Chemistry of β-(Phosphatoxy)alkyl and β-(Acyloxy)alkyl Radicals. Migration Reactions: Scope and Stereoselectivity of β-(Phosphatoxy)alkyl Rearrangement. Mechanism of β-(Phosphatoxy)alkyl and β-(Acyloxy)alkyl Migration

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Abstract: An in depth study of the mechanism of the β-(phosphatoxy)alkyl radical migration is presented. Examples are presented which define the scope and limitations of the migration and show that, in certain cases, it is highly stereoselective. It is shown that phosphoranyl radicals are not intermediates in this rearrangement. A series of experiments with stereochemically-, ^{18}O-, and deuterium-labeled probes indicate that the migration is intramolecular, proceeds through competing 1,2- and 2,3-pathways, and does not involve fragmentation to a cage pair followed by recombination. The deuterium-labeled probe is also applied to the β-(acyloxy)alkyl migration with the same result. The changing proportions of 1,2- and 2,3-shifts in going from the β-(phosphatoxy)alkyl to the β-(acyloxy)alkyl migration are discussed in terms of the conformational equilibria of the two different esters and the Curtin−Hammett principle.

Introduction

Electrophilic radicals are known to abstract hydrogen atoms from the sugar−phosphate backbone of oligonucleotides. When they do so from a C4′ site, as is known to be the case with Fe−bleomycin[1] and enediyne-derived arene-1,4-diyls,[2,3] a β-(phosphatoxy)alkyl radical is generated. The reaction of hydroxyl radicals with DNA also leads, *inter alia*, to the formation of β-(phosphatoxy)alkyl radicals.[4] An understanding of the chemistry of β-(phosphatoxy)alkyl radicals is therefore central to that of the mechanism of action of these antitumor antibiotics and of radiation therapy.[5] Remarkably, despite this central importance in the oxidative degradation of DNA and voluminous literature on phosphoranyl radical chemistry,[6] almost nothing was known of the fundamental free radical chemistry of phosphate esters in general and of β-(phosphatoxy)alkyl radicals in particular when this project was undertaken in early 1992. Since that time, in parallel with our own efforts,[7,8] this situation has been addressed by Giese and co-workers,[9] as well as by the Saito group.[10] Previously, Schulte-Frohlinde and co-workers had monitored the release ($k = 3 \times 10^4$ s^{-1}) of diisobutyl phosphate from triisobutyl phosphate on radiolysis at pH 4.5−5 in water and concluded that this was due to hydrogen atom abstraction by a hydroxyl radical to give a β-(phosphatoxy)alkyl radical followed by decomposition to give an isobutene cation radical and diisobutyl phosphate.[11] The formation of cation radicals on decomposition of nucleotide C4′ radicals in aqueous media was later elegantly confirmed by Giese.[9b,g] Levin and co-workers reported that methyl and phenyl radicals displaced ethyl radicals from triethyl phosphate, imply-

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Table 1. β-(Phosphatoxy)alkyl Radical Rearrangements

entry	substrate (concn (M))	Bu_3SnH (equiv, concn (M), addition time (h))	products (yield (%))	migration/reduction ratio
1	**1a** (6.25×10^{-3})	1.2, 1.5×10^{-2}, 25	**2a** (20), **3a** (80)	4/1
2	**6** (2.0×10^{-2})	1.5, 3.6×10^{-2}, 17	**24** (0), **25** (100)	>95/5
3	**7** (2.0×10^{-2})	1.5, 3.6×10^{-2}, 17	**26** (0), **27** (75)	>95/5
4	**8** (7.5×10^{-3})	1.2, 9.0×10^{-3}, 17	**28**(100), **29** (0)	<5/95
5	**11** (5.0×10^{-3})	*a*	**11** (73) **30** (27), **33** (0)	>95/5
6	**18** (5.0×10^{-3})	1.2, 1.2×10^{-2}, **14**	**35** (69), **37** (0), **38** (<5)	>95/5
7	**19** (9.0×10^{-3})	1.1, 4.5×10^{-2}, 12	**38** (79), **40** (0), **35** (<5)	>95/5
8	**21** (6.0×10^{-3})	1.1, 1.1×10^{-2}, 18	**41** (100), **42** (0)	>95/5
9	**23** (5.0×10^{-3})	1.3, 1.7×10^{-2}, 12	**43** (82), **44** (18)	4.78/1
10	**45** (3.0×10^{-2})	1.5, 9.0×10^{-2}, 13	**46** (60), **47** (40), **49** (0)	40/60
11	**51** (2.0×10^{-2})	1.3, 2.5×10^{-2}, 16	**52** (95), **53** (5), **54** (0)	5/95

[a] See Experimental Section.

ing the intermediacy of phosphoranyl radicals, but yields were reportedly very low even though the phosphate was used as the solvent.[12] In phosphorus(III) chemistry, Bentrude has examined the chemistry of photochemically generated diradicals and cation radicals β, γ to phosphites and has shown their rearrangement to dialkylallyl phosphonates to proceed via cyclic phosphoranyl radicals.[13]

In contemplating an investigation of the chemistry of simple β-(phosphatoxy)alkyl radicals, we were struck by their obvious similarity to β-(acyloxy)alkyl radicals **A** whose rearrangements (→**B**, eq 1) have been the subject of intense study[14] since their independent discovery by Surzur and Tanner.[15] Also of interest in this context was the much studied[16] Schenck rearrangement (**C** → **D**, eq 2)[17] of allylic hydroperoxyl radicals, a reaction which has now been shown to proceed via a dissociative mechanism.[18] The investigation set out below was undertaken in order to determine whether simple β-(phosphatoxy)alkyl radicals **E** would, given the opportunity, undergo a migration reaction to **F** (eq 3) and, if so, by what mechanism.

(1)

(2)

(3)

Results and Discussion

Substrate **1a** was selected for the initial exploratory study with the expectation that the rearrangement of a primary alkyl to secondary benzyl radical would provide a sufficient thermodynamic driving force for the anticipated β-(phosphatoxy)alkyl radical rearrangement. In the event dropwise addition of tributyltin hydride and AIBN to a solution of **1a** in benzene at reflux over 25 h resulted in the isolation of a mixture of the reduced substrate **2a** and the anticipated migration product **3a** in the ratio 1/4 (Table 1, entry 1). The reaction mixture was devoid of byproducts, most notably styrene. Blank experiments demonstrated the thermal stability of the substrate under the reaction conditions and so eliminated the possibity that **3a** arose by the thermal rearrangement of **1a** to **4**, followed by simple stannane reduction. Sodium borodeuteride reduction of phenacyl bromide provided 2-bromo-1-deuterio-1-phenylethanol, which was converted to **1b** with diphenylphosphoryl chloride. Reaction of **1b** with tributyltin hydride and AIBN led to the formation of a mixture of **2b** and **3b** in the ratio 1/4. Significantly, no evidence was found for the regioisomerically labeled product **5** which would have resulted from a neophyl rather than the (phosphatoxy)alkyl migration. Thus, not only was the existence of the β-(phosphatoxy)alkyl radical rearrangement established, but it was also shown to occur to the exclusion of the neophyl rearrangement.

Several other substrates (**6**–**8**) were prepared uneventfully by phosphorylation of the corresponding bromohydrins. The

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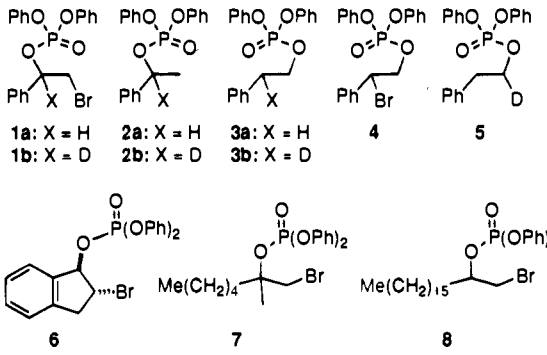
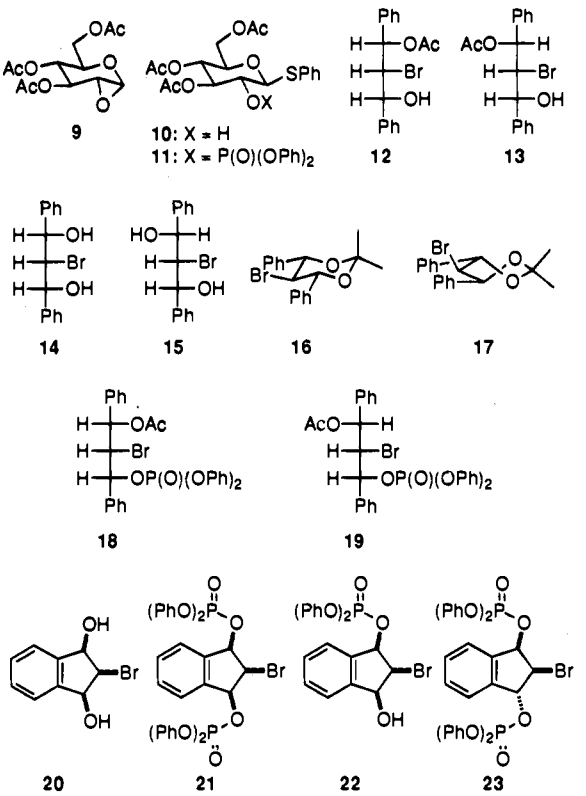


carbohydrate-based substrate **11** was prepared by treatment of Brigl's anhydride (**9**)[19] with thiophenol to give the thioglucoside **10**, followed by phosphorylation. Reaction of 1,3-diphenyl-3-acetoxy-1(*E*)-propene[20] with NBS in DMSO gave an approximately 1/1 mixture of the two diasteromeric acetoxybromohydrins **12** and **13** which were separated by chromatography on silica gel and recrystallization. The first of these (**12**) corresponded to the known[21] *ribo*-isomer, and this assignment was confirmed by $LiAlH_4$ reduction to the diol **14** and then conversion to the acetonide **16**, whose ^1H NMR spectrum revealed it to be in the chair conformation with the bromine equatorial. $LiAlH_4$ reduction of the second acetoxybromohydrin (**13**) gave a bromo diol devoid of symmetry, and so of the *arabino* configuration, as was confirmed by conversion, via **15**, to acetonide **17** which was shown to be in the twist boat conformation.[22] The *arabino*-diol **15** could have arisen from the acetoxybromohydrin **13** or its known C2 epimer. A distinction was readily made on the grounds of the observed melting points, with that of **13** being 110−112 °C and the literature value for the C2 epimer being 120−121 °C. Phosphorylation of diols **12** and **13** gave the phosphate esters **18** and **19**, respectively. Borohydride reduction of 2,2-dibromoindan-1,3-dione gave a mixture of monobromo diols from which the major isomer **20** was isolated by crystallization. The *syn*-diol configuration of **20** was revealed by its symmetry, evident from ^1H and ^{13}C NMR spectroscopy. The coupling constant $^3J_{H1-H2}$ was found to be 4.5 Hz, prompting us to assign the *all-syn* configuration indicated. This is based on the inspection of molecular models for both configurations at C2. The H1−C1−C2−H2 torsion angle in the *all-syn* diastereomer **20** is never more than ~20° and so should give rise to significant ^3J coupling, whereas in the C2 epimer H1 and H2 are approaching an orthogonal arrangement, leading to the expectation of a minimal ^3J coupling. The *all-syn* geometry of **20** is readily understood in terms of an initial reduction of 2,2-dibromoindan-1,3-dione to the monobromide followed by further reduction anti to the remaining bulky bromine substituent. Phosphorylation of **20** with diphenylphosphoryl chloride in the usual manner provided the symmetric diphosphate **21**, whereas treatment with bis(tributyltin) oxide and then diphenylphosphoryl chloride yielded the monophosphate **22**, albeit in meager yield. Mitsunobu reaction[23] of **22** then gave the *trans*-diphosphate **23**.

Each of the above substrates was subjected to reaction with tributyltin hydride in the usual manner, leading to the formation of rearrangement and reduction products as indicated in Table



1. The indan-derived bromo phosphate **6** underwent a very clean, high-yield rearrangement (Table 1, entry 2) to **25**. Inspection of the crude reaction mixture by ^1H NMR revealed no evidence of the reduction product **24**. The radical derived from **6** therefore rearranges significantly more rapidly than that from **1**. This is best explained by the more rigid nature of the indan system in which the scissile C−O bond is close to prealigned with the C2 radical. The tertiary phosphate **7** also suffered rearrangement in high yield and to the exclusion of any reduction reaction (Table 1, entry 3). However, the closely analogous secondary phosphate **8**, under the same conditions, provided only the reduction product **28** (Table 1, entry 4). The contrast in migration tendencies between the radicals derived from **7** and **8** could be interpreted in terms of any of several factors, or combinations thereof. Firstly, it may be that the formation of a secondary, as opposed to a tertiary, radical from a primary radical does not provide a sufficient thermodynamic driving force for the rearrangement. Secondly, the transition state for migration might be less stabilized for **8** than for **7**, as would be the case if there is significant cation radical like character, *vide infra*. Thirdly, the additional methyl group in **7** might predispose the system toward the reactive conformation.

With the carbohydrate system **11**, we observed a rather sluggish reaction which could not be driven to completion despite the repeated addition of tributyltin hydride. Nevertheless, inspection of the crude reaction mixture revealed the presence of only two products, the glucal **30** and the substrate **11** (Table 1, entry 5). The glucal could result from the decomposition of either the reduction (**33**) or the rearrangement (**31**) product, or both. An authentic sample of the reduction product **33** was synthesized by phosphorylation of alcohol **32**, itself prepared by the stannane reduction of 3,4,6-triacetylglucopyranosyl chloride, and shown to be stable under the reaction conditions. On the other hand, 2-deoxyglycosyl derivatives, especially the anomeric phosphates,[24] are notoriously unstable with respect to oxenium ion, and so glycal, formation. It was therefore most likely that **31** was the precursor to the glucal

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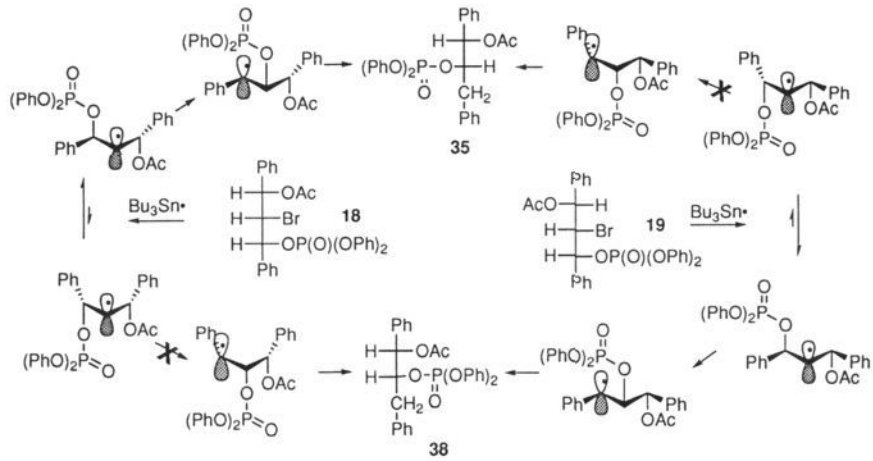
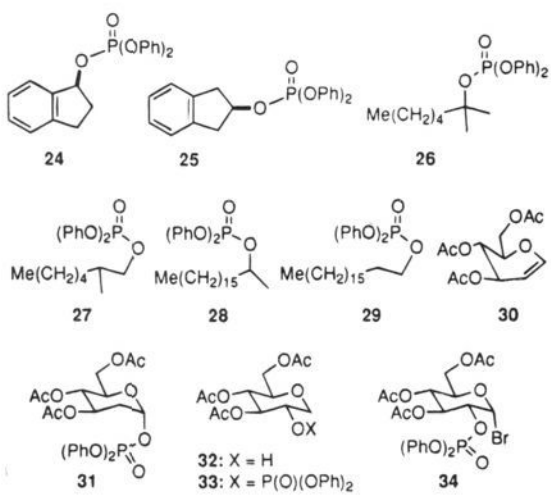
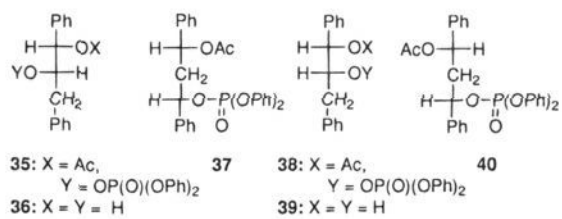
Scheme 1



isolated. Our suspicions were confirmed when Giese used the bromide **34** to study the identical rearrangement under photochemical conditions at room temperature.[9c,d] Under these conditions the rearrangement product was observed by NMR spectroscopy but was too unstable to be isolated with a half-life in deuteriochloroform solution at room temperature of only a few hours. The Giese group also measured the rate constant for this particular migration and found it to be 8×10^6 s^{-1} at 27 °C, and so 4 orders of magnitude faster than the comparable β-(acyloxy)alkyl migration of the 2,3,4,6-tetra-*O*-acetyl-1-glucopyranosyl radical. This seemingly contrathermodynamic rearrangement (**11** → **31**) involving formation of a secondary alkyl radical at the expense of an alkoxyalkyl (anomeric) radical is best understood in terms of the formation of an anomeric C−O bond in place of a simple secondary alkyl C−O bond, as was pointed out by Giese in explanation of the β-(acyloxy)-alkyl migration of the 2,3,4,6-tetra-*O*-acetyl-1-glucopyranosyl radical.[14h,m]



