Photo-Arbuzov Rearrangements of Benzylic Phosphites. Stereochemistry at Migratory Carbon

Worawan Bhanthumnavin, Atta Arif, and Wesley G. Bentrude*

Department of Chemistry, University of Utah, Salt Lake City, Utah 84112

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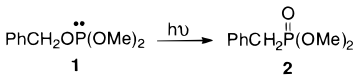
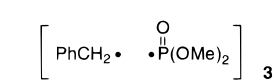
The stereochemistry of the photo-Arbuzov rearrangement of the benzylic phosphite *trans*-(*R,R′*)-**10** to the corresponding phosphonate, **11**, has been determined by ^{31}P NMR spectroscopy and X-ray crystallography. The reaction is shown to occur with predominant *retention of configuration* at the stereogenic migratory carbon center of configuration *R′* in starting *trans*-(*R,R′*)-**10** and the predominant product *cis*-(*R,R′*)-**11**. Thus, reaction of optically active phosphoramidite **13** (*R*/*S* ratio 98/2, 96% ee) with 1-phenylethanol of high optical purity (*R′*/*S′* ratio, 97/3, 94% ee) gives phosphite *trans*-**10** (cis/trans ratio ≥ 97/3) almost entirely as the single enantiomer, *trans*-(*R,R′*)-**10**. Irradiation of *trans*-(*R,R′*)-**10** in acetonitrile with 254 nm ultraviolet light converted it cleanly to two diastereomers of phosphonate *cis*-**11** in 80/20 ratio (^{31}P NMR). The major (80%) isomer was isolated, recrystallized, and shown by X-ray crystallography to be *cis*-(*R,R′*)-**11**. The lesser (20%) product is identified, on the basis of its ^{31}P NMR chemical shift, as the diastereomer *cis*-(*R,S′*)-**11**. (Assignments derived from photorearrangement of totally racemic *cis*-**10** prepared from reaction of racemic 1-phenylethanol with racemic **13**.) The generation of *trans*-(*R,S′*)-**11** is attributed to the formation (Scheme 1) from *trans*-(*R,R′*)-**10** of short-lived, predominantly singlet, free radical pairs (**12a**) that largely (≃80%) undergo combination to form *cis*-(*R,R′*)-**11**. To a lesser extent (≃20%), the 1-phenylethyl radicals (**C**) of the pair **12a** are converted by rotation to **C′** to generate the stereochemically distinct radical pair **12b** that then combines to form *cis*-(*R,S′*)-**11**. *To a first approximation*, combination (k_{comb}) is four times as fast as rotation (k_{rot}). During the photorearrangement the trans/cis ratios of starting phosphite **10** and product phosphonate **11** are unchanged as is consistent with the generation of phosphinoyl radical **B** that is configurationally stable at phosphorus.

Introduction

This laboratory has reported studies of the facile photoinduced Arbuzov rearrangements of dialkyl benzyl phosphites, e.g., **1** → **2**,[1−5] and the useful application of this new photoreaction to the synthesis of acyclic nucleoside-based phosphonates.[4,5] The quantum yield for formation of phosphonate **2**, Φ_P, at 266 nm is 0.43.[6] At 75% phosphite conversion, the accountability yield of **2**, based on **1** consumed, is 67% and is accompanied by a 3% accountability yield of bibenzyl, $PhCH_2CH_2Ph$.[7] The formation of bibenzyl suggests that at least a portion of the reaction proceeds via radical pairs, **3**. However, ^{31}P CIDNP phenomena are not observed on irradiation of **1**[8] nor is the phosphinoyl radical $(MeO)_2P(O)^{\bullet}$ detected in CIDEP studies.[9] Both phenomena are observed when initial *triplet radical pairs* are generated by photolysis of the *p*-acetylbenzyl phosphite analogue of **1**.[9,10]



1 **2**



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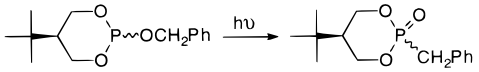
An earlier study of the photo-Arbuzov rearrangement of several cis/trans ratios of 2-benzyl-4-*tert*-butyl phosphite, **4**, established that the formation of phosphonate **5** proceeds with essentially complete *retention of stereochemistry at phosphorus*, as shown for *cis*-**4**[3] (*t*-Bu and P−O remain cis). This result says nothing, however, about the possibility that the photorearrangement of **4** to **5** proceeds via radical pair **6**. Thus, phosphinoyl radicals related to **A** were shown some time ago to be configurationally stable;[11] and a concerted 1,2-shift, a two-centered four-electron process, also most probably would involve retention of configuration at phosphorus.



