-59-4; 24'PS, 137944-03-7; (±)-25, 6118-14-5; 25P, 138051-42-0; 25'P, 138051-43-1; 25PS, 138051-44-2; 25'PS, 138051-45-3; (−)-26, 2216-51-5; 26P, 138051-46-4; 26'P, 138051-47-5; 26PS, 138051-48-6; 26'PS, 138051-49-7; (+)-27, 2216-52-6; 27P, 131897-22-8; 27'P, 131897-11-5; 27PS, 131897-32-0; 27'PS, 131897-12-6; (−)-28, 464-45-9; 28P, 137944-04-8; 28'P, 138051-50-0; 28PS, 138125-60-7; 28'PS, 137944-05-9; (±)-29, 56007-85-3; 29P, 137944-06-0; 29'P, 138051-51-1; 29PS, 137944-07-1; 29'PS, 138051-52-2; (±)-30, 18826-95-4; (S)-31, 687-47-8; 31P, 131897-23-9; 31'P, 131780-08-0; 31PS, 131897-33-1; 31'PS, 131780-09-1; (S)-32, 5928-67-6; 32P, 131897-24-0; 32'P, 131780-10-4; 32PS, 131897-34-2; 32'PS, 131780-11-5; (±)-33, 105120-61-4; 33P, 138125-61-8; 33'P, 137944-08-2; 33PS, 137944-09-3; 33'PS, 138051-53-3; (±)-34, 93059-59-7; 34P, 137944-10-6; 34'P, 138051-54-4; 34PS, 137944-11-7; 34'PS, 138051-55-5; (+)-35, 42151-56-4; 35P, 137944-12-8; 35'P, 138051-56-6; 35PS, 137944-13-9; 35'PS, 138051-57-7; (±)-36, 138051-58-8; 36P, 137944-14-0; 36PS, 137944-15-1; (±)-37, 19641-57-7; 37P, 137944-16-2; 37'P, 138051-59-9; 37PS, 137944-17-3; 37'PS, 138051-60-2; (±)-38, 34713-94-5; 38P, 137944-18-4; 38'P, 138051-61-3; 38PS, 137944-19-5; (±)-39, 98103-87-8; 39P, 137964-59-1; 39'P, 138125-62-9; 39PS, 137964-60-4; (±)-40, 111767-94-3; 40P, 137944-20-8; 40'P, 138051-62-4; 40PS, 137944-21-9; (±)-41, 86495-15-0; 41P, 137944-22-0; 41'P, 138051-63-5; 41PS, 137944-23-1; (S)-42, 7540-51-4; 42P, 131897-17-1; 42'P, 131779-97-0; 42PS, 138124-54-6; (±)-43, 111768-05-9; 43P, 137944-24-2; 43PS, 137944-25-3; (S)-44, 22323-82-6; 44P, 131897-15-9; 44'P, 131779-93-6; 44PS, 138051-64-6; (±)-45, 138051-65-7; 45P, 137944-26-4; 45'P, 138051-66-8; 45PS, 137944-27-5; 46, 134931-07-0; 46P, 138051-67-9; 46'P, 138051-68-0; 46PS, 138124-55-7; 46'PS, 138124-56-8; (±)-47, 131780-19-3; 47P, 138051-69-1; 47'P, 138051-70-4; 47PS, 138051-71-5; 47'PS, 138051-72-6; (±)-48, 52949-66-3; 49P, 137944-28-6; 49PS, 137944-29-7; erythro-(±)-51, 138124-57-9; threo-(±)-51, 138124-58-0; 51P (isomer 1), 137944-30-0; 51P (isomer 2), 138124-59-1; 51P (isomer 3), 138124-60-4; 51P (isomer 4), 138124-61-5; erythro-(±)-52, 138124-62-6; threo-(±)-52, 138124-63-7; 52P (isomer 1), 137944-31-1; 52P (isomer 2), 138124-64-8; 52P (isomer 3), 138124-65-9; 52P (isomer 4), 138124-66-0; erythro-(±)-53, 138051-73-7; threo-(±)-53, 114180-72-2; 53P (isomer 1), 137944-32-2; 53P (isomer 2), 138051-74-8; 53P (isomer 3), 138051-75-9; 53P (isomer 4), 138051-76-0; 53PS (isomer 1), 138125-63-0; 53PS (isomer 2), 137944-33-3; 53PS (isomer 3), 138124-67-1; 53PS (isomer 4), 138124-68-2; (±)-54, 91840-99-2; 54P, 137944-34-4; 54'P, 138051-77-1; 54PS, 137944-35-5; 54'PS, 138051-78-2; (±)-55, 110549-12-7; 55P, 137944-36-6; 55'P, 138051-79-3; 55PS, 137944-37-7; HMPT, 1608-26-0; Cl_3OP, 10025-87-3; Cl_3PS, 3982-91-0; (R,R)-N,N'-dimethylcyclohexane-1,2-diamine, 68737-65-5; (R,R)-N,N'-diisopropylcyclohexane-1,2-diamine, 137944-38-8; (R,R)-(−)-cyclohexane-1,2-diamine, 20439-47-8; (R,R)-diethyl 1,2-cyclohexanediylbiscarbamate, 75730-13-1; (R,R)-N,N'-dimethyl-1,2-diphenylethylene-1,2-diamine, 118628-68-5; (R,R)-N,N'-dimethyl-1,2-[bis(m-trifluoromethyl)phenyl]ethylene-1,2-diamine, 137944-39-9.

Supplementary Material Available: ^{1}H and ^{13}C NMR data for products 7, 10, 21, 12PO, 15PO, 16PO, 19PS, 24PS, 25PS, 29PS, 34PS, 38PS, 40PS, 42PS, 44PS, 45PS, 46PS, and 47PS and ^{31}P, ^{1}H, and ^{13}C NMR spectra of products 15P, 15PS, 16PO, 18P, 18PS, 19P, 19PS, 22, 22PS, 25P, 25PS, 27P, 27PS, 31P, 31PS, 32P, 32PS, 33P, 33PS, 34P, 34PS, 35P, 35PS, 39P, 39PS, 42P, 42PS, 44P, 44PS, 45P, 45PS, 47PS, 48PS, 54P, 54PS (78 pages). Ordering information is given on any current masthead page.

1,2- vs 1,4-Addition of Nucleophilic Organometallics to Nonracemic 2-(1-Naphthyl)- and 2-Cinnamyl-1,3-oxazolidines

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We herein report our results where the addition of organomagnesium reagents to 2-(1-naphthyl)- and 2-cinnamyl-1,3-oxazolidines *occurred consistently in a 1,4-conjugate manner, while lithium, cerium, and copper organometallic reagents added in a 1,2-fashion.* The 1,4-conjugate addition pathway was primarily exploited by using (4*R*)-2-(1-naphthyl)-4-phenyl-1,3-oxazolidine (4) as a substrate to obtain, after $NaBH_4$ reduction of the intermediate aldehyde, *trans*-disubstituted 1,2-dihydronaphthalenes with enantiomeric excesses of 93–94%. The amino alcohol products resulting from 1,2-addition were oxidatively cleaved to afford enantiomeric enriched (*R*)-α-(1-naphthyl)alkylamines **6a** and **6b** in >99% ee.

We have previously reported our results concerning nucleophilic addition to (4*R*)-2-aryl-4-phenyl-1,3-oxazolidines **1** wherein diastereomerically enriched amino alcohols **2** were obtained in moderate to good yields.[3a,b] In that

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