Substrates **18** and **19** were conceived with a view to establishing a competition between the β-(phosphatoxy)alkyl and β-(acyloxy)alkyl migrations. Treatment of both **18** and **19** with tributyltin hydride and AIBN in benzene at reflux resulted in isolation in each case of the product of the β-(phosphatoxy)-alkyl migration but not that of the β-(acyloxy)alkyl migration (Table 1, entries 6 and 7). Thus, in agreement with the rate constants measured by Giese (*vide supra*), we can confidently say that, for a comparable substrate, the phosphate migration is several orders of magnitude faster than the acyloxy migration. Inspection of the crude reaction mixtures for substrates **18** and **19** revealed both migrations to occur with a very high degree of stereoselectivity. Thus, for **18** only the *threo*-product could be detected, while **19** gave rise only to the *erythro*-product. The *diastereoselectivity of these two migrations is therefore at least* 95%. The configuration of the two products **35** and **38** was determined, after isolation, by hydrolysis to the corresponding diols **36** and **39** and comparison with literature data.[25] The stereoselectivity of both reactions is best understood in terms of a migration of the phosphate group along one face of the alkyl moiety, from a conformation in which the dipoles of the acetate and phosphate esters are antiparallel and the carbon termini have a *trans* relationship (Scheme 1). Highly stereoselective, suprafacial (acyloxy)alkyl and even (phosphatoxy)-alkyl migrations have been observed on rigid carbohydrate[14i,j] and steroid frameworks,[14g,h,l,m] but the above examples represent the first in conformationally labile systems. We note, however, that highly stereoselective examples of the Schenck rearrangement have been described by the Porter group in conformationally labile systems, and these for a reaction that has been demonstrated to occur by a fragmentation−in cage recombination pathway.[16,18]

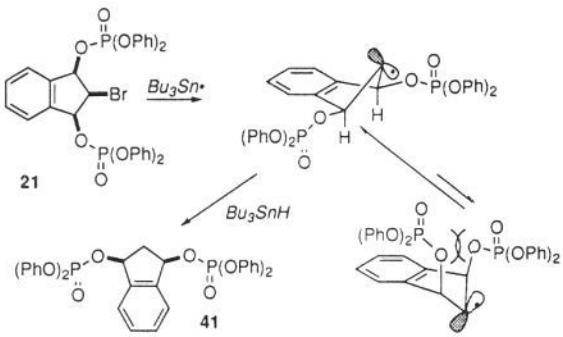


The contrast between the examples of entries 8 and 9 of Table 1 serves to confirm the stereoelectronic requirement, implicit in the above discussion, for the scissile C−O bond to line up coplanar with the initial radical in order for the migration to occur. In the case of the radical derived from **21** such a conformation would result in a severe steric interaction between the two phosphate esters and so is significantly disfavored with the result that migration is not observed (Scheme 2). On the

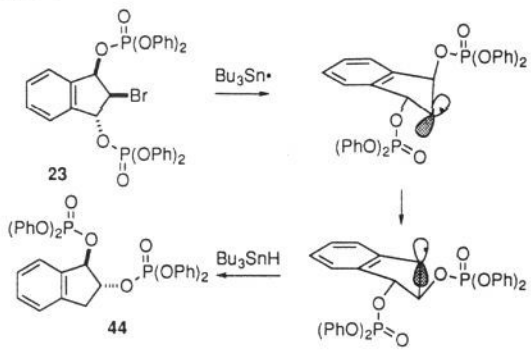
(24) (a) Williams, N. R.; Wander, J. D. In *The Carbohydrates*; Pigman, W., Horton, D., Eds.; Academic: New York, 1980; Vol. IB, p 761. (b) Percival, M. D.; Withers, S. G. *Can. J. Chem.* **1988**, *66*, 1970.

(25) Hambley, T. W.; Rideout, J. A.; Taylor, W. C. *Aust. J. Chem.* **1990**, *43*, 1327.

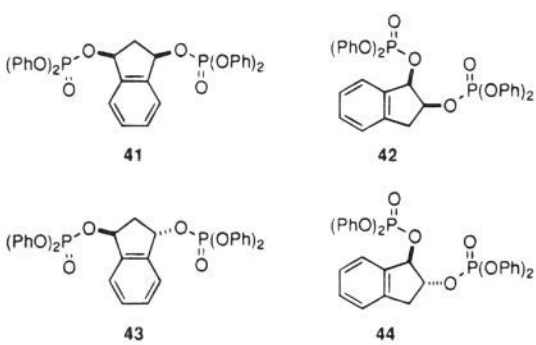
Scheme 2



Scheme 3

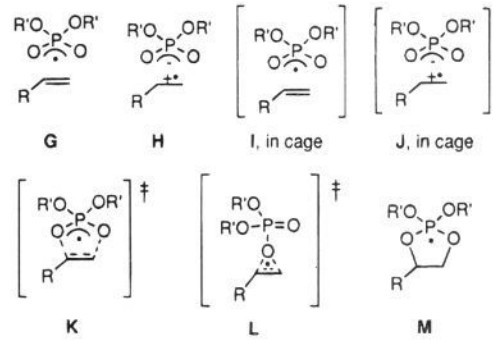


other hand, appropriate conformations are readily accessible to the radical from **23** with the result that migration is facile (Scheme 3).



Extending the analogy between the β-(acyloxy)alkyl and the β-(phosphatoxy)alkyl radical migration leads to the consideration of several mechanistic hypotheses. Thus, it is reasonable to consider four distinct fragmentation−recombination pathways: (i) **G**, fragmentation to an alkene and a phosphatoxy radical and eventual recombination; (ii) **H**, fragmentation to an alkene cation radical and a phosphate anion and eventual recombination; (iii) **I** and **J**, pathways as in **G** and **H** but with recombination within the solvent cage. It is also appropriate to consider a five-center−five-electron pericyclic mechanism, **K**, and a three-center−three-electron pericyclic mechanism, **L**, amounting to 2,3- and 1,2-shifts, respectively. Finally, it is necessary to consider a stepwise mechanism proceeding through a cyclic phosphoranyl radical, **M**, as the intermediate.

Contemplation of the above experiments permits a number of conclusions to be drawn. The highly stereoselective nature of the rearrangements of **18** and **19** to **35** and **36**, respectively, excludes any mechanism (**G** or **H**) in which fragmentation is followed by free diffusion and eventual recombination. However, as shown by Porter for the Schenck rearrangement,[16,18] such stereoselectivity does not permit the exclusion of cage



mechanisms (**I** and **J**). Further evidence against pathway **G** was provided by crossover experiments: no support for the formation of **25** was found when **1a** was allowed to react with tributyltin hydride in the presence of indene, and similarly **4** was not formed when the rearrangement of **6** was performed in the presence of styrene. The successful rearrangement of **7** to **27**, when contrasted with the failure of that of **8** to **29**, strongly mitigates against the intermediacy of a cyclic phosphoranyl radical (**M**). The radicals derived from both **7** and **8** might reasonably be expected to close to cyclic phosphoranyl radicals at roughly comparable rates. That derived from **7** would then undergo ring opening to give the tertairy radical and, eventually, **27**. Any phosphoranyl radical derived from **8**, which does not lead to the secondary radical, would have to be trapped, leading to the eventual isolation of an octadecane-1,2-diol derivative, which was not the case. Against this line of reasoning is the possible acceleration of closure to a cyclic phosphoranyl radical caused by the methyl group in **7** and its derived radical. It was therefore necessary to design an experiment to settle, unequivocally, the question of involvement of phosphoranyl radicals.

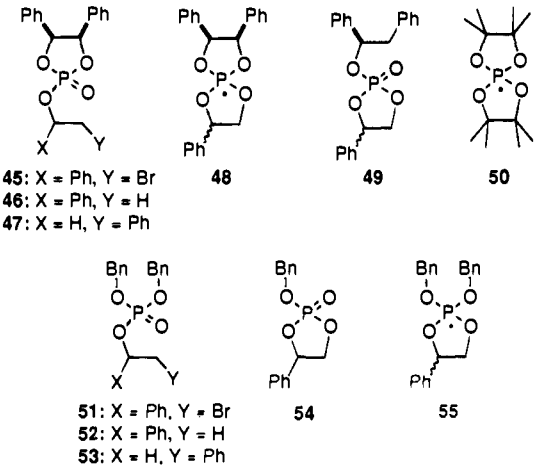
We reasoned that substrate **45** would be an adequate probe. Rearrangement by any pathway other than **M** would provide only the reduction and migration products **46** and **47**, respectively, whereas involvement of the cyclic phosphoranyl radical **48** would lead, additionally, to the isolation of **49**. Some considerable difficulty was experienced in the synthesis of **45** owing to a combination of steric hindrance and the well-known[26] susceptibility of such compounds to hydrolytic ring opening. Eventually, we had recourse to the phosphoramidite method as practiced in nucleotide chemistry,[27] with the additional modification that the phosphite, precursor to **45**, was oxidized with a benzene solution of *tert*-butyl hydroperoxide in order to prevent hydrolysis of the dioxaphospholane ring. In the event **49**, of which an authentic sample containing all four diastereomers was on hand, could not be detected in the crude reaction mixture from treatment of **45** with tributyltin hydride in benzene at reflux (Table 1, entry 10). There remained the possibility, however, that the formation of **48** was retarded because of the strain inherent in this spirocyclic system, leading to the operation of an alternative rearrangement mechanism in this particular case. Furthermore, there was the possibility that any small amount of **48** formed did not suffer fragmentation but was trapped by the stannane, leading to a spirocyclic phosphorane. Spirocyclic phosphoranyl radicals such as **50** are known to be unusually stable and to resist fragmentation up to 120 °C, permitting their trapping by addition to alkenes.[28] Substrate **51** was therefore prepared, again by means of phosphoramidite

(26) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70.

(27) (a) Barone, A. D.; Tang, T.-Y.; Caruthers, M. H. *Nucleic Acid Res.* **1984**, *12*, 4051. (b) Banworth, W.; Trzeciak, A. *Helv. Chim. Acta* **1987**, *70*, 175.

(28) Griller, D.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1416.

chemistry, and subjected to reaction with tributyltin hydride and AIBN in benzene at reflux (Table 1, entry 11). This migration was rather slow, leading to the observation of very significant quantities of reduced product **52** and only a small amount of the rearrangement product **53**. However, no evidence for the formation of the alternative product **54**, derived from fragmentation of the putative phosphoranyl radical **55**, and of which an authentic sample was prepared, was observed. Cyclic phosphoranyl radicals **M** were therefore eliminated from consideration as intermediates in the β-(phosphatoxy)alkyl radical rearrangement.

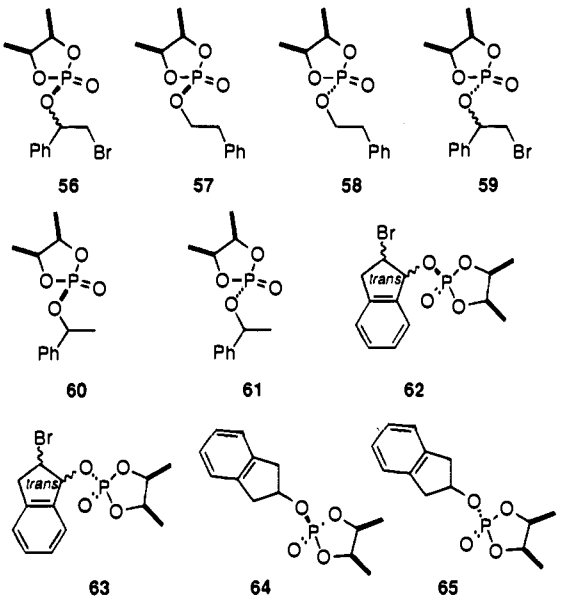


To test the possibility of the β-(phosphatoxy)alkyl migration occurring via a cage fragmentation−recombination pathway, or by a 1,2- or 2,3-concerted shift, a stereochemical probe was designed. Thus, rearrangement of the *trans*-bromo phosphate **56** via a 1,2-pathway would result in the formation of **57**, with retention of the configuration of phosphorus, while the 2,3-pathway would involve inversion at phosphorus and the formation of **58**. Likewise, the *cis*-stereoisomer **59** would provide **58** and **57** by the 1,2- and 2,3-pathways, respectively. Operation of a fragmentation−recombination pathway would be signaled by the formation of a mixture of **57** and **58** in the same ratio from either **56** or **59**. The β-bromoalkyl phosphate esters **56** and **59** were prepared by phosphorylation of styrene bromohydrin with *meso*-2-chloro-4,5-dimethyl-2-oxo-1,3,2-dioxaphospholane[29] followed by chromatographic separation into the *cis*- and *trans*-isomers about the dioxaphospholane ring. Authentic samples of **57** and **58**, as well as of the reduction products **60** and **61**, were similarly prepared. The *cis* and *trans* assignments about the phospholane ring, crucial to the correct interpretation of the results, are securely based on ^{1}H and ^{31}P NMR chemical shifts supported by comparison with the work of Lowe[30] and others,[29,31] which itself is crystallographically derived. A second series of compounds (**62**−**65**) based on *trans*-indan bromohydrin was synthesized and assigned analogously. The consistency of the assignments was reinforced when, for each pair of diastereomers prepared, the *trans*-isomer eluted more slowly on silica gel than the *cis*-isomer. It is also noteworthy that for each pair of diastereomers the more hindered *trans*-isomer was considerably more susceptible to hydrolysis than the *cis*-isomer and suffered extensive degradation on purification by silica gel chromatography.

(29) Corriu, R. J. P.; Lanneau, G. F.; LeClercq, D. *Tetrahedron Lett.* **1986**, *42*, 5591.
(30) Cullins, P. M.; Jarvest, R. L.; Lowe, G.; Potter, B. V. L. *J. Chem. Soc., Chem. Commun.* **1981**, 245.
(31) (a) Cooper, D. B.; Hall, C. H.; Harrison, J. M.; Inch, T. D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1969. (b) Denny, D. Z.; Chen, G. Y.; Denny, D. B. *J. Am. Chem. Soc.* **1969**, *91*, 6838.