4 **5**

(1) Omelanzcuk, J.; Sopchik, A. E.; Lee, S.-G.; Akutagawa, K.; Cairns, S. M.; Bentrude, W. G. *J. Am. Chem. Soc.* **1988**, *110*, 6908.
(2) Bentrude, W. G.; Lee, S.-G.; Akutagawa, K.; Ye, W.; Charbonnel, Y.; Omelanczuk, J. *Phosphorus Sulfur* **1987**, *30*, 105.
(3) Cairns, S. M.; Bentrude, W. G. *Tetrahedron Lett.* **1989**, *30*, 1025.
(4) Bentrude, W. G.; Mullah, K. B. *J. Org. Chem.* **1991**, *56*, 7218.
(5) Mullah, K. B.; Bentrude, W. G. *Nucleosides Nucleotides* **1994**, *13*, 127.
(6) Ganapathy, S. Unpublished results from this laboratory.
(7) Somasekharan, B. B. V. Unpublished results from this laboratory.
(8) Landis, M. S.; Sluggett, G. W.; Turro, N. J. Unpublished results, Columbia University.
(9) Koptyug, I. V.; Ghatlia, N. D.; Sluggett, G. W.; Turro, N. J.; Ganapathy, S.; Bentrude, W. G. *J. Am. Chem. Soc.* **1995**, *117*, 9486.
(10) Koptyug, I. V.; Sluggett, G. W.; Ghatlia, N. D.; Landis, M. S.; Turro, N. J.; Ganapathy, S.; Bentrude, W. G. *J. Phys. Chem.* **1996**, *100*, 14581.
(11) Reiff, L. P.; Aaron, H. S. *J. Am. Chem. Soc.* **1970**, *92*, 5275. Szafraniec, L.; Reiff, L. P.; Aaron, H. S. *J. Am. Chem. Soc.* **1970**, *92*, 6391. Farnham, W. B.; Murray, R. K., Jr.; Mislow, K. *J. Chem. Soc. D* **1971**, 146.

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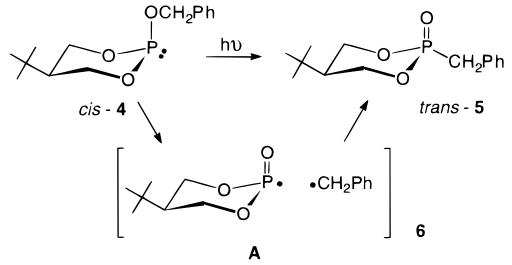
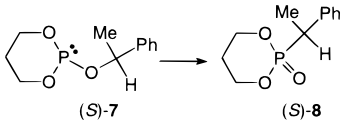
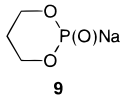


However, it is clear that were the benzylic carbon of the radical pair **3** or **6** a stereogenic center, loss of stereochemistry at that carbon center would accompany the photorearrangement were it to proceed via a radical pair of sufficient lifetime. Because the chemical yields of phosphonates in photo-Arbuzov reactions are reasonably good,[1−5] the stereochemistry in question is of interest from a synthetic, as well as mechanistic, standpoint. This process, if stereoselective, potentially provides an attractive way to introduce, in stereoselective fashion, a stereogenic carbon center of known configuration attached directly to phosphorus. Stereoselective carbon−phosphorus bond formation involving a secondary carbon is not readily accomplished by other means, e.g., via thermal Arbuzov reaction chemistry.[12]

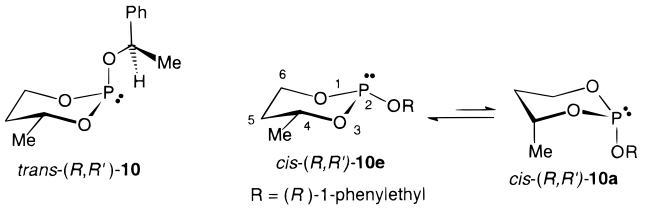
We reported earlier in preliminary fashion the results of a study of the stereochemistry at the migratory carbon of the photo-Arbuzov rearrangement of phosphite (*S*)-**7** to **8** under direct irradiation conditions.[1] Added chiral shift reagent, optically pure *t*-BuPhP(S)OH,[13] differentiated the methyl signals (^{1}H NMR at 400 MHz) for the two enantiomers of phosphonate **8** (diastereotopic phosphonate−shift reagent complexes). The reaction was judged to proceed with *at least 90% retention* of configuration at carbon to yield predominantly (*S*)-**8**.[1]



The absolute stereochemistry of the major enantiomer of **8** was determined by its preparation by way of two reactions of presumably predictable stereochemistry. Thus, the thermal reaction of 2-trimethylsilyloxy-1,3,2-dioxaphosphorinane with (*R*)-MePhCHBr took place with 95% stereoselectivity and presumably with the *inversion* of configuration at the stereogenic carbon center expected of such an Arbuzov reaction[12] to yield (*S*)-**8**. However, the specific reaction in question is facilitated kinetically by the trimethylsilyl group which evidently aids the departure of bromine from the secondary carbon center through formation of the silicon−bromine bond. Therefore, the possibility must be considered that a concerted, five-centered (P−O−Si−Br−C) process took place *with retention of configuration at carbon*. The other reaction employed the S_N2 displacement of bromide from the stereocenter of (*R*)-MePhCHBr by the sodium derivative **9**. Unfortunately, the yield of presumed (*S*)-**8** was very low and proceeded with only about 50% stereoselectivity.