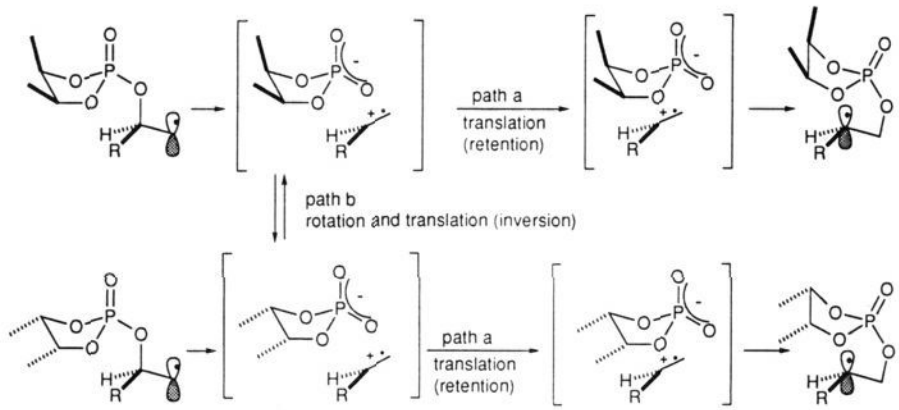
Table 2. Rearrangements of Stereochemically- and ^{18}O-Labeled Phosphates

entry	substrate	product ratio	migration/ reduction ratio	phosphorus retention/ inversion ratio
1	**56**	**57/58/60** = 20.3/8.7/71	1/2.4	2.33/1
2	**59**	**57/58/60** = 6.0/17.0/77	1/3.3	2.84/1
3	**62**	**64/65** = 58/42	>95/5	1.38/1
4	**63**	**64/65** = 25/75	>95/5	3.0/1
5	[^{18}O]-**1a**	[^{18}O]-**3a**/[^{18}O]-**2a** = 3.0/1	3.0/1	1.5/1

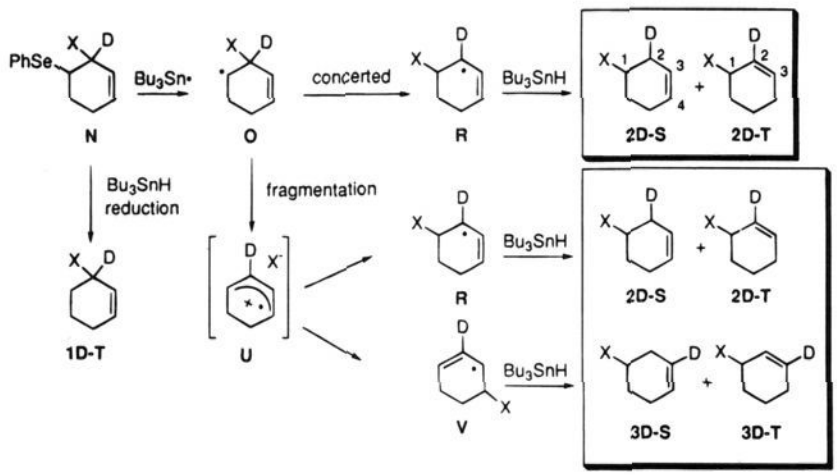


Each of the substrates **56**, **59**, **62**, and **63** was reacted with tributyltin hydride in benzene at reflux in the usual manner. The crude reaction mixtures were analyzed by ^{1}H and ^{31}P NMR spectroscopy, leading to the ratios presented in Table 2, entries 1−4. Several conclusions can be drawn. As noted above, the indene bromohydrin-based series rearranges significantly faster than that based on styrene bromohydrin. None of the four rearrangements studied goes with complete retention or inversion of stereochemistry at phosphorus: each proceeds with an excess of retention over inversion of stereochemistry at phosphorus. For a given pair of diastereomers the *cis*-substrate proceeds with a greater excess of retention of configuration. To corroborate these results, an ^{18}O-labeled probe, **1a**, was prepared by hydrolysis of phenacyl bromide dimethyl acetal with ^{18}O-labeled water, borohydride reduction, and phosphorylation with diphenylphosphoryl chloride. Reduction with $LiAlH_4$ gave 1-phenylethanol which, on examination by ^{13}C NMR, was shown to have an ^{18}O/^{16}O ratio of 2.01/1 in keeping with the 70% ^{18}O content of the water purchased. Treatment of this substance with tributyltin hydride and AIBN in benzene at reflux gave a mixture of reduced ([^{18}O]-**2a**) and rearranged ([^{18}O]-**3a**) products. After chromatographic separation the rearranged product was reduced with $LiAlH_4$ to 2-phenylethanol and then examined by GC/MS. The ^{18}O/^{16}O ratio was found to be 1.21/1, indicating that the rearrangement of [^{18}O]-**1a** proceeds with a 1.5/1 ratio of retention over inversion of configuration at phosphorus (Table 2, entry 5). These results are clearly not compatible with either a pure 1,2-shift (**L**) or a pure 2,3-shift (**K**), but with a situation in which 1,2- and 2,3-shift mechanisms exist in parallel with a marginally lower activation energy for the former. However, it is also possible to explain the observed slight preponderance of retention at phosphorus in terms of a fragmentation mechanism followed by almost instantaneous recollapse as would, for example, be the case if an intimate phosphate anion/alkene

Scheme 4



Scheme 5



cation radical (**J**) were the caged species (Scheme 4). This hypothesis simply requires that translation of one of the two caged species by 1−1.5 Å followed by recombination is faster than rotation of the phosphate by 180°. This state of affairs was very much akin to that of the β-(acyloxy)alkyl migration where distinction between a competing three- and five-center concerted paths and a fragmentation to a carboxylate anion/alkene radical cation cage pair followed by immediate recollapse to product had evaded all previous researchers.[14] A more subtle probe was evidently required.

Consider the deuterium-labeled system **N** in which X is the migrating ester,[32] be it an acyloxy or a phosphatoxy group (Scheme 5). Treatment with tributyltin hydride will lead to the homoallylic radical **O** which may rearrange to an allylic radical by either of two pathways. The concerted path (three- or five-centered) will give rise to the allylic radical **R** which will be quenched by the stannane at either terminus, giving rise to the homoallylic and allylic esters **2D-S** and **2D-T**, respectively. On the other hand, fragmentation of **O** will lead to the cage pair **U** and, following recombination at either terminus, the allylic radicals **R** and **V**. As before **R** will provide **2D-S** and **2D-T** on reaction with the stannane, while **V** will furnish **3D-S** and **3D-T**. Thus, the concerted pathway will lead to the formation of one homoallylic ester labeled at C2 and one allylic ester labeled at C2. On the other hand, the fragmentation pathway will provide two homoallylic esters, one labeled at C3 and the other at C2, and two allylic esters, labeled at C2 and C3, respectively. Reduction of the intial radical **N** will provide a further allylic product, **1D-T**. On this basis, provided sufficient resolution is available, inspection of the olefinic region of the ^{1}H NMR spectrum of the reaction mixture should enable a distinction to be made between the cage and concerted processes.

Before undertaking this experiment, it was necessary to verify (i) that the various olefinic signals could be adequately resolved by ^{1}H NMR spectroscopy and (ii) that the formation of an allylic radical was sufficient to drive the phosphatoxy (and acyloxy) radical migrations. Phosphate **68** was prepared in the usual manner from **66**. Controlled hydrolysis of 1-methoxycyclohexa-1,4-diene provided 3-cyclohexenone which was reduced with sodium borohydride to give the homoallylic alcohol **67**, followed by phosphorylation to give **72**. Fortunately, the olefinic ^{1}H signals in both **68** and **72**, which were rigorously assigned through decoupling experiments, could be fully resolved at 300 MHz in $CDCl_3$ solution. Deprotonation of cyclohexenone with LDA and quenching with phenylselenenyl chloride gave **75** which, on treatment with Luche's reagent, provided the selenocyclohexenol **76**. Phosphorylation of **76** then gave the radical precursor **78**.[33] Treatment of **78** with tributyltin hydride and AIBN in benzene at reflux provided a crude reaction mixture, which was shown by ^{1}H NMR spectroscopy to consist of a mixture of **68** and **72** in the approximate ratio 1:2. The formation of the allylic phosphate **68** does not permit any conclusions to be drawn as it can arise by simple reduction of

(32) The cyclohexene-based system **N** was chosen in preference to one based on esters of 3-hydroxy-4-(phenylselenio)-1-butene in order to avoid problems from further rearrangements provoked by closure of the substituted homoallylic radical to the corresponding cyclopropylmethyl radical followed by an alternative ring opening.

(33) Attempted use of the analogous diphenyl phosphate resulted only in decomposition.

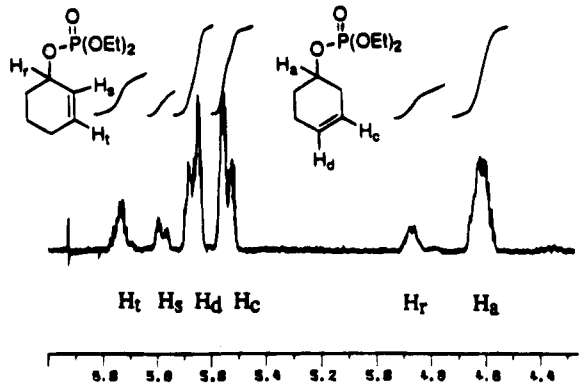
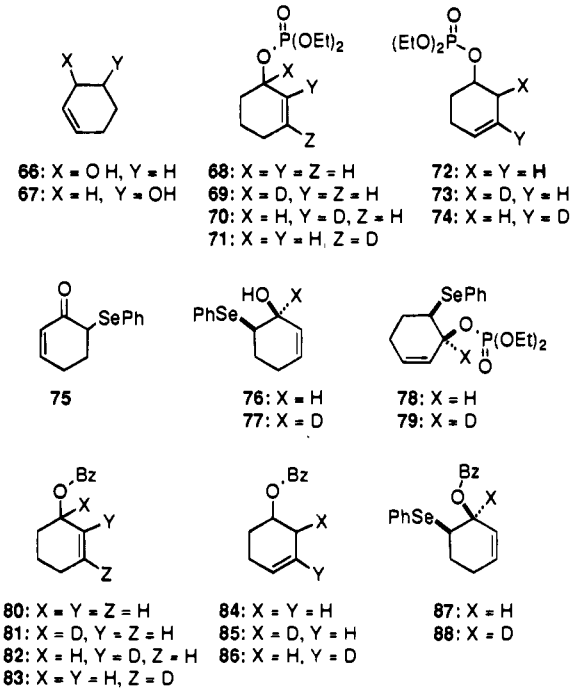


Figure 1. Partial 300 MHz ^{1}H NMR spectrum resulting from the treatment of **79** with tributyltin hydride and AIBN in benzene at reflux.

the initial radical **N**, as well as by either of the two rearrangement pathways, but that of **72** puts the migration beyond doubt.



The deuterated substrate **79** was readily prepared by reduction of **75** with $NaBD_4/CeCl_3$ to **77** followed by phosphorylation. Reaction of **79** with tributyltin hydride and AIBN in the usual manner resulted in a mixture of homoallylic and allylic phosphates with the partial ^{1}H NMR spectrum given in Figure 1. The most striking feature of this spectrum is the equal intensity, within the limits of experimental error, of the olefinic signals H_c and H_d of the homoallylic ester, which is therefore assigned structure **73** (=**2D-S**), as opposed to **74** (=**3D-S**). On the other hand, the corresponding signals H_s and H_t of the allylic ester are unequal in intensity, with H_s being diminished. This outcome is best interpreted in terms of the nondissociative pathway which predicts no labeling of H_c and H_d as in **73** and complete labeling of H_s as in **70**. The incomplete suppression of H_s observed is rationalized in terms of formation of **69** (**1D-T**) by the direct reduction pathway. The alternative, cage mechanism **U** would give rise to an unequal ratio of H_c and H_d, with the former being diminished. It is also possible to estimate from the integration that approximately 50% of the allylic phosphate arises from the direct reduction pathway and 50% from quenching of the rearranged radical **R** [X = OP(O)-$(OEt)_2$]. Similarly, it can be estimated that approximately 80%

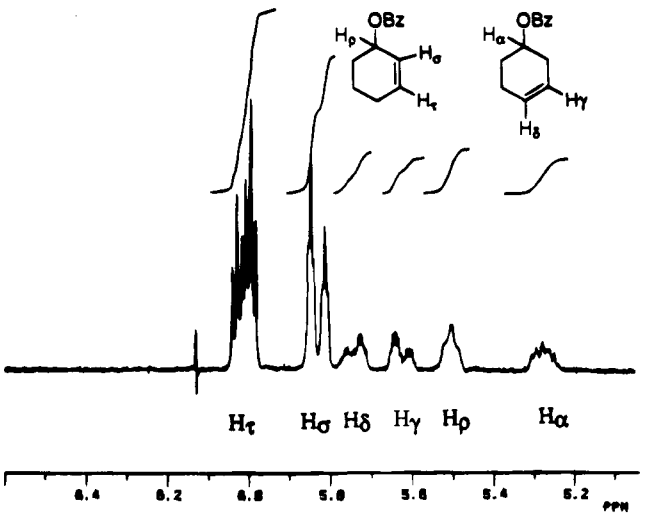


Figure 2. Partial 300 MHz ^{1}H NMR spectrum resulting from the treatment of **88** with tributyltin hydride and AIBN in benzene at reflux.

of radical **R** [X = OP(O)$(OEt)_2$] is quenched by Bu_3SnH proximal to the phosphate ester and 20% at the distal site.

The same experiment was applied to the β-(acyloxy)alkyl migration. Thus, authentic samples of **80** and **84** were prepared and their olefinic signals shown to be resolved by ^{1}H NMR spectroscopy. The unlabeled substrate **87** was prepared and subjected to reaction with tributyltin hydride under the usual conditions, resulting in a 4:1 mixture of **80** and **84**. The significantly higher proportion of the allylic, rather than the homoallylic, product found simply reflects the much slower nature of the acyloxy migration as opposed to the phosphatoxy migration. The deuterium-labeled substrate, on treatment with tributyltin hydride in the usual manner, gave rise to the partial ^{1}H NMR spectrum shown in Figure 2. Following the logic applied to the phosphatoxy migration, it is immediately obvious from the 1/1 ratio of H_δ and H_γ that this rearrangement also proceeds, within the limits of experimental error, exclusively by a nondissociative pathway. Furthermore, inspection of the integrals leads to the conclusion that approximately 80% of the allylic benzoate arises from the direct reduction pathway and that the rearranged radical **R** [X = OC(O)Ph] is quenched by Bu_3SnH with approximately equal rates at both termini.

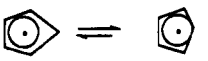
Is the cage pathway **U** (Scheme 5) truly excluded by the above experiments? This depends on the structure, delocalized or localized, of the cyclohexa-1,3-diene cation radical, its rate of conformational inversion, and its rate of rotational diffusion. ESR spectroscopy of the cyclohexa-1,3-diene cation radical in a $CFCl_3$ matrix at 77 K reveals four distinct hyperfine splittings indicative of a frozen half-chair conformation with two internal olefinic hydrogens, two terminal olefinic hydrogens, and a pseudoequatorial and pseudoaxial hydrogen on each methylene.[34] On warming to 130 K, the four methylene hydrogens are found to be equivalent, indicating rapid conformational inversion on the ESR time scale at this temperature.[34] The actual barrier to inversion is not known, but it is reasonable to assume that it will not be greater than the 3.1 kcal·mol^{-1} measured by Raman spectroscopy,[35] or 2.2 kcal·mol^{-1} estimated by molecular mechanics calculations,[36] for cyclohexa-1,3-diene itself.[37,38] Rotational diffusion constants for cyclohexanes in

(34) (a) Tabata, M.; Lund, A. *Chem. Phys.* **1983**, *75*, 379. (b) Shibata, T.; Egawa, Y.; Kubodera, H.; Kato, T. *J. Chem. Phys.* **1980**, *73*, 5963.
(35) Carreira, L. A.; Carter, R. O.; Durig, J. R. *J. Chem. Phys.* **1973**, *59*, 812.
(36) Kao, J. *J. Am. Chem. Soc.* **1987**, *109*, 3817.
(37) For an NMR investigation of cyclohexa-1,3-diene see: Auf der Meyde, W.; Lüttke, W. *Chem. Ber.* **1978**, *111*, 2384.

$CDCl_3$ solution at 35 °C, as determined by measurement of relaxation times by ^{13}C NMR spectroscopy, are in the range $10^{10}-10^{11}$ rad·s^{-1}.[39] These properties are such that any fragmentation pathway leading to the diphenyl phosphate anion and the cyclohexa-1,3-diene cation radical as separate entities, within a solvent cage, would result in scrambling of the deuterium label. The only type of fragmentation pathway that may be admitted is one in which recombination occurs before the radical cation becomes delocalized over the complete π-framework: this, of course, is experimentally indistinguishable from pericyclic (three-center−three-electron or five-center−five-electron) mechanisms with significant polar character at the transition state.

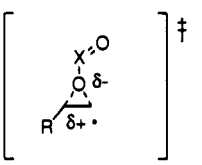
Thus, we are left with two competing, odd electron, pericyclic mechanisms. Such odd electron pericyclic reactions, with the possible exception of several radical aminium cation radical catalyzed processes,[40] and photoinduced cycloadditions,[41] are unknown. In view of this relative lack of precedent it is of interest to consider the structures of the cyclopropenyl and cyclopentadienyl radicals as first-generation models for the transition states of such odd electron pericyclic reactions. The ESR spectrum of the trimethylcyclopropenyl radical **89**,[42] generated by photolysis of di-*tert*-butyl peroxide in the presence of 1,2,3-trimethylcyclopropene, shows it to be an equilibrating mixture of three equivalent σ-radicals at 240 K in cyclopropane and to be a localized σ-radical at 113 K in propane.[43] Parallel phenomena are observed with the tri-*tert*-butylcyclopropenyl radical.[44] Calculations suggest that a three-electron π-cyclopropenyl radical would be antiaromatic.[45] The 2,3-di-*tert*-butyl-1-(3,5-di-*tert*-butylphenyl)cyclopropenyl radical has a π-structure, owing to extensive benzylic delocalization.[46] The cyclopentadienyl radical **90** and its peralkylated analogues have been extensively investigated by Davies.[47] Above 70 K it is a π-radical with D_{5h} symmetry, prompting the Davies group to call it the simplest π-annulene radical which has been prepared. However, below 70 K the ESR spectrum is consistent with a π-radical having C_{2v} symmetry and oscillating between an elongated and a compressed pentagon.[48]

89

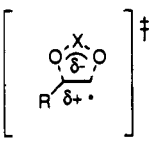


90

Radicals **89** and **90** are only very crude models, but the lessons are clear. The transition state for the three-center−three-electron migration favored in the β-(phosphatoxy)alkyl migration is likely to have a high degree of localization and is probably best represented as in **91**. The five-center−five-electron process most common in the β-(acyloxy)alkyl migration will be best represented by a distorted, polarized pentagon, **92**, as originally suggested by Ingold,[14e] and supported by the calculations of Radom and Beckwith.[14f]



91, X = $(R'O)_2P$ or R'C



92, X = $(R'O)_2P$ or R'C

The remaining question concerns the different partitioning between the three-center mechanism **91** and the five-center mechanism **92** adopted by the β-(phosphatoxy)alkyl and β-(acyloxy)alkyl migration. In a preliminary communication,[7b] based on an inspection of literature X-ray crystal structures of five-membered cyclic phosphate esters and the ground state conformation of carboxylate esters, we suggested that the mechanism was influenced by the O=P−O−R torsional angle in phosphate esters and by the O=C−O−R torsion angle in carboxylate esters. Thus, the X-ray crystal structure of methyl ethylene phosphate **93** reveals an O=P−O−Me torsion angle of 180°,[49] as does that of **94**.[50] The diphenyl derivative **95**, on the other hand, crystallizes as a 1/1 mixture of two conformers with O=P−O−Me torsion angles of 180° and 33°, respectively.[51] With methyl pinacol phosphate (**96**) the switch over is complete and the methyl group eclipses the P=O double bond.[52] Recent molecular orbital calculations on **93**, however, suggest that while the crystal structure conformation is an energy minimum, the conformation with the O=P−O−Me torsion angle of 0° is 2.5−3.3 kcal·mol^{-1} more stable.[53] The barrier to rotation about the P−O bond was calculated to be 5.7 kcal·mol^{-1}.[53] For the more general case of acyclic phosphate esters it is reasonable to expect both a lower barrier and a smaller difference in energy between the various conformations about

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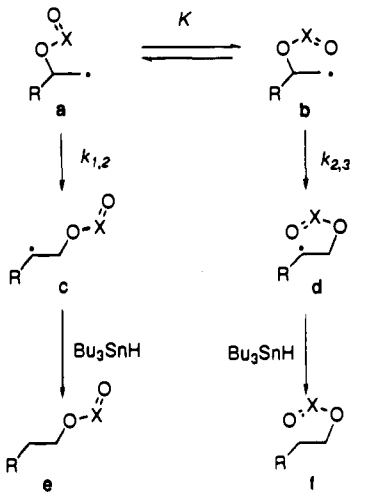
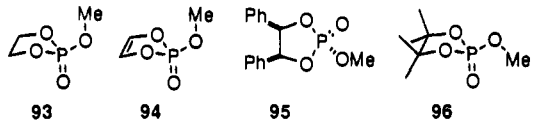
Scheme 6



the P—OR bond.[54] With carboxylate esters the situation is clearer, and it is widely appreciated that the *Z*-conformation is preferred by 3−4 kcal·mol^{-1}.[55] Calculations on methyl formate give the *Z*-conformer to be more stable than the *E*-conformer by between 3.68 and 5.56 kcal·mol^{-1}, with the barrier to inversion 11.4 kcal·mol^{-1}.[56]



93 **94** **95** **96**

For such a system of equilibrating conformers (Scheme 6) the basic tenets of the Curtin−Hammett principle[57] apply. Thus, when **a** and **b** are rapidly equilibrating with respect to the reaction rate ($k_{1,2}$ and $k_{2,3}$), the product ratio is given by **f/e** = $Kk_{2,3}/k_{1,2}$. Consider first the β-(acyloxy)alkyl migration (Scheme 6, X = CR′), for which more kinetic information is available. A conservative value for *K* of 10^3 and, for a typical case, a minimum value of **f/e** of 10^2 predicts a rate constant ratio $k_{2,3}/k_{1,2}$ of 10^{-1}. Thus, although the rate constant for the 1,2-shift is greater than that for the 2,3-shift, the equilibrium of the reacting conformers is such that the 2,3-shift will predominate. For the β-(phosphatoxy)alkyl migration [Scheme 6, X = P(OR′)$_2$] recall that (i) it is typically at least $10^2\times$ faster than a corresponding acyloxy migration and (ii) the 1,2-shift predominates. The prediction is therefore that either the $k_{2,3}/k_{1,2}$ ratio is lower than for the acyloxy migration or the equilibrium constant *K* is smaller, or both. At this stage, in support of this hypothesis, we simply draw attention to the two pairs of diastereomeric phosphates **56** and **58**, and **62** and **63**. For reasons of steric hindrance, as supported by the X-ray crystal structure analyses of **93**−**96**, we expect the equilibrium constant for *K* (Scheme 6) to be greater in **58** than in **56**, and greater in **63** than in **62**, leading, as is observed (Table 2), to a greater proportion of 1,2-shift in **58** than in **56**, and likewise in **63** than in **62**. Further analysis must await a full, solution phase, conformational analysis of **56**, **58**, **62**, and **63**, which will be undertaken in due course.

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Experimental Section

General Procedures. Melting points were recorded on a Thomas hot stage microscope and are uncorrected. ^{1}H, ^{13}C, and ^{31}P NMR spectra were run in $CDCl_3$ at 300, 75, and 121 MHz, respectively. ^{1}H and ^{13}C chemical shifts are downfield from tetramethylsilane as the internal standard. ^{31}P chemical shifts are quoted with respect to external H_3PO_4. All solvents were dried and distilled by standard procedures. All reactions were run under a dry nitrogen or argon atmosphere. THF was distilled, under N_2, immediately prior to use from sodium benzophenone ketyl. Ether refers to diethyl ether. Microanalyses were conducted by Midwest Microanalytical, Indianapolis.

2-Bromo-1-phenylethyl Diphenyl Phosphate (1a). A solution of styrene bromohydrin (4.02 g, 20 mmol) and DMAP (2.70 g, 22 mmol) in CH_2Cl_2 (25 mL) was treated with a solution of diphenyl chlorophosphate (5.37 g, 20 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature overnight before being quenched by saturated NH_4Cl (50 mL). The organic layer was separated and washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated to dryness *in vacuo*. Column chromatography on silica gel (eluant hexane/ether, 1/1) gave the title compound (7.23 g, 83.5%) as a white solid: mp 48−50 °C; ^{1}H NMR δ 3.60 (1H, ddd, J = 2.3, 5.2, 10.9 Hz), 3.72 (1H, dd, J = 7.2, 10.9 Hz), 5.71 (1H, dt, J = 5.3, 7.6 Hz), 7.36−6.92 (15H, m); ^{13}C NMR δ 34.6 (d, J = 8.5 Hz), 80.7 (d, J = 5.3 Hz), 119.9 (d, J = 4.9 Hz), 120.2 (d, J = 4.8 Hz), 125.2, 125.4, 126.6, 128.6, 129.2, 129.5, 129.7, 136.6, 150.2 (d, J = 6.6 Hz), 150.2 (d, J = 7.6 Hz); ^{31}P NMR δ −12.28. Anal. Calcd for $C_{20}H_{18}BrO_4P$: C, 55.45; H, 4.19. Found: C, 55.57; H, 4.24.

1-Phenylethyl Diphenyl Phosphate (2a). Preparation of an Authentic Sample. Phosphorylation of 1-phenylethyl alcohol as described for **1a** gave, after column chromatography (eluant hexane/ether, 1/2), the title compound (98%) as a colorless oil: ^{1}H NMR δ 1.65 (3H, dd, J = 0.62, 6.5 Hz), 5.71 (1H, quintet, J = 6.9 Hz), 7.01−7.35 (15H, m); ^{13}C NMR δ 23.9 (d, J = 5.5 Hz), 78.8 (d, J = 6.1 Hz), 120.0 (d, J = 5.4 Hz), 120.7 (d, J = 4.2 Hz), 125.1, 125.2, 125.9, 128.3, 128.4, 129.5, 129.6, 129.9, 140.6 (d, J = 4.5 Hz), 150.4 (d, J = 6.6 Hz), 150.5 (d, J = 6.6 Hz); ^{31}P NMR δ −12.06. This product was unstable and decomposed substantially, within 24 h of isolation, on standing at room temperature.

2-Phenylethyl Diphenyl Phosphate (3a). Preparation of an Authentic Sample. Phosphorylation of 2-phenylethyl alcohol as described for **1a** gave, after column chromatography (eluant hexane/ether, 1/2), the title compound (87%) as a colorless oil: ^{1}H NMR δ 3.01 (2H, t, J = 6.9 Hz), 4.44 (2H, quartet, J = 7.2 Hz), 7.13−7.34 (15H, m); ^{13}C NMR δ 36.6 (d, J = 7.5 Hz), 69.4 (d, J = 7.5 Hz), 120.0 (d, J = 4.5 Hz), 125.3, 126.8, 128.6, 129.0, 136.7, 150.5 (d, J = 6.7 Hz); ^{31}P NMR δ −11.43. Anal. Calcd for $C_{20}H_{19}O_4P$: C, 67.79; H, 5.41. Found: C, 67.82; H, 5.50.

***trans*-2-Bromo-1-indanyl Diphenyl Phosphate (6).** To a solution of 2-bromo-1-indanol (533 mg, 2.5 mmol) and DMAP (367 mg, 3.0 mmol) in CH_2Cl_2 (10 mL) was added dropwise a solution of diphenyl chlorophosphate (806 mg, 3.0 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was heated to reflux for 2.5 h. After cooling to room temperature, saturated NH_4Cl (10 mL) was added and the organic layer separated, washed with saturated $NaHCO_3$, water, and brine, and then dried (Na_2SO_4). Removal of solvent *in vacuo* gave essentially pure **6** (1.08 g, 97%) as a thick oil. Attempted purification by column chromatography on silica gel resulted in complete decomposition: ^{1}H NMR δ 3.24 (1H, dd, J = 4.0, 17.1 Hz), 3.71 (1H, dd, J = 6.5, 17.1 Hz), 4.56 (1H, ddd, J = 3.2, 4.0, 6.6 Hz), 6.12 (1H, dd, J = 3.1, 7.0 Hz), 7.16−7.41 (14H, m); ^{13}C NMR δ 14.1, 50.3 (d, J = 6.4 Hz), 88.8 (d, J = 6.4 Hz), 120.1 (d, J = 4.4 Hz), 124.8, 125.4, 126.0, 127.6, 129.8 (d, J = 5.0 Hz), 130.2, 137.3 (d, J = 5.0 Hz), 141.0, 150.3 (d, J = 7.5 Hz), 150.4 (d, J = 6.7 Hz); ^{31}P NMR δ −12.44.

2-Indanyl Diphenyl Phosphate (25). Preparation of an Authentic Sample. To a stirred solution of 2-indanol (134 mg, 1.0 mmol) and DMAP (183 mg, 1.5 mmol) in THF (15 mL) was introduced diphenyl chlorophosphate (311 μL, 1.5 mmol). After stirring at room temperature for 30 min, the solid part was filtered off and the filtrate

concentrated *in vacuo*. Column chromatography on silica gel (eluant DCM) gave **25** (359 mg, 98%) as a colorless oil: ^{1}H NMR δ 3.19 (2H, dd, J = 3.4, 16.8 Hz), 3.31 (2H, dd, J = 7.3, 16.9 Hz), 5.49 (1H, m), 7.18−7.37 (14H, m); ^{13}C NMR δ 40.6 (d, J = 5.3 Hz), 52.1, 81.0 (d, J = 6.2 Hz), 120.1 (d, J = 4.6 Hz), 124.6, 125.3, 126.9, 129.7, 139.5, 150.4 (d, J = 7.6 Hz); ^{31}P NMR δ −11.81. Anal. Calcd for $C_{21}H_{19}O_4P$: C, 68.8; H, 5.23. Found: C, 68.60; H, 5.30.

1-Bromo-2-methyl-2-heptanyl Diphenyl Phosphate (7). A solution of 1-bromo-2-methyl-2-heptanol (580 mg, 3.0 mmol), DMAP (440 mg, 3.6 mmol), and diphenyl chlorophosphate (967 mg, 3.6 mmol) in CH_2Cl_2 (25 mL) was heated to reflux under N_2 for 24 h. After cooling to room temperature, saturated NH_4Cl (30 mL) was added and the organic layer separated, washed with brine, dried (Na_2SO_4), and concentrated to dryness. Column chromatography on silical gel (eluant ether/petroleum ether, 1/3) gave **7** (1.064 g, 80%) as a colorless oil: ^{1}H NMR δ 0.86 (3H, t, J = 5.0 Hz), 1.26 (6H, br s), 1.67 (3H, s), 1.91 (2H, br s), 3.63 (2H, s), 7.16−7.42 (10H, m); ^{13}C NMR δ 13.9, 22.4, 23.0, 24.0 (d, J = 2.0 Hz), 31.6, 38.8 (d, J = 3.9 Hz), 38.8 (d, J = 5.1 Hz), 87.0 (d, J = 7.6 Hz), 120.1 (d, J = 5.4 Hz), 125.2, 129.6, 150.6 (d, J = 7.7 Hz); ^{31}P NMR δ −16.48. Anal. Calcd for $C_{20}H_{26}BrO_4P$: C, 54.43; H, 54.9. Found: C, 54.36; H, 5.85.

1-Bromo-2-octadecyl Diphenyl Phosphate (8). A solution of 1-bromo-2-octadecanol (350 mg, 1 mmol) and DMAP (147 mg, 1.2 mmol) in CH_2Cl_2 (10 mL) was treated with diphenyl chlorophosphate (322 mg, 1.2 mmol) and then heated to reflux for 7 h. After cooling, saturated ammonium chloride was added and the organic layer separated, washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated under vacuum. Column chromatography on silica gel (eluant hexane/ether, 1/1) gave **8** as a white solid (565 mg, 97%): mp 29−30 °C; ^{1}H NMR δ 0.88 (3H, t, J = 6.7 Hz), 1.25 (28H, br s), 1.77 (2H, q, J = 7.2 Hz), 3.52 (2H, d, J = 4.8 Hz), 4.67−4.77 (1H, m), 7.17−7.37 (10H, m); ^{13}C NMR δ 14.1, 22.6, 24.4, 29.1, 29.3, 29.4, 29.6 (5C), 31.9, 33.4 (d, J = 5.4 Hz), 34.3 (d, J = 4.3 Hz), 78.9 (d, J = 6.5 Hz), 120.0 (d, J = 4.4 Hz), 120.1 (d, J = 5.4 Hz), 125.3, 129.7, 150.4 (d, J = 4.4 Hz), 150.4 (d, J = 3.3 Hz); ^{31}P NMR δ −11.99. Anal. Calcd for $C_{30}H_{46}BrO_4P$: C, 61.96; H, 7.97. Found: C, 62.21; H, 8.20.

General Protocol for Rearrangements of 1, 6, 7, and 8 with Bu_3SnH. To a solution of the appropriate radical precursor in benzene (20 mL) was added a solution of *n*-Bu_3SnH (1.2−1.5 equiv) and AIBN (5−10 mol %) in benzene (20 mL) at reflux under Ar with the aid of a motor-driven syringe pump over a period of 17−25 h (Table 1). After the addition was complete, heating was continued for another 2 h before cooling to room temperature. After removal of the solvent, the reaction products were identified either by comparision of their ^{1}H NMR spectra with those of the authentic samples or by isolation by column chromatography on silica gel.

2-Methyl-1-heptanyl Diphenyl Phosphate (27): ^{1}H NMR δ 0.87 (3H, t, J = 6.9 Hz), 0.92 (3H, d, J = 6.8 Hz), 1.09−1.37 (8H, m), 1.81 (1H, m), 3.99−4.14 (2H, m), 7.16−7.37 (10H, m); ^{13}C NMR δ 11.0, 16.4, 22.5, 26.3, 31.9, 32.6, 33.8 (d, J = 6.9 Hz), 74.0 (d, J = 6.7 Hz), 120.1 (d, J = 4.6 Hz), 125.2, 129.7, 150.6 (d, J = 7.6 Hz); ^{31}P NMR δ −11.23. Anal. Calcd for $C_{20}H_{27}O_4P$: C, 66.29; H, 7.51. Found: C, 66.19; H, 7.52.