Because of the necessity that the predominant absolute stereochemistry at the migratory carbon of these processes be known with great certainty, we turned to the photo-Arbuzov rearrangement of a phosphite (**10**) with known geometry at C4 of the ring (unchanged during photorearrangement) and at the stereogenic carbon of the 1-phenylethyl group. Free radical pairs (**12**) from photolysis of phosphite **10** (Scheme 1), were they sufficiently long-lived, would yield phosphonate **11** with some *loss of stereochemistry at the migratory carbon*, as a result of rotation of the 1-phenylethyl radical (**C**) to expose its opposite face (**C′**) to the phosphinoyl radical, **B**, prior to the combination of **B** with **C′**. Thus, less than stereospecific conversion of *trans-(R,R′)*-**10** to *cis*-(*R,R′*)-**11** would raise the possibility of the involvement of radical pairs (**12**). As noted above, a truly concerted 1,2-shift most likely would be *completely retentive* at the migratory, benzylic stereogenic carbon.



Throughout this paper *R* and *R′* refer to the configurations at the stereogenic carbons in the ring and 1-phenylethyl substituents, respectively. For economy of presentation, single enantiomer representations of **10**, **11**, and **12**, etc. are used in discussion of the reactions of the racemic materials, as well as those of the same molecules with high configurational purity and the specific geometries shown for ring C4 (*R*) and the 1-phenylethyl group (*R′* or *S′*) in Scheme 1 and elsewhere.

The primary goal of the study reported here is the determination, for the photorearrangement of **10**, of the predominant stereochemistry, retention or inversion, at the migratory 1-phenylethyl. Indeed, an X-ray crystallographic determination of the structure of the stereochemically predominant photorearrangement product from *trans*-(*R,R′*)-**10** reveals the relative stereochemistries of the two carbon centers in product phosphonate **11** (Figure 1) and, thereby, leads to the conclusion that the *predominant* overall stereochemistry at the stereogenic, migratory carbon is *retention*. The partial loss of stereochemistry actually observed at the carbon in question is consistent with the intermediacy of the radical pairs shown in Scheme 1. The retention of stereochemistry at phosphorus earlier found to accompany the photorearrangement of **10** confirms the results found earlier for **4** → **5**.

Results and Discussion

The stereochemical properties of the six-membered rings (1,3,2-dioxaphosphorinanes) of molecules such as **10** and **11** have been thoroughly studied by this group

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(13) Harger, M. J. P. *J. Chem. Soc., Perkin Trans 2* **1980**, 1505; **1978**, 326.

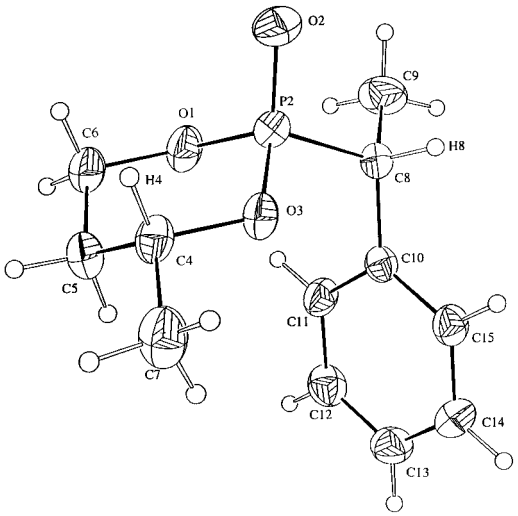


Figure 1. ORTEP structure for *cis-(R,R′)*-**11**.

Scheme 1

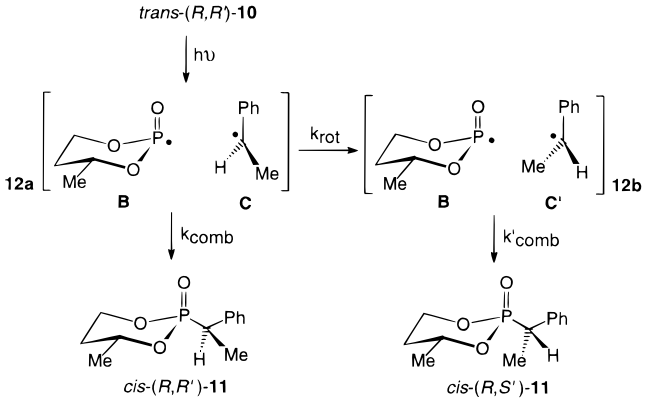


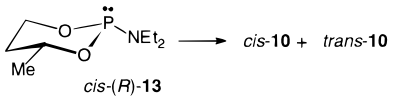
Table 1. Crystal Data for *cis-(R,R′)*-11

empirical formula	$C_{12}H_{17}O_3P$
formula weight	240.23
space group	$P2_12_12_1$
crystal system	orthorhombic
cell dimensions	
a, Å	6.0934(11)
b, Å	7.938(2)
c, Å	25.748(4)
$\alpha = \beta = \gamma$ (deg)	90
n, Å^3	1245.4(4)
D_{calcd}, g/cm^3	1.281
absorptn coeff, cm^{-1}	0.211
2θ range for data collection, deg	2.69−24.95

and others.[14] The cis or trans relationship of the methyl at C4 to the substituent on phosphorus is readily assigned in both phosphite **10** and phosphonate **11** from their relative ^{31}P chemical shifts. With both three- and four-coordinated phosphorus, the cis or trans diastereomer with the greater population of conformer with substituent on phosphorus *axial* will display the more-upfield ^{31}P chemical shift. The strong preference of an alkoxy group attached to phosphorus to be axial[14] means that the chair conformer shown for *trans*-**10** will be populated nearly exclusively. For *cis*-**10** two chair conformers, **10a** and **10e**, and perhaps a twist form will be populated. The near-exclusive population by *cis*-**11** of the chair conformation shown, with both ring substituents equatorial,[14] ensures that its ^{31}P NMR chemical shift will be *downfield* of that for its trans counterpart. Furthermore, the inversion barrier at phosphorus for phosphite **10** is sufficiently high that *cis*- and *trans*-**10** will not be interconverted at room temperature. Thus, this reaction system also allows the stereochemistry of the photorearrangement *at phosphorus* to be ascertained.