2-Octadecanyl Diphenyl Phosphate (28): mp 36.5−37 °C; ^{1}H NMR δ 0.88 (3H, t, J = 6.7 Hz), 1.26 (28H, br s), 1.44 (3H, d, J = 6.2 Hz), 1.50−1.75 (2H, m), 4.73 (1H, quintet, J = 6.4 Hz), 7.15−7.36 (10H, m); ^{13}C NMR δ 14.1, 21.5 (d, J = 3.2 Hz), 22.7, 25.0, 29.3, 29.4, 29.5, 29.5, 29.69, 29.7 (6C), 31.9, 37.3 (d, J = 6.1 Hz), 78.5 (d, J = 6.7 Hz), 120.1 (d, J = 4.4 Hz), 120.1 (d, J = 4.4 Hz), 125.1, 129.7, 150.7 (d, J = 8.7 Hz); ^{31}P NMR δ −11.96. Anal. Calcd for $C_{30}H_{47}O_4P$: C, 71.68; H, 9.42. Found: C, 71.45; H, 9.28.

***S*-Phenyl 1-Deoxy-1-thio-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (10).** A solution of Brigl's anhydride[19] (**9**) (1.44 g, 5 mmol) in CH_2Cl_2 (25 mL) and PhSH (550 mg, 5.0 mmol) was heated to reflux for 12 h. After removal of the solvent, the title compound[58] was separated from the unreacted starting material by preparative TLC (eluant EtOAc/hexane, 1/1) (0.9 g, 45%) as a highly hygroscopic foam: ^{1}H NMR ($CDCl_3$), δ 2.03 (3H, s), 2.07 (3H, s), 2.09 (3H, s), 2.51 (1H, d, J = 2.9 Hz), 3.50 (1H, td, J = 2.7, 9.4 Hz), 3.73 (1H, ddd, J = 2.6, 4.8, 10.0 Hz), 4.18 (1H, dd, J = 2.7, 12.3 Hz), 4.24 (1H, dd, J = 4.9, 12.3 Hz), 4.57 (1H, d, J = 9.8 Hz), 4.98 (1H, t, J = 9.7 Hz), 5.15 (1H, t, J = 9.3 Hz), 7.33−7.36 (3H, m), 7.55−7.58 (2H, m).

***S*-Phenyl 1-Deoxy-1-thio-2-*O*-(diphenoxyphosphoryl)-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (11).** A solution of **10** (187 mg, 0.56 mmol) and DMAP (73 mg, 0.60 mmol) in CH_2Cl_2 (10 mL) was treated with diphenyl chlorophosphate (161 mg, 0.6 mmol) dissolved in CH_2Cl_2 (5 mL). After refluxing under Ar for 24 h, the reaction mixture was cooled to room temperature, washed with saturated NH_4Cl, water, and brine, dried (Na_2SO_4), and concentrated in *vacuo*. Purification by preparative TLC (eluant EtOAc/hexane, 2/1) gave **11** (235 mg, 67%) as a solid: mp 130−132 °C; ^{1}H NMR δ 1.84 (3H, s), 2.01 (3H, s), 2.08 (3H, s), 3.77 (1H, ddd, J = 3.2, 4.2, 10.0 Hz), 4.20 (1H, d, J = 3.0 Hz), 4.21 (1H, d, J = 4.5 Hz), 4.60 (1H, quartet, J = 9.8 Hz), 5.00 (1H, t, J = 9.8 Hz), 7.15−7.45 (15H, m); ^{13}C NMR δ 20.5 (2C), 20.6, 61.9, 68.3, 75.6, 75.7 (d, J = 6.6 Hz), 85.9 (d, J = 6.6 Hz), 119.9 (d, J = 5.4 Hz), 120.2 (d, J = 4.4 Hz), 125.4, 128.4, 128.8, 129.6, 129.8, 131.1, 133.5, 150.3, 169.4, 170.2, 170.5; ^{31}P NMR δ −12.94. Anal. Calcd for $C_{30}H_{31}OPS$: C, 57.14; H, 4.95; S, 5.08. Found: C, 56.70; H, 5.18; S, 4.98.

Rearrangement of 11 with Bu_3SnH. To a solution of **11** (63 mg, 0.10 mmol) in benzene (20 mL) at reflux was added a solution of Bu_3SnH (35 mg, 0.12 mmol) and AIBN (2 mg, 0.012 mmol) in benzene (20 mL) over 17 h using a motor-driven syringe pump. After a further 2 h at reflux, another portion of Bu_3SnH (40 mg, 0.137 mmol) and AIBN (4 mg, 0.024 mmol) in benzene (20 mL) was added over 8 h. After the addition was complete, heating was continued for another 2 h before the reaction mixture was cooled to room temperature. Removal of the solvent *in vacuo* followed by ^{1}H NMR examination of the crude reaction mixture revealed the formation of tri-*O*-acetyl-D-glucal (**30**), identified by comparision with the spectrum of a commercial sample, as the only product, together with unreacted **11** in the ratio of **30/11** = 27/73.

(±)-*ribo*-3-Acetoxy-2-bromo-1,3-diphenyl-1-propanol (12) and (±)-*arabino*-3-Acetoxy-2-bromo-1,3-diphenyl-1-propanol (13). 3-Acetoxy-1,3-diphenyl-1(*E*)-propene[20] (3.40 g, 13.5 mmol) was dissolved in 50 mL of DMSO followed by the addition of 2.4 mL of H_2O. Freshly recrystallized NBS (2.88 g, 16.2 mmol) was then added to the stirred reaction mixture. After stirring for 8 h at room temperature, the reaction mixture was poured into aqueous $NaHCO_3$ solution (100 mL) and extracted with CH_2Cl_2 (2 × 150 mL). The combined extracts were washed with 2 M HCl (1 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo to give crude **12** and **13** in an approximately 1/1 ratio. Purification by column chromatography (8/1 hexane/ether) gave first a fraction containing **12** and **13** (2.16 g) in an approximately 10/1 ratio. Recrystallization of this fraction from hexane/ether gave 1.83 g of **12** as white crystals: mp 97−98 °C (lit.[21] mp 104−105 °C); ^{1}H NMR δ 1.99 (3H, s), 4.67 (2H, m), 6.23 (1H, d, J = 4.70 Hz), 7.51−7.34 (10H, m); ^{13}C NMR δ 21.1, 60.0, 74.1, 74.9, 127.0, 128.0, 128.2, 128.5, 128.60, 128.64, 136.4, 140.5, 169.4; IR (CH_2Cl_2) 3588, 1740 cm^{-1}. Anal. Calcd for $C_{17}H_{17}O_3Br$: C, 58.47; H, 4.91. Found: C, 58.23; H, 5.20. Further elution yielded another fraction containing **12** and **13** (2.46 g) in an approximately 1/8 ratio. Recrystallization of this fraction from hexane/CH_2Cl_2 gave 2.1 g of **13** as white crystals: mp 110−112 °C; ^{1}H NMR δ 2.28 (3H, s), 4.30 (1H, dd, J = 2.29, 8.52 Hz), 4.76 (1H, d, J = 8.52 Hz), 6.43 (1H, d, J = 2.29 Hz), 7.33−7.42 (10H, m); ^{13}C NMR δ 21.1, 60.3, 74.6, 75.3, 127.7, 128.8, 128.9, 129.2, 129.3, 129.4, 137.0, 141.3, 169.0; IR (CH_2Cl_2) 3578, 1737 cm^{-1}. Anal. Calcd for $C_{17}H_{17}O_3Br$: C, 58.47; H, 4.91. Found: C, 58.41; H, 4.95. The combined yield of **12** and **13** was 83%.

***ribo*-1-Acetoxy-2-bromo-3-(diphenylphosphatoxy)-1,3-diphenylpropane (18).** A solution of bromohydrin **12** (3 g, 8.59 mmol), diphenyl chlorophosphate (6.92 g, 25.8 mmol), dry pyridine (20 mL), and catalytic DMAP in dry CH_2Cl_2 (10 mL) was stirred for 12 h, with heating from a water bath. The reaction mixture was then diluted with CH_2Cl_2 (150 mL), washed with 2 M HCl (2 × 100 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give crude **18**. Purification by flash column chromatography (gradient elution 8/1 hexane/ether to 100% ether) yielded **18** (3.95 g, 79%) as a pale yellow oil. Recrystallization from hexane/THF gave **18** as white crystals: mp 77−79 °C; ^{1}H NMR δ 2.06 (3H, s), 4.73 (1H, t, J = 7.71 Hz), 5.67 (1H, t, J = 7.71 Hz), 5.74 (1H, d, J = 7.71 Hz), 6.87 (2H, d, J = 8.15 Hz), 7.35−7.08 (18H,

(58) Bols, M. *Acta Chem. Scand.* **1993**, *47*, 829.

m); ^{13}C NMR δ 21.1, 57.8 (d, J = 9.61 Hz), 74.7, 79.9 (d, J = 5.13 Hz), 119.9 (d, J = 5.03 Hz), 120.5 (d, J = 4.65 Hz), 125.2 (d, J = 1.01 Hz), 125.6 (d, J = 1.01 Hz), 128.05, 128.18, 128.23, 128.7, 129.4, 129.6, 129.87, 129.88, 135.0 (d, J = 2.53 Hz), 136.2, 150.2 (d, J = 7.08 Hz), 150.3 (d, J = 7.58 Hz), 169.4; ^{31}P NMR δ −12.86 (d, J = 6.40 Hz); IR (CH_2Cl_2) 1742, 1596, 1496, 1226, 1190 cm^{-1}. Anal. Calcd for $C_{29}H_{26}O_6BrP$: C, 59.91; H, 4.51. Found: C, 59.98; H, 4.57.

***arabino*-1-Acetoxy-2-bromo-3-(diphenylphosphatoxy)-1,3-diphenylpropane (19).** A solution of bromohydrin **13** (2.5 g, 7.16 mmol), diphenyl chlorophosphate (5.77 g, 21.5 mmol), dry pyridine (20 mL), and catalytic DMAP in dry CH_2Cl_2 (10 mL) was stirred for 12 h, with heating from a water bath. The reaction mixture was then diluted with CH_2Cl_2 (150 mL), washed with 2 M HCl (2 × 100 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give crude **19**. Purification by flash column chromatography (gradient elution 4/1 hexane/ether to 100% ether) yielded 3.54 g (85%) of **19** as a white solid. Recrystallization from hexane/CH_2Cl_2 gave **19** as white crystals: mp 153 °C; ^{1}H NMR δ 2.14 (3H, s), 4.47 (1H, dd, J = 3.26, 8.43 Hz), 5.75 (1H, t, J = 8.43 Hz), 6.20 (1H, d, J = 3.26 Hz), 6.81 (2H, d, J = 8.19 Hz), 7.41−7.13 (18H, m); ^{13}C NMR δ 20.9, 59.2 (d, J = 10.1 Hz), 72.5, 80.6 (d, J = 5.40 Hz), 119.9 (d, J = 4.88 Hz), 120.1 (d, J = 3.38 Hz), 125.2 (d, J = 1.23 Hz), 125.4 (d, J = 1.43 Hz), 126.4, 128.0, 128.42, 128.45, 129.4, 129.6, 129.8, 136.4 (d, J = 4.58 Hz), 137.9, 150.2 (d, J = 7.49 Hz), 150.4 (d, J = 7.25 Hz), 169.4; ^{31}P NMR δ −12.77 (d, J = 8.49 Hz); IR (CH_2Cl_2) 3072, 3039, 1749, 1584, 1490, 1449 cm^{-1}. Anal. Calcd for $C_{29}H_{26}O_6BrP$: C, 59.91; H, 4.51. Found: C, 59.67; H, 4.57.

***ribo*-2-Bromo-1,3-indandiol (20).** A solution of 2,2-dibromo-1,3-indandione[59] (15 g, 0.049 mol) in MeOH (200 mL) was cooled to 0 °C, and $NaBH_4$ (7.47 g, 0.197 mol) was added portionwise over a 1 h period. After stirring for an additional 4 h at that temperature, the reaction mixture was quenched with saturated NH_4Cl solution (100 mL) and left sitting at 0 °C overnight. A white solid precipitated and was filtered off, yielding 8.9 g of crude **20** as a pale yellow semisolid. Recrystallization from ligroin/THF yielded **20** (5.54 g, 42%) as white crystals: mp 199−200 °C; ^{1}H NMR δ 4.95 (1H, t, J = 4.46), 5.15 (2H, d, J = 4.46 Hz), 7.61−7.45 (4H, m); ^{13}C NMR δ 65.6, 74.1, 125.7, 130.8, 140.8; IR (CH_2Cl_2) 3354, 3260 cm^{-1}. Anal. Calcd for $C_9H_9O_2Br$: C, 47.19; H, 3.96. Found: C, 47.19; H, 3.99.

***ribo*-2-Bromo-1,3-bis(diphenylphosphatoxy)indan (21).** A solution of **20** (257 mg, 1.12 mmol), diphenyl chlorophosphate (1.05 g, 3.92 mmol), pyridine (20 mL), and catalytic DMAP in CH_2Cl_2 (30 mL) was heated on a water bath for 18 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with 2 M HCl (100 mL) and saturated K_2CO_3 solution (100 mL), dried (Na_2SO_4), and concentrated *in vacuo*, yielding 1.3 g of crude **21**. Purification by flash chromatography (gradient elution 6/1 hexane/ether to 100% ether) gave 482 mg (62%) of **21** as a pale yellow oil. Recrystallization from hexane/ether gave **21** as white crystals: mp 78−80 °C; ^{1}H NMR δ 4.69 (1H, m), 5.80 (2H, t, J = 5.10 Hz), 7.39−7.04 (24H, m); ^{13}C NMR δ 52.5 (t, J = 7.04 Hz), 79.4 (d, J = 5.33 Hz), 120.4 (d, J = 4.65 Hz), 120.5 (d, J = 4.33 Hz), 125.4 (d, J = 1.43 Hz), 125.5 (d, J = 1.43 Hz), 126.0, 129.7 (d, J = 1.05 Hz), 129.8 (d, J = 1.20 Hz), 130.7, 138.3, (d, J = 3.15 Hz), 150.2 (d, J = 7.08 Hz), 150.5 (d, J = 7.81 Hz); ^{31}P NMR δ −11.74 (d, J = 7.10 Hz); IR (CH_2Cl_2) 1591, 1491, 1285, 1189 cm^{-1}. Anal. Calcd for $C_{33}H_{27}O_8BrP_2$: C, 56.83; H, 3.90. Found: C, 56.79; H, 3.86.

***ribo*-2-Bromo-3-(diphenylphosphatoxy)-1-indanol (22).** A solution of **20** (750 mg, 3.27 mmol) and bis(tributyltin) oxide (2.93 g, 4.91 mmol) were refluxed in benzene, while azeotroping water with a Dean−Stark apparatus, for 18 h. The reaction mixture was then brought to room temperature and diphenyl chlorophosphate (1.76 g, 6.54 mmol) added, followed by an additional 3 h of stirring at that temperature. The solvent was then evaporated *in vacuo*, and the residue diluted in CH_3CN (50 mL) and washed with hexane (3 × 50 mL), yielding crude **22**. Purification by column chromotography (gradient elution 5/1 hexane/ether to 3/1 hexane/ether) gave 436 mg (28%) of **22** as a pale yellow syrup: ^{1}H NMR δ 4.89 (2H, m), 5.79 (1H, dd, J = 3.84, 8.55 Hz), 7.50−7.15 (14H, m); ^{13}C NMR δ 62.0 (d, J = 4.50 Hz), 73.2, 79.0 (d, J = 5.48 Hz), 120.3 (d, J = 4.88 Hz), 120.4 (d, J = 4.95 Hz), 124.9, 125.2, 125.6, 129.4, 129.80, 129.83 (d, J = 1.00 Hz), 129.9 (d, J = 1.00 Hz), 130.2, 137.1 (d, J = 4.31 Hz), 141.6, 150.3 (d, J = 7.07 Hz), 150.4 (d, J = 7.58 Hz); ^{31}P NMR δ −11.94 (d, J = 8.64 Hz); IR (CH_2Cl_2) 3533, 1592, 1491 cm^{-1}. Anal. Calcd for $C_{21}H_{18}BrO_5P$: C, 54.68; H, 3.93. Found: C, 54.58; H, 3.91.

***arabino*-2-Bromo-1,3-bis(diphenylphosphatoxy)indan (23).** Diethyl azodicarboxylate (378 mL, 2.41 mmol) was added dropwise to a stirred solution of **22** (370 mg, 0.802 mmol), triphenylphosphine (631 mg, 2.41 mmol), and diphenyl phosphate (602 mg, 2.41 mmol) in dry benzene under N_2. The reaction was stirred for 1 h at room temperature followed by an additonal 24 h at reflux. The solvent was concentrated *in vacuo* and ether added. The mixture was kept at 0 °C overnight, resulting in the formation of a white precipitate. The precipitate was filtered and washed with ether, and the filtrate collected and concentrated *in vacuo* to give crude **23**. Purification by column chromotography (gradient elution 5/1 hexane/ether to 100% ether) gave 302 mg (54%) of **23** as a pale yellow syrup: ^{1}H NMR δ 7.38−7.13 (22H, m), 7.01 (2H, d, J = 8.21 Hz), 6.14 (1H, dd, J = 5.39, 7.61 Hz), 5.98 (1H, t, J = 5.77 Hz); ^{13}C NMR δ 53.4 (dd, J = 6.06, 6.83 Hz), 79.4 (d, J = 4.04 Hz), 85.4 (d, J = 5.56 Hz), 120.1 (d, J = 1.13 Hz), 120.2 (d, J = 1.13 Hz), 120.22, 120.3, 120.4, 125.3, 125.4, 125.5, 125.6, 126.0, 129.73 (d, J = 2.12 Hz), 129.74 (d, J = 3.15), 129.9 (d, J = 2.85 Hz), 129.9 (d, J = 2.85 Hz), 130.3, 130.8, 137.5 (d, J = 2.78 Hz), 138.6 (d, J = 3.80 Hz), 150.0−150.5 (m, 4C); ^{31}P NMR δ −11.71 (d, J = 5.2 Hz), −11.86 (d, J = 7.02 Hz); IR (CH_2Cl_2) 1591, 1490, 1285 cm^{-1}. Owing to slow decomposition, we have been unable to obtain microanalytical data on this compound.

Rearrangement of 18 to (±)-*threo*-1-Acetoxy-2-(diphenylphosphatoxy)-1,3-diphenylpropane (35). Tributyltin hydride (33 μL, 0.12 mmol) and catalytic AIBN in benzene (10 mL) were added over 14 h via a motor-driven syringe pump to **18** (60 mg, 0.10 mmol) in benzene (20 mL) at reflux under N_2. After the addition was complete, the reaction mixture was allowed to reflux for an additional 6 h. The solvent was then evaporated *in vacuo*, and the remaining crude reaction mixture was diluted in CH_3CN (50 mL) and washed with hexane (3 × 50 mL) to yield 58 mg of crude **35** containing <5% of the *erythro*-isomer **38** and the reduced product **37** as judged by ^{1}H NMR. Purification by column chromatography (eluent 6/1 hexane/ether) yielded 32 mg (69%) of **35** as a colorless oil. Recrystallization from ligroin/THF gave **35** as a white solid: mp 46−47 °C; ^{1}H NMR δ 7.33−7.04 (18H, m), 6.95 (2H, d, J = 8.70 Hz), 5.84 (1H, d, J = 7.11 Hz), 5.22 (1H, m), 2.91 (1H, dd, J = 3.84, 13.6 Hz), 2.80 (1H, dd, J = 7.20, 13.6 Hz), 1.96 (3H, s); ^{13}C NMR δ 21.0, 37.9 (d, J = 3.75 Hz), 75.9 (d, J = 4.50 Hz), 87.2 (d, J = 6.60 Hz), 119.8, 120.0, 125.0 (d, J = 1.13 Hz), 125.2 (d, J = 1.25 Hz), 126.8, 127.7, 128.0, 128.2, 128.8, 129.4, 129.6, 129.7, 135.5, 136.1, 150.5 (d, J = 7.03 Hz), 150.6 (d, J = 7.04 Hz); ^{31}P NMR δ −12.1 (d, J = 8.55 Hz); IR (CH_2Cl_2) 1742, 1591, 1491 cm^{-1}. Anal. Calcd for $C_{29}H_{27}O_6P$: C, 69.32; H, 5.42. Found: C, 69.22; H, 5.16.

Rearrangement of 19 to (±)-*erythro*-1-Acetoxy-2-(diphenylphosphatoxy)-1,3-diphenylpropane (38). Tributyltin hydride (120 μL, 0.45 mmol) and catalytic AIBN in benzene (10 mL) were added over 12 h via a motor-driven syringe pump to **19** (200 mg, 0.34 mmol) in benzene (40 mL) at reflux under N_2. After the addition was complete, the reaction mixture was allowed to reflux for an additional 6 h. The solvent was then evaporated *in vacuo*, and the remaining crude reaction mixture was diluted in CH_3CN (50 mL) and washed with hexane (3 × 50 mL) to yield 193 mg of crude **38** containing <5% of the *threo*-isomer **35** and the reduced product **40** as judged by ^{1}H NMR spectroscopy. Purification by column chromatography (4/1 hexane/ether) yielded 173 mg (79%) of **38** as a colorless oil. Recrystallization from hexane/ether gave **38** as white crystals: mp 79 °C; ^{1}H NMR δ 2.02 (3H, s), 2.84 (1H, dd, J = 3.83, 14.6 Hz), 2.94 (1H, dd, J = 7.66, 14.6 Hz), 5.28 (1H, m), 5.91 (1H, d, J = 3.80 Hz), 6.90 (2H, d, J = 8.18 Hz), 7.43−7.12 (18H, m); ^{13}C NMR δ 21.0, 37.3 (d, J = 4.80 Hz), 75.8 (d, J = 4.13 Hz), 81.9 (d, J = 6.45 Hz), 169.7, 119.93 (d, J = 4.80 Hz), 119.99, (d, J = 4.88 Hz), 125.1 (d, J = 1.05 Hz), 125.2 (d, J = 1.35 Hz), 126.9, 128.0, 128.4, 128.61, 128.63, 129.4, 129.6, 129.7, 135.1, 135.9, 150.5 (d, J = 7.42 Hz), 150.7 (d, J = 7.19 Hz); ^{31}P NMR δ −11.72 (d, J = 8.31 Hz); IR (CH_2Cl_2) 1741, 1593, 1492, 1456 cm^{-1}. Anal. Calcd for $C_{29}H_{27}O_6P$: C, 69.32; H, 5.42. Found: C, 68.94; H, 5.56.

Attempted Rearrangement of 21. Isolation of *cis*-1,3-Bis(diphenylphosphatoxy)indan (41). Tributyltin hydride (34 μL, 0.127 mmol)

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and catalytic AIBN in benzene (10 mL) were added over 18 h via a motor-driven syringe pump to **21** (80 mg, 0.115 mmol) in benzene (20 mL) at reflux under N_2. After the addition was complete, the reaction mixture was allowed to reflux for an additional 6 h. The solvent was then evaporated *in vacuo*, and the remaining crude reaction mixture was diluted in CH_3CN (50 mL) and washed with hexane (3 × 50 mL) to yield 73 mg of crude **41** free of **42** as judged by ^1H NMR spectroscopy. In a further experiment, a solution of **21** (520 mg, 0.75 mmol), tributyltin hydride (261 μL, 0.975 mmol), and catalytic AIBN was refluxed in benzene under nitrogen for 18 h. The solvent was then evaporated *in vacuo*, and the remaining residue was diluted in CH_3CN (50 mL) and washed with hexane (3 × 50 mL), yielding crude **41**. Purification by flash chromotography (gradient elution 10/1 hexane/EtOAc to 3/1 hexane/EtOAc) gave 483 mg (95%) of **41** as a clear oil: ^1H NMR δ 2.39 (1H, dt, J = 3.83, 14.0 Hz), 2.97 (1H, dt, J = 7.10, 14.4 Hz), 5.88 (2H, m), 7.39−7.15 (24H, m); ^{13}C NMR δ 41.4, 79.2 (d, J = 4.33 Hz), 120.1 (d, J = 3.53 Hz), 120.2 (d, J = 3.83 Hz), 125.40, 125.49, 129.70, 129.74, 130.1, 140.1 (d, J = 6.00 Hz), 150.4 (d, J = 6.10 Hz); ^{31}P NMR δ −11.67 (d, J = 7.57 Hz); IR (CH_2Cl_2) 1542, 1492, 1282 cm^{-1}. Anal. Calcd for $C_{33}H_{28}O_8P_2$: C, 64.50; H, 4.59. Found: C, 64.36; H, 4.60.

Rearrangement of 23. *trans*-1,3-Bis(diphenylphosphatoxy)indan (43) and *trans*-1,2-Bis(diphenylphosphatoxy)indan (44). Tributyltin hydride (45 μL, 0.166 mmol) and catalytic AIBN in benzene (10 mL) were added over 12 h via a motor-driven syringe pump to **23** (89 mg, 0.128 mmol) in benzene (25 mL) at reflux under N_2. After the addition was complete, the reaction mixture was allowed to reflux for an additional 6 h. The solvent was then evaporated *in vacuo*, and the remaining crude reaction mixture was diluted in CH_3CN (50 mL) and washed with hexane (3 × 50 mL) to yield 82 mg of a mixture of **43** and **44** in the ratio 1/4.78. The reduced product **43**, extremely unstable with respect to isomerization to its *cis*-isomer, was identified with the aid of an authentic sample. Repeated preparative TLC (eluent ether/hexane, 3/1) enabled the isolation of a pure sample of **44**: ^1H NMR δ 3.06 (1H, dd, J = 4.30, 16.6 Hz), 3.49 (1H, dd, J = 6.45, 16.6 Hz), 5.38 (1H, m), 6.08 (1H, dd, J = 3.36, 7.58 Hz), 7.34−7.10 (23H, m), 7.39 (1H, d, J = 7.52 Hz); ^{13}C NMR δ 37.2 (d, J = 4.90 Hz), 83.8 (dd, J = 9.38, 11.8 Hz), 85.9 (dd, J = 9.79, 15.5 Hz), 120.2−120.1 (4C, m), 125.1, 125.5−125.4 (4C, m), 126.0, 127.8, 129.7, 129.80, 129.81, 130.2, 136.6 (d, J = 4.89 Hz), 139.6, 150.4−150.3 (4C, m); ^{31}P NMR δ −12.00 (d, J = 8.25 Hz), −12.31 (δ, J = 5.95 Hz); IR (CH_2Cl_2) 1591, 1490 cm^{-1}. Anal. Calcd for $C_{33}H_{28}O_8P_2$: C, 64.50; H, 4.59. Found: C, 64.39; H, 4.68.

***trans*-1,3-Bis(diphenylphosphatoxy)indan (43). Preparation of an Authentic Sample.** A 9/1 mixture of *trans*- and *cis*-1,3-indandiol (90 mg, 0.61 mmol), diphenyl chlorophosphate (0.36 g, 1.34 mmol), pyridine (25 mL), and catalytic DMAP was stirred at room temperature for 18 h. The reaction mixture was then diluted with CH_2Cl_2 (100 mL), washed with 2 M HCl (1 × 100 mL) and saturated $NaHCO_3$ solution (1 × 100 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give 0.27 g of crude *trans*- and *cis*-1,3-bis(diphenylphosphatoxy)indan in a 1/1 ratio. Purification of 70 mg of the 1/1 diphosphate mixture was achieved by preparative TLC on silica gel (eluent ethyl acetate/hexane, 2/1), giving 9 mg of the title compound as a pale yellow oil: ^1H NMR δ 4.69 (2H, t, J = 5.21 Hz), 6.19 (2H, q, J = 5.21 Hz), 7.41−7.13 (24H, m); ^{13}C NMR δ 42.2 (t, J = 4.54 Hz), 80.9 (d, J = 5.85 Hz), 120.1 (d, J = 3.15 Hz), 120.2 (d, J = 3.08 Hz), 125.5 (d, J = 4.27 Hz), 125.6 (d, J = 3.83 Hz), 129.77, 129.85, 130.5, 140.6, (d, J = 5.78 Hz), 150.4 (d, J = 5.48, 2C); ^{31}P NMR δ −11.60 (d, ^3J = 6.34). Owing to isomerization on standing, it was not possible to obtain a microanalysis of this substance.

2-(2-Bromo-1-phenylethoxy)-*cis*-4,5-diphenyl-2-oxo-1,3,2-dioxaphospholane (45). A mixture of 2-(*N*,*N*-diisopropylamino)-*cis*-4,5-diphenyl-1,3,2-dioxaphospholane (515 mg,1.5 mmol), styrene bromohydrin (271 mg, 1.35 mmol), and tetrazole (105 mg, 1.5 mmol) in DCM (15 mL) was stirred at room temperature for 24 h. Saturated $NaHCO_3$ (20 mL) was then added and the reaction mixture extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and evaporated to dryness under vacuum to give the crude phosphite (569 mg, 95%) as a viscous oil, which was ~90% pure by ^1H NMR, and a 7/3 mixture of diastereomers: ^1H NMR δ 3.65 (minor) and 3.72 (major) (2H, dd for the minor with J = 5.1, 7.3 Hz; d for the major with J = 6.0 Hz), 5.53−5.76 (3H, m), 6.87−7.44 (15H, m); ^{31}P NMR δ 139.43 (minor) and 150.53 (major). This substance was then taken up in dry benzene (10 mL) and treated with *tert*-butyl hydroperoxide (5.5 M in 2,2,4-trimethylpentane, 0.3 mL, dried over 4 Å molecular sieves) in benzene (15 mL). After 5 min, solid NaS_2O_3 (0.5 g) was added. After stirring for 5 min, the reaction mixture was quickly filtered and the filtrate concentrated *in vacuo* to give **45** (580 mg, 94%) as a 7/3 mixture of diastereomers as determined by ^{31}P NMR in the form of a syrup. The product thus obtained was 90% pure by ^1H NMR. No further purification was attempted due to rapid decomposition on silica gel or basic alumina and upon exposure to trace amounts of moisture: ^1H NMR δ 3.70−3.87 (2H, m), 5.73−6.01 (3H, m), 6.99−7.48 (5H, m); ^{13}C NMR δ 35.2 (minor) (d, J = 6.7 Hz) and 35.4 (major) (d, J = 6.8 Hz), 80.5 (minor) (d, J = 6.7 Hz) and 81.0 (major) (d, J = 4.5 Hz), 83.5 (minor) and 83.6 (major) (d, J = 4.5 Hz), 126.4, 126.5, 126.6, 126.7, 128.0, 128.4, 128.5, 128.5, 128.8, 129.3; ^{31}P NMR δ 14.71 (minor) and 15.36 (major).

2-(1-Phenylethoxy)-*cis*-4,5-diphenyl-2-oxo-1,3,2-dioxaphospholane (46). Preparation of an Authentic Sample. This compound was prepared from 1-phenylethanol (37 mg, 0.30 mmol) and 2-(*N*,*N*-diisopropylamino)-*cis*-4,5-diphenyl-1,3,2-dioxaphospholane according to the protocol described for **45** above. The crude product (120 mg) was about 85% pure with contamination by a small amount of 1-phenylethanol. No further purification was attempted due to rapid decomposition on silica gel or basic alumina and upon exposure to a trace amount of moisture: ^1H NMR δ 1.77 (minor) and 1.81 (major) (3H, 2d, J = 6.5 Hz for both diastereomers), 5.70−5.94 (3H, m), 6.92−7.50 (15H, m); ^{13}C NMR δ 23.8 (minor) (d, J = 5.6 Hz) and 24.0 (major) (d, J = 5.7 Hz), 78.5 (minor) (d, J = 5.7 Hz) and 79.2 (major) (d, J = 4.5 Hz), 83.2, 83.3, 125.9, 126.3, 126.4, 126.6, 126.8, 127.6, 127.8, 127.9, 127.9, 128.2, 128.3, 133.7, 133.8, 134.0, 134.1, 144.2, 140.8, 140.9, 141.0; ^{31}P NMR δ 14.90 (minor) and 15.60 (major).

2-(2-Phenylethoxy)-*cis*-4,5-diphenyl-2-oxo-1,3,2-dioxaphospholane (47). Preparation of an Authentic Sample. This compound was prepared from 2-phenylethanol (37 mg, 0.30 mmol) and 2-(*N*,*N*-diisopropylamino)-*cis*-4,5-diphenyl-1,3,2-dioxaphospholane according to the protocol described for **45** above. The crude product (114 mg), an approximately 6/4 mixture of diastereomers as determined by ^{31}P NMR, was about 95% pure with contamination by a small amount of 1-phenylethanol. No further purification was attempted due to rapid decomposition on silica gel or basic alumina and upon exposure to a trace amount of moisture: ^1H NMR δ 3.11 (*trans*) and 3.16 (*cis*) (2H, 2d, J = 7.0 for *trans* and 6.8 Hz for *cis*), 4.51 (*trans*) and 4.62 (*cis*) (2H, 2(td), J = 7.0 and 9.1 Hz for both *trans* and *cis*), 5.64 (*trans*) and 5.91 (*cis*) (2H, 2d, J = 7.9 for *trans* and 8.2 Hz for *cis*), 6.91−7.36 (15H, m); ^{13}C NMR δ 36.9 (d, J = 8.4 Hz) (*trans*) and 37.1 (d, J = 5.6 Hz) (*cis*), 69.3 (d, J = 5.7 Hz) (*trans*) and 70.3 (d, J = 5.7z) (*cis*), 83.4 (d, J = 2.3 Hz), 126.4, 126.5, 126.8, 127.1, 127.9, 128.0, 128.4, 128.5, 128.6, 129.1, 129.1, 137.0; ^{31}P NMR ($CDCl_3$) δ 15.50 (*trans*) and 16.57 (*cis*).