An initial study was carried out using *racemic* phosphite **10**. This was to demonstrate that the two diastereomers of a given cis or trans phosphite or phosphonate can be distinguished by ^{31}P NMR. Thus if the racemic *R,S′/S,R′* diastereomer has a different ^{31}P chemical shift from its racemic *R,R′/S,S′* counterpart, it will be possible to check the diastereomeric purity of a phosphite whose stereochemistry is predominantly *trans*-(*R,R′*)-**10** and to monitor by ^{31}P NMR the stereochemistry of its photorearrangement to phosphonates (*R,R′*)- and (*R,S′*)-*cis*-**11**.

To this end racemic phosphoramidite **13** was prepared by reaction of tris(diethylamino)phosphine with racemic 1,3-butanediol in refluxing benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid. The ^{31}P chemical shift in $CDCl_3$ ($\delta(^{31}P) = 145.0$) of the *major* isomer of racemic **13** was downfield of that of its counterpart ($\delta(^{31}P) = 141.2$) which allowed the major product to be designated as the cis diastereomer shown, *cis*-**13**,[14,15] i.e., methyl and diethylamino groups cis (cis/trans ratio 96/4 from ^{31}P NMR integrals). The thermo-



dynamically most stable conformation of *cis*-2-dialkylamino-4-methyl-1,3,2-dioxaphosphorinanes is known to be the chair form shown for *cis*-**13** with both ring substituents equatorial.[15]

Racemic (*R/S*) phosphoramidite **13** was reacted with racemic (*R′/S′*)-1-phenylethanol in acetonitrile in the presence of 1*H*-tetrazole to give phosphite **10** in 60% yield following distillation. Two pairs of peaks were observed in the ^{31}P NMR spectrum $CDCl_3$ of **10**. The major set (single peaks of *equal* areas at δ 127.7 and 127.8) corresponds to the two trans diastereomers of **10**, the *R,R′/S,S′* isomer and the *S,R′/R,S′* isomer.[15] This clearly demonstrates that *the two racemic diastereomers of trans-**10** can be easily differentiated by ^{31}P NMR*. A second pair of very weak, equal-intensity resonances at δ 131.8 and 131.9 can be assigned to the cis diastereomers. By integration of the ^{31}P NMR signals, the trans/cis ratio was determined to be ≥97/3. The very predominant amount of the thermodynamically more stable trans phosphite arises from equilibration of the trans and cis forms of **10** at distillation temperatures.

A 0.02 M deoxygenated acetonitrile solution of the racemic phosphite **10** (trans/cis ≥ 97/3) in a quartz tube was irradiated at 254 nm. Consumption of **10**, monitored by GC, was complete in approximately 100 min. A ^{31}P NMR spectrum (CH_3CN) of the photolysis mixture showed the reaction to be very clean. Two major product peaks

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(15) Mosbo, J. A.; Verkade, J. G. *J. Am. Chem. Soc.* **1972**, *94*, 8224; **1973**, *95*, 4659. Bentrude, W. G.; Tan, H. W. *J. Am. Chem. Soc.* **1972**, *94*, 8222; **1973**, *95*, 4666. Cogne, A.; Gumaraes, A. G.; Martin, J.; Nardin, R.; Robert, J.-B.; Stec, W. J. *J. Magn. Reson.* **1974**, *6*, 629.

of nearly equal areas in the phosphonate region (δ 30.3 and 30.4) accounted for over 90% of total peak area. Each phosphonate peak corresponds to one of the two diastereomers (as a 50/50 pair of enantiomers, *R,R′*/*S,S′* and *R,S′*/*S,R′*) of product phosphonate *cis*-**11**, whose cis geometry was subsequently confirmed by X-ray crystallography on a pure *R,R′* isomer (see below). Peaks for the diastereomers of racemic phosphonate *trans*-**11**, expected to appear at somewhat *higher* field,[14] were too small to be observed. Following purification by HPLC as a mixture, the two diastereomers of phosphonate *cis*-**11** (approximately 50/50 by HPLC) showed equal-intensity ^{31}P chemical shifts at δ 25.2 and 25.4 ppm (solvent changed to $CDCl_3$). *These results show that the chemical shift of the cis-R,R′/S,S′ enantiomeric pair of cis-**11** can be differentiated from that of the diastereomeric cis-R,S′/S,R′* enantiomers.

By use of (*R*)-(−)-1,3-butanediol (*R*/*S* = 98/2), optically active (*R*)-**13** (cis/trans ratio >95/5, ^{31}P NMR) was prepared by the procedure described for racemic **13**. The *R*/*S* ratio at the stereogenic ring carbon (C4) is expected to be unchanged on cyclization or on subsequent conversion of **13** to **10**. Thus, when distilled phosphoramidite (*R*)-**13** was reacted with (*R*)-(+)-1-phenylethanol (97/3 *R*/*S*), the desired chiral phosphite *trans*-(*R,R′*)-**10** (^{31}P NMR) was formed in predominant amounts. As expected from the work with racemic materials, the ^{31}P NMR spectrum displayed peaks in two regions. The more downfield region (δ about 131 ppm, as for the racemic materials), which can be assigned to the *cis isomer*, showed low intensity, hardly discernible resonances (trans/cis ≥ 97/3). The other set, a pair of peaks, was assigned to the *trans isomer* (δ = 127.6, major; 127.7, minor; ratio = 96/4). The more intense peak (δ = 127.6) clearly belongs to the *R,R′* enantiomer (with perhaps a trace of *S,S′* present). The minor peak (δ = 127.7) can be assigned to nearly equal amounts of the *R,S′* and *S,R′* enantiomers of the other diastereomer of *trans*-**7**.

Phosphonate *cis*-(*R,R′*)-**11** was shown to be the major phosphonate product of the photolysis of *trans*-(*R,R′*)-**10** (0.01 M in acetonitrile), carried out in the manner described for racemic *trans*-**10**. More than 95% of the starting material was consumed in about 70 min. Analysis of the photolytic mixture by ^{31}P NMR (CH_3CN) indicated that *trans*-**10** was converted to product phosphonate **11** with peaks in the *cis*-phosphonate region at δ 30.2 and 30.4. The area ratio of the dominant, more-*downfield* peak (demonstrated by X-ray crystallography to be the *R,R′* isomer; see below) to its weaker, *higher-field* counterpart (very predominantly the *R,S′* isomer) was 80/20. The two diastereomers of *cis*-**11** (*R,R′* (major) + *S,S′*(minor), 80%, $\delta(^{31}P)$ = 25.7, $CDCl_3$; and *R,S′*(major) + *S,R′*(minor), 20%, $\delta(^{31}P)$ = 25.3, $CDCl_3$)) were separated by HPLC. The isolated yield of the major phosphonate was 68%. Subsequently, an X-ray quality crystal of the major (80%) phosphonate enantiomer, *cis*-**11**, was grown by diffusion of pentane into an ethereal solution of the phosphonate. The X-ray crystal structure, suitably refined (Experimental Section), establishes the structure as *cis*-(*R,R′*)-**11**, as is displayed in the ORTEP drawing, Figure 1. One concludes, therefore, that *the predominant overall stereochemistry at the 1-phenylethyl migratory carbon in the photo-Arbuzov rearrangement of **10** is retention; i.e., trans-(R,R′)-**10** → cis-(R,R′)-**11***.

Furthermore, the trans/cis ratio of phosphite **10** used in the photolyses, whether the racemic compound or the very predominantly *R,R′* material, was greater than 97/3. Photoproduct phosphonate **11**, at near-total consumption of phosphite **10**, showed (^{31}P NMR) the formation of only a trace of trans isomer. This reaction is, therefore, *essentially stereospecific at phosphorus (trans-**10** → cis-**11**)*. This result is in accord with our earlier finding for the rearrangements of *cis*- and *trans*-**4**.[3]

Although retention at the stereogenic 1-phenylethyl carbon center is the major reaction course of the photorearrangement of phosphite **10**, it is very significant that some loss of stereochemistry at that carbon center is observed. Thus, as noted, photolysis of *trans*-(*R,R′*)-**10** gave photoproduct *cis*-**11** as an 80/20 mixture of major diastereomers (*R,R′*)/(R,S′) of *cis*-**11** as a result of *partial loss of stereochemistry* at the 1-phenylethyl carbon center. This ratio (80/20) was the same at 30%, 46%, and 95% conversions of phosphite. Additionally, the HPLC-purified 80/20 mixture of diastereomers was irradiated in acetonitrile for a period of 2 h, typical of the time of irradiations in the conversions of **10** to **11**, without an observed change in ratio. Clearly, the product phosphonate is configurationally stable at the migratory carbon atom. Similarly, if the configuration at ring C4 of the chiral phosphite **10** were to have undergone racemization, a change in *R*/*S* product ratio with phosphite **10** conversion, leading to formation of *cis*-(*S,R′*)-**10**, would have been observed by ^{31}P NMR.