Rearrangement of 45 with Bu_3SnH. To a solution of **45** (551 mg, 1.2 mmol) in benzene (40 mL) at reflux was added a solution of Bu_3SnH (524 mg, 1.8 mmol) and AIBN (10 mg, 0.06 mmol) in benzene (20 mL) over 13 h. After the addition was complete, the reaction mixture was heated to reflux for a further 2 h. After cooling to room temperature, the solvent was removed under vacuum. Examination of the crude reaction mixture by ^1H NMR revealed complete consumption of **45** with formation of **46** and **47** (**46**/**47** = 60/40). The *cis*/*trans*-isomer ratio of **47** was determined to be 62/38.

2-Bromo-1-phenylethyl Dibenzyl Phosphate (51). A solution of bis(diisopropylamino)(benzyloxy)phosphine (372 mg, 1.1 mmol),[27b] benzyl alcohol (108 mg, 1.0 mmol), and diisopropylaminium tetrazolide (171 mg, 1.0 mmol)[27a] in CH_2Cl_2 (20 mL) was stirred for 5 h at room temperature before a solution of styrene bromohydrin (201 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was introduced. After stirring overnight at room temperature, the reaction was quenched by adding saturated $NaHCO_3$ (15 mL). The reaction mixture was extracted with CH_2Cl_2 (2 × 15 mL) and the combined organic extracts washed with brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was then taken up in benzene (15 mL) and treated with *tert*-butyl hydroperoxide (5.5 M in 2,2,4-trimethylpentane, 0.2 mL, dried over 4 Å molecular sieves). Removal of the solvent followed by column chromatography on silica

gel (eluant ether/hexane, 3/2) gave the title compound (250 mg, 54%) as a colorless oil: ^{1}H NMR δ 3.54 (1H, ddd, J = 2.2, 5.1, 10.7 Hz), 3.63 (1H, dd, J = 7.4, 10.9 Hz), 4.83 (2H, br d, J = 7.4 Hz), 4.98 (1H, dd, J = 7.5, 11.7 Hz), 5.04 (1H, dd, J = 7.4, 11.6 Hz), 5.48 (1H, dt, J = 5.2, 7.5 Hz), 7.12–7.32 (15H, m); ^{13}C NMR δ 35.3 (d, J = 8.7 Hz), 69.2 (d, J = 5.6 Hz), 69.4 (d, J = 5.6 Hz), 79.4 (d, J = 5.5 Hz), 126.7, 127.8, 127.9, 128.4, 128.5, 128.5, 128.5, 128.7, 129.2, 135.7, 137.5; ^{31}P NMR δ −1.60. Anal. Calcd for $C_{22}H_{22}BrO_4P$: C, 57.3; H, 4.81. Found: C, 57.55; H, 4.86.

Dibenzyl 1-Phenylethyl Phosphate (52). Preparation of an Authentic Sample. A solution of tribenzyl phosphite[60] (635 mg, 1.8 mmol) in CH_2Cl_2 (7 mL) was treated with I_2 (457 mg, 1.8 mmol) at 0 °C. After stirring for 5 min at this temperature, this solution was added dropwise to a stirred solution of 1-phenylethanol (183 mg, 1.5 mmol) and pyridine (486 μL, 6 mmol) in CH_2Cl_2 (10 mL) at −40 °C. After the addition was complete, the reaction was brought to room temperature over 30 min and quenched with aqueous sodium bisulfite (10%, 15 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 7 mL). The combined extracts were washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated to dryness. Column chromatography on silica gel (eluant hexane/EtOAc, 2/1) gave **52** (178 mg, 31%) as a colorless oil: ^{1}H NMR δ 1.60 (3H, d, J = 6.5 Hz), 4.88 (2H, d, J = 7.7 Hz), 4.96 (1H, dd, J = 7.8 and 11.4 Hz), 5.04 (1H, dd, J = 11.4 and 11.8 Hz), 5.51 (1H, quintet, J = 6.8 Hz), 7.19–7.36 (15**H**, m); ^{13}C NMR δ 24.1 (d, J = 5.4 Hz), 68.9 (d, J = 5.2 Hz), 69.0 (d, J = 4.9 Hz), 77.1 (d, J = 5.6 Hz), 125.9, 127.7, 127.9, 128.1, 128.3, 128,-34, 128.4, 128.45, 128.5, 135.8 (d, J = 6.5 Hz), 135.8 (d, J = 6.5 Hz), 141.4 (d, J = 4.4 Hz); ^{31}P NMR δ −1.16. Anal. Calcd for $C_{22}H_{23}O_4P$: C, 69.10; H, 6.06. Found: C, 69.32; H, 6.23.

Dibenzyl 2-Phenylethyl Phosphate (53). Preparation of an Authentic Sample. This compound was prepared from 2-phenylethanol (183 mg, 1.5 mmol) in the same way as for the preparation of **52**. Column chromatography on silica gel (eluant hexane/EtOAc, 2/1) gave **53** (210 mg, 37%) as a colorless oil: ^{1}H NMR δ 2.91 (2H, t, J = 7.0 Hz), 4.18 (2H, quartet, J = 7.0 Hz), 4.95 (4H, d, J = 8.1 Hz), 7.15–7.36 (15H, m); ^{13}C NMR δ 36.6 (d, J = 7.2 Hz), 68.1 (d, J = 5.9 Hz), 69.1 (d, J = 5.5 Hz), 124.3, 126.7, 127.9, 128.5, 128.53, 129.0, 135.9 (d, J = 6.5 Hz), 137.1; ^{31}P NMR δ −0.55. Anal. Calcd for $C_{22}H_{23}O_4P$: C, 69.10; H, 6.06. Found: C, 68.93; H, 6.14.

Rearrangement of 51 with Bu_3SnH. To a solution of **51** (185 mg, 0.4 mmol) in benzene (20 mL) at reflux was added a solution of Bu_3SnH (146 mg, 0.5 mmol) and AIBN (3.5 mg, 0.02 mmol) in benzene (20 mL) over 16 h. After the addition was complete, the reaction mixture was heated to reflux for a further 2 h. After cooling to room temperature, the solvent was removed under vacuum. Inspection of the crude reaction mixture by ^{1}H NMR revealed complete consumption of **51** and formation of the direct reduction product **52** and the rearrangement product **53** in the ratio of 95/5.

Preparation of ^{18}O-Labeled 2-Bromo-1-phenylethyl Diphenyl Phosphate 1 from ^{18}O-Labeled Styrene Bromohydrin. A solution of styrene bromohydrin labeled with ^{18}O ($^{18}O/^{16}O$ = 2.01/1 by ^{13}C NMR)[61] (200 mg, 1.00 mmol), diphenyl chlorophosphate (547 mg, 2.00 mmol), dry pyridine (10 mL), and catalytic DMAP in dry CH_2Cl_2 (10 mL) was stirred for 18 h at room temperature. The reaction mixture was then diluted with CH_2Cl_2 (50 mL), washed with 2 M HCl (2 × 100 mL), dried (Na_2SO_4), and concentrated *in vacuo*, yielding crude **1**. Purification by flash column chromatography (gradient elution 8/1 hexane/Et_2O to 100% Et_2O) gave 269 mg (63%) of **1** as pale yellow syrup, whose spectral data matched those of authentic **1**. Examination of the product by GC/MS showed a 2.08/1 $^{18}O/^{16}O$ ratio for $[M - CH_2Br]^+$. A ^{13}C NMR spectrum recorded with a relaxation delay of 2 s showed two fully resolved benzylic carbon doublets at δ 80.70 and 80.67 in the ratio 2.08/1.

Rearrangement of ^{18}O-Labeled 1. Tri-*n*-butyltin hydride (131 μL, 0.488 mmol) and catalytic AIBN in benzene (10 mL) were added over 12 h via a motor-driven syringe pump to a solution of **1** (163 mg, 0.38 mmol) at reflux under N_2 in benzene (75 mL). After the addition was complete, the reaction mixture was allowed to reflux for an additional 6 h. The solvent was then evaporated *in vacuo*, and the remaining crude reaction mixture was diluted in CH_3CN (50 mL) and washed with hexane (3 × 50 mL) to yield 139 mg of crude product. Examination of the crude reaction mixture by NMR showed **3** and **2** in a 3.00/1 ratio. Column chromatography (gradient elution 6/1 hexane/Et_2O to 100% Et_2O) yielded **3** (68 mg). Examination by GC/MS was not possible due to the absence of a reliable molecular ion or fragment ion. A solution of **3** (50 mg, 0.141 mmol) in THF (25 mL) at 0 °C was treated with $LiAlH_4$ (12 mg, 0.310 mmol) over 10 min. The reaction was stirred for 3 h and then diluted with Et_2O (50 mL), washed with a 1/1 brine/2 M HCl solution (1 × 50 mL), and dried (Na_2SO_4) and the solvent evaporated *in vacuo* to yield crude 2-phenylethanol (33 mg). Examination by GC/MS showed a 1.21/1 $^{18}O/^{16}O$ ratio for $[M]^+$.

General Protocol for the Preparation of Phospholanes 56–65. To a solution of *meso*-2,3-butanediol (271 mg, 3.0 mmol) and Et_3N (673 mg, 6.6 mmol) in dry Et_2O (10 mL) was added dropwise $POCl_3$ (506 mg, 3.3 mmol) at 0 °C under an argon atmosphere. After stirring at this temperature for 30 min, triethylammonium chloride was removed by filtration and the filtrate concentrated *in vacuo*. The residue was taken up in dry benzene (10 mL) and DMAP (403 mg, 3.3 mmol) added, followed by the appropriate alcohol (2.0 mmol). The reaction mixture was then heated to reflux under Ar for 20–30 h. After cooling to room temperature, the solid part was filtered off, the filtrate was concentrated to dryness, and the products were isolated by column chromatography on silica.

***trans*-2-(2-Bromo-1-phenylethoxy)-*cis*-4,5-dimethyl-2-oxo-1,3,2-dioxaphospholane (56) and the *cis*-Isomer 59.** These compounds were prepared from styrene bromohydrin (402 mg, 2.0 mmol) by the standard protocol. Chromatographic separation (eluant ether) gave **56** (R_f = 0.50; 131 mg, 20%) and **59** (R_f = 0.67; 240 mg, 36%) as colorless oils. Data for **56**: ^{1}H NMR δ 1.33 (3H, d, J = 6.4 Hz), 1.39 (3H, d, J = 6.4 Hz), 3.62 −3.73 (2H, m), 4.67–4.85 (2H, m), 5.68 (1H, ddd, J = 5.3, 6.7, 8.4 Hz), 7.35–7.42 (5H, m); ^{13}C NMR δ 15.3 (d, J = 6.8 Hz), 15.4 (d, J = 7.9 Hz), 35.4 (d, J = 6.8 Hz), 78.2 (d, J = 6.8 Hz), 78.22 (d, J = 6.8 Hz), 80.0 (d, J = 4.5 Hz), 126.4, 128.7, 129.1, 137.4; ^{31}P NMR δ 15.46. Anal. Calcd for $C_{12}H_{16}BrO_4P$: C, 43.01; H, 4.81. Found: C, 43.17; H, 5.00. Data for **59**: ^{1}H NMR δ 1.32 (3H, d, J = 6.3 Hz), 1.37 (3H, d, J = 6.3 Hz), 3.64 (1H, ddd, J = 1.8, 5.1, 10.9 Hz), 3.68–3.82 (1H, m), 4.62–4.76 (2H, m), 5.63 (1H, m), 7.35–7.38 (5**H**, m); ^{13}C NMR δ 15.6 (d, J = 5.6 Hz), 15.64 (d, J = 5.8 Hz), 35.4 (d, J = 7.5 Hz), 78.0 (d, J = 2.9 Hz), 79.8 (d, J = 5.4 Hz), 126.4 (d, J = 4.5 Hz), 128.8, 129.2, 137.5 (d, J = 3.0 Hz); ^{31}P NMR δ 14.13. Anal. Calcd for $C_{12}H_{16}BrO_4P$: C, 43.01; H, 4.81. Found: C, 43.20; H, 4.85.

***trans*-2-(2-Phenylethoxy)-*cis*-4,5-dimethyl-2-oxo-1,3,2-dioxaphospholane (57) and the *cis*-Isomer 58. Authentic Samples.** These compounds were prepared by the general protocol from 2-phenylethanol (245 mg, 2.0 mmol). Chromatographic separation (eluant ether) gave **57** (R_f = 0.27; 10 mg, 3%) and **58** (R_f = 0.50; 175 mg, 46%) both as oils. Data for **57**: ^{1}H NMR δ 1.26 (6H, d, J = 6.3 Hz), 3.01 (2H, t, J = 7.0 Hz), 4.35 (2H, dt, J = 9.4 and 7.0 Hz), 4.67–4.79 (2H, m), 7.20–7.33 (5H, m); ^{13}C NMR δ 15.3 (d, J = 5.6 Hz), 36.9 (d, J = 5.7 Hz), 69.2 (d, J = 6.5 Hz), 77.9, 126.7, 128.5, 129.0, 137.0; ^{31}P NMR δ 14.40. Data for **58**: ^{1}H NMR δ 1.34 (6H, d, J = 6.3 Hz), 3.01 (2H, t, J = 7.1 Hz), 4.32 (2H, dt, J = 9.0, 7.1 Hz), 4.55 (2H, m, J_{P-H} = 9.5 Hz), 7.21–7.34 (5H, m); ^{13}C NMR δ 15.6 (d, J = 6.3 Hz), 36.9 (d, J = 5.9 Hz), 68.8 (d, J = 6.5 Hz), 77.7, 126.7, 128.5, 129.0, 137.0; ^{31}P NMR δ 15.00. Both **57** and **58** proved very susceptible to hydrolysis which has prevented us from obtaining microanalytical or HRMS data.

***trans*-2-(1-Phenylethoxy)-*cis*-4,5-dimethyl-2-oxo-1,3,2-dioxaphospholane (60) and the cis-Isomer 61.** These compounds were prepared by the standard protocol from 1-phenylethanol (245 mg, 2.0 mmol). Chromatographic separation (eluant Et_2O) gave **60** (R_f = 0.33; 51 mg, 10%) and **61** (R_f = 0.50; 81 mg, 16%), both as oils. Both compounds underwent significant decomposition on column chromatography. Data for **60**: ^{1}H NMR δ 1.27 (3H, d, J = 6.4 Hz), 1.35 (3H, d, J = 6.4 Hz), 1.66 (3H, d, J = 6.6 Hz), 4.64–4.81 (2H, m), 5.63 (1H, quintet, J = 6.6 Hz), 7.27–7.37 (5H, m); ^{13}C NMR δ 15.3 (d, J = 4.5 Hz), 15.4 (d, J = 5.7 Hz), 24.1 (d, J = 4.5 Hz), 77.8 (d, J = 2.3 Hz), 77.9 (d, J = 2.3 Hz), 79.0 (d, J = 5.7 Hz), 125.9, 128.2, 128.5, 141.3; ^{31}P NMR δ 15.63; HRMS calcd for $C_{12}H_{17}O_4P$ 256.0864, found 256.0865. Data for **61**: ^{1}H NMR δ 1.32 (3H, d, J = 6.3 Hz), 1.36 (3H, d, J = 6.3 Hz), 1.66 (3H, d, J = 6.6 Hz), 4.53–4.89 (2H, m), 5.60 (1H, quintet,

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J = 6.7 Hz), 7.28−7.40 (5H, m); ^{13}C NMR δ 15.6 (d, J = 5.5 Hz), 15.7 (d, J = 5.4 Hz), 24.0 (d, J = 5.0 Hz), 77.6 (d, J = 1.7 Hz), 77.7 (d, J = 2.3 Hz), 77.74 (d, J = 2.3 Hz), 125.8, 128.2, 128.5, 141.3 (d, J = 5.7 Hz); ^{31}P NMR δ 14.33; HRMS calcd for $C_{12}H_{17}O_4P$ 256.0864, found 256.0870.