Evidence for the formation of short-lived radical pairs on irradiation of phosphite **10** comes from the measured formation of 2−3% of 1-phenylethyl radical dimer, PhMeCHCHMePh. In Scheme 1 are shown the stereochemical events involving free radical pairs (**12a** and **12b**) that lead on photolysis of very predominantly *trans*-(*R,R′*)-**10** to a mixture of *cis*-(*R,R′*)-**11** and *cis*-(*R,S′*)-**11**. Analysis of the photorearrangement of **10** in terms of Scheme 1 is complicated somewhat by the presence of two stereogenic centers, neither of which is totally optically pure. However, to a first approximation, it can be assumed that the *trans*-**10** studied is purely the (*R,R′*) isomer and that rotation of the 1-phenylethyl radical (**C** → **C′**) is irreversible. One then concludes that the ratio k_{comb}/k_{rot} is 4 (i.e., 80/20); that is, one out of five **C** radicals undergoes rotation (**C** → **C′**) and combination to form (*R,S′*)-*cis*-**11**, whereas four out of five (80%) undergo combination to give *cis*-(*R,R′*)-**11**. Of course in fact some of pair **12b** reverts back to **12a** and combines to form *cis*-(*R,R′*)-**11**, decreasing the *apparent* value of k_{rot}. At the same time approximately 3% of starting *trans*-**10** is the *S,R′*/*R,S′* material. Its photolysis will yield primarily the *S,R′*/*R,S′* phosphonates with ^{31}P chemical shift the same as that of pure *R,S′* phosphonate, adding to the apparent amount of *cis*-(*R,S′*)-**11** formed by rotation−combination. In addition a minor amount of *R,R′* and *R,S′* phosphonates, formed in equal amounts by random re-encounter of cage−free radical pairs, will contribute to the apparent ratio (*R,R′*)/(*R,S′*) measured by ^{31}P NMR.

Conclusions. The primary goal of the present research is to establish the dominant stereochemistry of the photorearrangement of phosphite **10** at the stereogenic, migratory C1 carbon of the 1-phenylethyl group. Indeed, *retention is primarily observed*. Nonetheless, it also can be concluded that *to a first approximation the rate constant (k_{comb}) for combination of radical pair **12a** is four times that for rotation (k_{rot}) to give radical pair **12b** (**C** → **C′**)*. The free radical pairs, therefore, must be

relatively short-lived as they predominantly undergo combination rather than rotation. A more precise treatment of the relative rate constants for rotation and radical pair combination, and their relation to the well-studied reaction stereochemistry of carbon radical pairs, will be reserved for a subsequent publication reporting the study of the photorearrangement, monitored by chiral HPLC, of the six-membered ring phosphite **7** which contains only a single stereogenic center. Studies that consider the possibility of formation of an ion pair analogous to free radical pairs **3** and **12** also will be addressed in subsequent publications.

Experimental Section

General Procedures and Materials. Air-sensitive materials were transferred by syringe or cannula and/or in a glovebag under an argon atmosphere. Except for distillation prior to use, commercial solvents (spectrophotometric grade) were used as received. Diethyl ether was dried over sodium/benzophenone. Acetonitrile, methanol, and *n*-pentane were Merck Omnisolv grade. Methanol and $CHCl_3$ were Mallinckrodt HPLC quality solvents. Flash chromatography of products prior to their purification by HPLC was conducted on Merck silica gel 60, 230−400 mesh. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, GA. High-performance liquid chromatographic (HPLC) separations of products were obtained under isocratic conditions monitored by a UV absorbance detector and employed a 10 mm i.d. semipreparative or a 21.4 mm i.d. preparative Dynamax silica HPLC column.

Spectroscopic and Physical Data. ^{1}H and ^{13}C NMR chemical shifts (δ) are reported in parts per million relative to internal tetramethylsilane with the solvent as an internal standard. ^{31}P chemical shifts are referenced to external 85% phosphoric acid. Melting points are uncorrected. Ultraviolet (UV) spectra were obtained in acetonitrile solutions. Wavelength maxima (λ_{max}) are reported in nm with extinction coefficients (ϵ) in L mol^{-1} cm^{-1}. Low- and high-resolution mass spectra (LRMS and HRMS, EI, 70 eV) were obtained on gas chromatograph/mass spectrometers operated in the EI or CI mode (15 m × 0.25 mm DB-1 capillary column).

Procedure for the Irradiation of Racemic *trans*-10 and *trans*-(*R,R′*)-10. Solutions (0.01−0.02 M) of phosphite in spectrophotometric grade acetonitrile in septum-stoppered quartz tubes were deoxygenated with an argon purge and then irradiated in a Rayonet preparative scale photochemical reactor at 254 nm. Reactions were monitored by GC to >90% consumption of phosphite. Products were isolated by HPLC using $CHCl_3$ (1.1% methyl alcohol as stabilizer).

X-ray Crystallography. A colorless prism of *cis*-(*R,R′*)-**11** from photorearrangement of *trans*-(*R,R′*)-**10** was grown by diffusion of pentane into an ether solution of *cis*-**11** made from the *major* (80%) portion, separated by HPLC, of an 80/20 mixture of diastereomers of *cis*-**11**. The crystal was mounted on a glass fiber for data collection on a CAD4 diffractometer. Cell constants were obtained from 25 reflections with $21.0 < 2\theta < 28$. The space group was determined from systematic absences ($h00$ $h = 2n$, $0k0$ $k = 2n$, $00l$ $l = 2n$) and subsequent least-squares refinements. Standard reflections showed no decay during data collection. Lorentz and polarization corrections, and an empirical absorption correction, based upon a series of ψ scans, were applied to the data. The structure was solved by standard heavy-atom techniques using the Molen/VAX package. Non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms positions were calculated and added to the structure factor calculations using riding model refinements. All refinements were done using SHELXL-93. Determination of absolute configuration was carried out by refining the Flack absolute structure parameters (SHELXL-93). Key crystal data are contained in Table 1.

Racemic *N,N*-Diethyl-4-methyl-1,3,2-dioxaphosphorinan-2-amine (13). A solution of tris(diethylamino)phosphine[16] (8.0 g, 50 mmol) and 1,3-butanediol (4.8 g, 53 mmol) in 100 mL of benzene was purged with argon for 10 min. To the magnetically stirred solution was added a catalytic amount of *p*-toluenesulfonic acid (0.10 g). The flask was fitted with a reflux condenser equipped with an argon inlet. The solution was refluxed for 4 h to complete consumption of the phosphorus triamide (^{31}P NMR). Benzene was removed under vacuum (30 °C, 20 mmHg). Pentane was added (50 mL) to precipitate the amine salt of *p*-toluenesulfonic acid, which was removed by filtration in a Schlenck apparatus. Distillation under reduced pressure gave pure **13** (6.5 g, 34 mmol, 65%) as a colorless liquid collected at −78 °C: bp 60−61 °C (1.5 mmHg), cis/trans ratio ≥ 97/3 by ^{31}P NMR. For *cis*-**13**: ^{31}P NMR (121 MHz, $CDCl_3$) δ 145.0; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.73 (m, 1 H), 1.03 (t, 6 H, $^3J_{HH} = 7.0$ Hz), 1.19 (dd, 3 H, $^4J_{HP} = 1.5$ Hz, $^3J_{HH} = 6.0$ Hz), 1.78 (m, 1 H), 3.17 (m, 4 H), 3.71−3.80 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.32 (d, $^3J_{CP} = 3.1$ Hz), 23.22 (d, $^3J_{CP} = 6.2$ Hz) 35.14 (d, $^3J_{CP} = 9.9$ Hz), 38.15 (d, $^3J_{CP} = 21.3$ Hz), 63.95 (d, $^2J_{CP} = 6.8$ Hz), 71.07 (d), $^2J_{CP} = 6.2$ Hz). For *trans*-**13**: ^{31}P NMR (121 MHz, $CDCl_3$) δ 141.2.

(*R*)-*N,N*-Diethyl-4-methyl-1,3,2-dioxaphosphorinan-2-amine ((*R*)-13). A reaction of tris(diethylamino)phosphine (3.5 g, 22 mmol) and 98/2 *R*/*S* 1,3-butanediol (1.8 g, 20 mmol) was carried out as described for racemic **13**. Distillation under reduced pressure gave pure (*R*)-**13** (2.6 g, 13.6 mmol, 68%) as a colorless liquid, cis/trans ratio ≥ 95/5 by ^{31}P NMR.

Racemic 2-(1-Phenylethoxy)-4-methyl-1,3,2-dioxaphosphorinane (10). A solution of *N,N*-diethyl-4-methyl-1,3,2-dioxaphosphorinane-2-amine (**13**) (3.2 g, 17 mmol) and a catalytic amount of 1*H* tetrazole (100 mg) in 25 mL of freshly distilled acetonitrile was magnetically stirred under an argon sweep. To the solution was added dropwise a solution of 1-phenylethanol (1.8 g, 15 mmol) in acetonitrile (10 mL). After 1 h the solvent was removed under vacuum. Diethyl ether was added. The precipitated solids were filtered off under argon in a Schlenck apparatus and washed with dry ether (2 × 5 mL) which was removed under vacuum. The crude product was distilled to give 2.1 g (9 mmol, 60%) of **10** as a colorless liquid: bp 85−86 °C (0.95 mmHg); trans/cis ratio ≥ 97/3 (^{31}P NMR, $CDCl_3$, δ 127.7, 127.8, 131.8, 131.9. See Results section for relative intensities).