***trans*-2-(*trans*-2-Bromo-1-indanoxy)-*cis*-4,5-dimethyl-2-oxo-1,3,2-dioxaphospholane (62) and the *cis*-Isomer 63.** These compounds were prepared from *trans*-indene bromohydrin (426 mg, 2.0 mmol) by the standard protocol. Chromatographic separation (eluant EtOAc/hexane, 1/1) gave **62** (R_f = 0.36; 250 mg, 36%) and **63** (R_f = 0.50; 152 mg, 22%). Data for **62**: mp 65−67 °C; ^{1}H NMR δ 1.27 (3H, d, J = 6.3 Hz), 1.34 (3H, d, J = 6.3 Hz), 3.26 (1H, dd, J = 5.3, 16.7 Hz), 3.79 (1H, dd, J = 6.8, 16.7 Hz), 4.55 (1H, ddd, J = 4.2, 5.3, 6.9 Hz), 4.74−4.85 (2H, m), 6.03 (1H, dd, J = 4.2, 7.7 Hz), 7.24−7.58 (4H, m); ^{13}C NMR δ 15.3 (d, J = 3.8 Hz), 15.4 (d, J = 5.1 Hz), 41.0, 50.5 (d, J = 5.7 Hz), 78.2, 88.3 (d, J = 5.7 Hz), 124.7, 125.8, 127.7, 129.9, 140.6; ^{31}P NMR δ 15.74. Anal. Calcd for $C_{13}H_{16}BrO_4P$: C, 44.98; H, 4.65. Found: C, 44.33; H, 6.39. Data for **63**: mp 105−106 °C; ^{1}H NMR δ 1.38 (3H, d, J = 6.2 Hz), 1.41 (3H, d, J = 6.2 Hz), 3.25 (1H, dd, J = 5.3, 16.7 Hz), 3.70 (1H, dd, J = 6.8, 16.7 Hz), 4.54 (1H, ddd, J = 4.1, 5.2, 6.8 Hz), 4.59−4.76 (2H, m), 6.00 (1H, dd, J = 4.1, 7.6 Hz), 7.25−7.58 (4H, m); ^{13}C NMR δ 15.7 (d, J = 6.0 Hz), 41.0, 50.5 (d, J = 5.7 Hz), 78.1, 88.1 (d, J = 5.7 Hz), 124.8, 125.6, 127.8, 129.9, 140.6; ^{31}P NMR δ 14.43. Anal. Calcd for $C_{13}H_{16}BrO_4P$: C, 44.93; H, 4.57.

***trans*-2-(2-Indanoxy)-*cis*-4,5-dimethyl-2-oxo-1,3,2-dioxaphospholane (64) and the *cis*-Isomer 65. Authentic Samples.** These compounds were prepared from 2-indanol (201 mg, 1.5 mmol) according to the standard protocol. Chromatographic separation (eluant EtOAc/hexane = 2/1) gave **64** (R_f = 0.28; 80 mg, 20%) and **65** (R_f = 0.42; 204 mg, 51%). Data for **64**: mp 105.5−106 °C; ^{1}H NMR δ 1.24 (6H, d, J = 7.7 Hz), 3.17 (2H, dd, J = 3.1, 16.8 Hz), 3.31 (2H, dd, J = 5.9, 17.1 Hz), 4.70 −4.77 (2H, m), 5.37 (1H, m), 7.17−7.26 (4H, m); ^{13}C NMR δ 15.2 (d, J = 5.6 Hz), 40.8 (d, J = 5.7 Hz), 77.9, 80.3 (d, J = 5.0 Hz), 124.6, 126.8, 139.9; ^{31}P NMR δ 15.79. Anal. Calcd for $C_{13}H_{17}O_4P$: C, 58.21; H, 6.39. Found: C, 58.11; H, 6.39. Data for **65:** mp 113−114 °C; ^{1}H NMR δ 1.35 (6H, d, J = 6.3 Hz), 3.16 (2H, dd, J = 3.0, 16.9 Hz), 3.31 (2H, dd, J = 5.9, 16.9 Hz), 4.55−4.64 (2H, m), 5.36 (1H, m), 7.17 −7.26 (4H, m); ^{13}C NMR δ 15.6 (d, J = 5.7 Hz), 40.9 (d, J = 5.5 Hz), 77.6, 80.1 (d, J = 5.7 Hz), 124.7, 126.9, 139.9; ^{31}P NMR δ 14.67. Anal. Calcd for $C_{13}H_{17}O_4P$: C, 58.21; H, 6.39. Found: C, 58.11; H, 6.39.

Rearrangements of 56, 59, 62, and 63 with Bu_3SnH. To a solution of the appropriate bromoalkyl phosphate (0.30 mmol) in benzene (40 mL) at reflux under N_2 were added tributyltin hydride (131 mg, 0.45 mmol) and AIBN (2.5 mg, 0.015 mmol) in benzene (20 mL) over 16 h with the aid of a motor-driven syringe pump. After the addition, the reaction mixture was refluxed for a further 2 h. After cooling to room temperature, the solvent was removed *in vacuo* and the crude reaction mixture examined by ^{1}H NMR and ^{31}P NMR with the aid of spectra of the corresponding authentic samples of all possible reaction products. The results are listed in Table 2.

Diethyl 1-Deuterio-cyclohex-2-enyl Phosphate (69). This compound was prepared from 1-deuterio-cyclohex-2-enol (prepared from $NaBD_4/CeCl_3\cdot 6H_2O$ reduction of cyclohexenone)[62] in the same way as for the preparation of **68** in 86% yield: ^{1}H NMR δ 1.33 (6H, t, J = 7.0 Hz), 1.52−2.10 (6H, m), 4.10 (4H, quintet, J = 7.1 Hz), 5.78 (1H, br d, J = 10.2 Hz), 5.94 (1H, td, J = 9.7, 10.2 Hz); ^{31}P NMR δ −0.65.

6-(Phenylseleno)cyclohex-2-enone (75). To a solution of diisopropylamine (3.50 mL, 25 mmol) in THF (25 mL) was slowly added BuLi (2 M in pentane, 12.5 mL, 25 mmol) at 0 °C under N_2. The reaction mixture was stirred for 20 min before a solution of 2-cyclohexen-1-one (1.923 g, 20 mmol) in THF (25 mL) was introduced. After stirring at 0 °C for 30 min, (TMS)Cl (3.26 g, 30 mmol) was added in one portion and the resulting mixture stirred at room temperature for 1 h before PhSeBr in THF (1.1 M, 20 mL) was slowly indroduced with stirring at room temperature. After stirring for 45 min, the reaction mixture was quenched by addition of dilute aqueous HCl (10%, 30 mL) followed by stirring for another 1.5 h. The reaction mixture was then extracted with ether (3 × 20 mL), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to dryness. Column chromatography on silica gel (eluant CH_2Cl_2/hexane, 9/1) gave the title compound (4.24 g, 84.5%) as a slightly yellow colored oil: ^{1}H NMR δ 2.17−2.62 (4H, m), 4.03 (1H, t, J = 4.6 Hz), 6.04 (1H, br d, J = 10.1 Hz), 6.91 (1H, m), 7.25−7.62 (5H, m); ^{13}C NMR δ 23.9, 29.1, 47.8, 127.6, 128.3, 128.9, 129.2, 149.3, 195.2. Anal. Calcd for $C_{12}H_{12}OSe$: C, 57.38; H, 4.82. Found: C, 57.41; H, 4.86.

***cis*-6-(Phenylseleno)cyclohex-2-enol (76).** To a solution of **75** (1.005 g, 4.0 mmol) and $CeCl_3\cdot H_2O$ (1.53 g, 4.1 mmol) in CH_3OH (15 mL) was added $NaBH_4$ (155 mg, 4.1 mmol) in portions over 15 min (**Caution**: highly exothermic reaction!). The resulting reaction mixture was stirred for another 10 min before water (25 mL) was added. After stirring for 10 min, the reaction mixture was extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated under vacuum. Column chromatography on silica gel (eluant CH_2Cl_2) gave the title compound (1.00 g, 99%) as a white solid: mp 58−60 °C; ^{1}H NMR δ 1.98−2.29 (4H, m), 2.50 (1H, br s), 3.57 (1H, dt, J = 9.8, 3.8 Hz), 4.16 (1H, br s), 5.76−5.89 (2H, m), 7.26−7.63 (5H, m); ^{13}C NMR δ 25.1, 25.6, 50.6, 65.2, 127.7, 128.4, 129.0, 129.2, 130.6, 134.3. Anal. Calcd for $C_{12}H_{14}OSe$: C, 56.92; H, 5.57. Found: C, 57.20: H, 5.72.

1-Deuterio-6-(phenylseleno)cyclohex-2-enol (77). This compound was prepared analogously to **76** by reduction of **75** with $NaBD_4$ in 95% yield: ^{1}H NMR δ 1.99−2.28 (4H, m), 2.49 (1H, s), 3.56 (1H, dd, J = 3.8, 9.8 Hz), 5.77−5.89 (2H, m), 7.26−7.61 (5H, m).

Diethyl 6-(Phenylseleno)cyclohex-2-enyl Phosphate (78). A solution of the alcohol **76** (380 mg, 1.5 mmol) in THF (10 mL) was treated with BuLi (2 M in pentane, 0.75 mL, 1.5 mmol) at 0 °C with stirring. After 5 min, diethyl chlorophosphate (390 mg, 2.25 mmol) in THF (5 mL) was introduced and the reaction mixture stirred at room temperature for 5 h. Water (15 mL) was then added and the reaction mixture extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and evaporated. Column chromatography on silica gel (eluant EtOAc/hexane, 1/1) gave **78** (456 mg, 78%) as a colorless oil: ^{1}H NMR δ 1.31−1.39 (6H, m), 2.02−2.27 (4H, m), 4.07−4.25 (4H, m), 5.05 (1H, m), 5.90−6.00 (2H, m), 7.26−7.62 (5H, m); ^{13}C NMR δ 16.1 (d, J = 6.8 Hz), 16.2 (d, J = 7.9 Hz), 25.7 (d, J = 35.5 Hz), 45.4 (d, J = 8.2 Hz), 63.7 (d, J = 5.7 Hz), 64.0 (d, J = 5.7 Hz), 73.0 (d, J = 5.4 Hz), 103.4 (d, J = 32.8 Hz), 125.5, 127.5, 129.1, 132.6, 134.5; ^{31}P NMR δ −1.02; HRMS calcd for $C_{16}H_{23}O_4SeP$ 390.04991, found 390.04987.

Diethyl 1-Deuterio-6-(phenylseleno)cyclohex-2-enyl Phosphate (79). This compound was prepared from the alcohol **77**, analogously to the preparation of **78**, in 77% yield as a colorless oil: ^{1}H NMR δ 1.31−1.39 (6H, m), 2.00−2.28 (1H, m), 3.47 (1H, br d, J = 10.5 Hz), 4.07−4.25 (4H, m), 5.90−6.01 (2H, m), 7.26−7.62 (5H, m); ^{31}P NMR δ −0.96.

1-Deuteriocyclohex-2-enyl Benzoate (81). A solution of 1-deuteriocyclohex-2-enol (49 mg, 0.50 mmol), DMAP (92 mg, 0.75 mmol), and benzoyl chloride (105 mg, 0.75 mmol) in CH_2Cl_2 (5 mL) was heated to reflux for 6 h. After cooling to room temperature, water (10 mL) was added and the reaction mixture extracted with CH_2Cl_2 (2 × 5 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to dryness. Column chromatography (hexane/CH_2Cl_2, 1/1) gave **81** (93 mg, 93%) as a colorless oil: ^{1}H NMR δ 1.65−2.20 (6H, m), 5.83 (1H, td, J = 2.0, 10.1 Hz), 6.01 (1H, td, J = 3.7, 10.1 Hz), 7.41−8.07 (5H, m).

6-(Phenylseleno)cyclohex-2-enyl Benzoate (87). A solution of the alcohol **76** (506 mg, 2.0 mmol), DMAP (367 mg, 3.0 mmol), and benzoyl chloride (422 mg, 3.0 mmol) in CH_2Cl_2 (10 mL) was heated to reflux under N_2 for 24 h. After cooling to room temperature, the reaction mixture was quenched by addition of water (20 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and evaporated to dryness. Column chromatography on silica gel (eluant CH_2Cl_2/hexane, 3/2) gave the title compound (664 mg, 93%) as a colorless oil: ^{1}H NMR δ 2.12−2.33 (4H, m), 3.66 (1H, dt, J = 10.2, 4.1 Hz), 5.62 (1H, t, J = 4.1 Hz), 5.92−6.30 (2H, m), 7.23−8.09 (10H, m); ^{13}C NMR δ 25.8, 26.1, 44.4, 69.9, 124.9, 127.6, 128.3, 129.1, 129.2, 129.8, 130.3, 132.5, 132.9, 134.5, 165.9. Anal. Calcd for $C_{19}H_{18}OSe$: C, 63.87; H, 5.08. Found: C, 63.65; H, 5.06.

1-Deuterio-6-(phenylseleno)cyclohex-2-enyl Benzoate (88). This compound was prepared from the alcohol **77** (305 mg, 1.2 mmol) in

(62) Luche, J. L. *J. Am. Chem. Soc.* **1979**, *100*, 2226.

the same way as for the preparation of **87**. Column chromatography (eluant CH_2Cl_2/hexane, 3/2) gave **88** (395 mg, 92%) as a colorless oil: ^{1}H NMR δ 2.09−2.33 (4H, m), 3.65 (1H, dd, J = 4.1, 10.6 Hz), 5.92−6.04 (2H, m), 7.23−8.09 (10H, m).

Rearrangement of 78 with Bu_3SnH. To a solution of **78** (195 mg, 0.50 mmol) in benzene (20 mL) at reflux under N_2 was added a solution of tributyltin hydride (218 mg, 0.75 mmol) and AIBN (4 mg, 0.025 mmol) in benzene (20 mL) over 5 h with the aid of a motor-driven syringe pump. A further portion of AIBN (13 mg, 0.08 mmol) in benzene (13 mL) was then added over 10 h. After the addition, heating was continued for another 5 h. After cooling to room temperature, the solvent was removed under vacuum and the residue subjected to column chromatography on silica gel (eluant EtOAc/hexane, 1/1) to give a mixture of **68** and **72** (70 mg, 58%) in a ratio of 2/3 as determined by ^{1}H NMR spectroscopy.

Rearrangement of 79 with Bu_3SnH. To a solution of **79** (195 mg, 0.50 mmol) in benzene (20 mL) at reflux under N_2 was added a solution of tributyltin hydride (218 mg, 0.75 mmol) and AIBN (8.2 mg, 0.025 mmol) in benzene (20 mL) over 12 h. After a further 3 h of reflux, another portion of AIBN (5 mg) was added, and heating was continued for a further 5 h. After cooling to room temperature, the solvent was removed under vacuum and the residue taken up in acetonitrile (15 mL), washed with hexane (2 × 15 mL), and concentrated to dryness. Column chromatography on silica gel (eluant EtOAc/CH_2Cl_2, 1/4) gave 45 mg (23%) of unreacted **79** and 41 mg (35%) of a mixture of the allylic phosphate esters (**69** + **70**) and the homoallylic phosphate ester **73** in the ratio of 1/2.3. A partial ^{1}H NMR spectrum of this sample is shown in Figure 1.

Rearrangement of 87 with Bu_3SnH. To a solution of **87** (129 mg, 0.26 mmol) in benzene (40 mL) at reflux under N_2 was added a solution of tributyltin hydride (175 mg, 0.60 mmol) and AIBN (4 mg, 0.025 mmol) in benzene (20 mL) over 16 h. After reflux for another 4 h, the reaction mixture was cooled to room temperature and the solvent removed *in vacuo*. Column chromatography on silica gel (eluant CH_2Cl_2/hexane, 1/1) gave an inseparable mixture of the two products **80** and **84** (66%) in a ratio of 81/19 together with the unreacted **87** (25%).

Rearrangement of 88 with Bu_3SnH. Reaction of **88** with tributyltin hydride under the same conditions as for **87** followed by column chromatography gave 82 mg (82%) of an inseparable mixture of the allylic benzoates (**81** + **82**) and the homoallylic benzoate **85** in a ratio of 4/1. A partial ^{1}H NMR spectrum is shown in Figure 2.

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Supporting Information Available: Text describing the preparation and spectral data for **1b**, **14**−**17**, **32**, **33**, **36**, **39**, **49**, **54**, **67**, **68**, **72**, **80**, **84**, 1-bromo-2-methyl-2-heptanol, 1-bromo-2-octadecanol, *trans*-1,3-indandiol, 2-(*N*,*N*-diisopropylamino)-*cis*-4,5-diphenyl-1,3,2-dioxaphospholane, and 2-(*N*,*N*-diisopropylamino)-4-phenyl-1,3,2-dioxaphospholane and figures showing the ^{1}H NMR and ^{13}C NMR spectra of **2**, **6**, **16**, **17**, **43**, **45**−**47**, **49** (^{1}H only), **54** (^{1}H only), **57**, **58**, **60**, **61**, and **78** (37 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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