(*R′*)-2-(1-Phenylethoxy)-(*R*)-4-methyl-1,3,2-dioxaphosphorinane ((*R,R′*)-10). Following the procedure for the racemic material, reaction of (*R*)-*N,N*-diethyl-1,3,2-dioxaphosphorinan-2-amine ((*R*)-**13**) (2.4 g, 13 mmol) and (*R*)-(+)-1-phenylethanol (1.4 g, 11 mmol; 97/3 *R*/*S* by HPLC on a CHIRALCEL OD column, 1.5% methanol in chloroform) gave on distillation 1.7 g (7.3 mmol, 66%) of *trans*-**10** (*R,R′*/*R,S′* = 96/4 as shown by integration of the ^{31}P NMR ($CDCl_3$) peaks at δ = 127.7, *R,R′* isomer; and 127.8, *R,S′* isomer). Peaks assignable to the cis isomer near δ 131 were barely discernible. For *trans*-(*R,R′*)-**7**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (dd, 3 H, $^4J_{HP} = 1.8$ Hz, $^3J_{HH} = 6.2$ Hz), 1.34−1.52 (m, 1 H), 1.60 (d, 3 H), $^3J_{HP} = 6.5$ Hz), 2.23−2.37 (m, 1 H), 3.62−3.75 (m, 1 H), 4.25−4.35 (m, 1 H), 4.67−4.77 (m, 1 H), 5.20 (dq, 1 H, $^3J_{HP} = 8.6$ Hz, $^3J_{HH} = 6.5$ Hz), 7.24−7.44 (m, 5 H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.59 (d, $^3J_{CP} = 7.0$ Hz), 25.07 (d, $^3J_{CP} = 3.7$ Hz), 35.60 (d, $^3J_{CP} = 4.7$ Hz), 57.42 (d, $^2J_{CP} = 2.5$ Hz), 65.74 (d, $^2J_{CP} = 4.7$ Hz), 70.95 (d, $^2J_{CP} = 20.5$ Hz), 126.10, 127.74, 129.05, 145.13 (d, $^3J_{CP} = 3.5$ Hz); UV (CH_3CN): 250 (ϵ 200), 256 (ϵ 225), 260 (ϵ 230), 266 (ϵ 205); GC-EIMS (70 eV) *m/z* (relative intensity) 240 $[M]^+$ (10), 185 (19), 106 (15), 105 $[CHCH_3Ph]^+$ (100), 104 (27), 103 (10), 79 (15), 78 (8), 77 $[Ph]^+$ (30), 58 (9); HRMS $[M]^+$ calcd for $C_{12}H_{17}O_3P$ 240.0915, found 240.0910.

***trans*-(*R′*)-2-(1-Phenylethyl)-2-oxo-(*R*)-4-methyl-1,3,2-dioxaphosphorinane ((*R,R′*)-11).** Following the procedure given above racemic phosphite **10** (trans/cis, ≥97/3) was converted to **11** in an essentially clean reaction, as shown by the lack of spurious peaks in the GC or ^{31}P NMR spectrum of the reactions mixture at 90−95% completion. ^{31}P NMR

(16) (a) Kosolapoff, G. M.; Maier, L. *Organic Phosphorus Compounds*; Wiley-Interscience: New York, 1973; Vol. 4, 5, 7. (b) Ivanov, B. E.; Zheltukhin, V. F. *Russ. Chem. Rev.* **1970**, *39*, 358.

chemical shifts for the product phosphonates, **11**, are given in the Results section. In a completely analogous fashion, a 0.01 M solution of *trans*-(*R*,*R*′)-**10** in acetonitrile was photolyzed. *cis*-(*R*,*R*′)-**11**, the major product (80/20 *R*,*R*′/*R*,*S*′ *cis*-**11** product mixture, δ^{31}P NMR = 25.7, major; 25.5, minor) of photolysis was isolated by HPLC (1.1% methyl alcohol in chloroform) as a white solid in 70% yield. Recrystallization from ether/pentane gave colorless needles, mp 89−90 °C, suitable for X-ray crystallograpy. For *cis*-(*R*,*R*′)-**11**: ^{31}P NMR (121 MHz $CDCl_3$) δ 25.7; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (dd, 3 H, $^4J_{HP}$ = 1.7 Hz, $^3J_{HH}$ = 6.1 Hz), 1.34−1.48 (m, 1 H), 1.63 (dd, 3 H, $^3J_{HP}$ = 26.1 Hz, $^3J_{HH}$ = 7.6 Hz), 1.56−1.64 (m, 1 H), 3.25 (dq, 1 H, $^3J_{HP}$ = 22.9 Hz, $^3J_{HH}$ = 7.5 Hz), 4.02−4.15 (m, 1 H), 4.39−4.49 (m, 1 H), 4.63−4.73 (m, 1 H), 7.32−7.34 (m, 5 H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.97 (d, $^2J_{CP}$ = 5.2 Hz), 22.17 (d, $^3J_{CP}$ = 7.8 Hz), 33.26 (d, $^3J_{CP}$ = 5.2 Hz), 38.44 (d, *C*HCH$_3$, $^1J_{CP}$ = 137.0 Hz), 64.95 (d, $^2J_{CP}$ = 7.3 Hz), 72.89 (d, $^2J_{CP}$ = 6.8 Hz), 127.06 (d, J_{CP} = 3.6 Hz), 128.29 (d, J_{CP} = 2.6 Hz), 128.67 (d, J_{CP} = 6.2 Hz), 137.74 (d, *ipso*-Ph, $^3J_{CP}$ = 7.3 Hz); UV (CH_3CN) 240 (ϵ 150), 248 (ϵ 191), 256 (ϵ 238), 262 (ϵ 170), 265 (ϵ 96); GC-EIMS (70 eV) *m*/*z* (relative intensity) 240 $[M]^+$ (58), 186 (19), 185 (14), 158 (6), 136 (36), 109 (8), 106 (8), 104 (22), 103 (8), 79 (8), 77 $[Ph]^+$ (10), 55 (11); HRMS $[M]^+$ calcd for $C_{12}H_{17}O_3P$ 240.0915, found 240.0928. Anal. Calcd for $C_{12}H_{17}O_3P$: C, 59.98; H, 7.14. Found: C, 59.88; H, 7.10.

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Supporting Information Available: For the X-ray structure of *cis*-(*R*,*R*′)-**11** tables of crystal data, bond lengths and angles, atomic coordinates, and anisotropic thermal parameters (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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