SET-Induced Photorearrangement of 2-Phenylallyl Phosphites. Stereochemistry at Phosphorus. Application to Cyclic Nucleotide Derivatives

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The stereochemistry at phosphorus of the SET-induced photorearrangement of diastereomeric 4-*tert*-butyl-2-phenylallyl-1,3,2-dioxaphosphorinanes (**8**) to the corresponding 2-phenylallylphosphonates (**9**), which involves excited singlet 1,4-dicyanonaphthalene (^{1}DCN*) as one-electron oxidant, was investigated. The rearrangement occurs with close to complete *retention of configuration at phosphorus*. The previously postulated mechanism for this photorearrangement is shown to be consistent with the stereochemical finding. Thus, one-electron reduction by DCN$^{\cdot-}$ of the presumably stereospecifically formed distonic cyclic 1,3-cation radical intermediate **15**, generated from *cis*-**8** (Scheme 2), yields the thermodynamically stable diradical **16**. β scission of **16** forms phosphonate *cis*-**9**. An alternative mechanism involving β scission of **15** to a styryl cation radical, prior to one-electron reduction to **15**, is discounted on the basis of unpublished trapping studies using MeOH. The direct, kinetically controlled formation of diradical **16** rather than the thermodynamically less stable **21** with CH_2 bonded apically to phosphorus is argued to be consistent with the essentially equal values of the quantum yield for phosphonate formation (ϕ_P) on SET-induced rearrangement of the *acyclic* 2-phenylallyl phosphite **1** and phosphite **7** with phosphorus incorporated in a six-membered (1,3,2-dioxaphosphorinane) ring. This mechanism is contrasted to that for the previously reported *triplet-sensitized* photorearrangements of phosphites **1** and **7**, which have greatly different ϕ_P values. For these reactions, kinetic formation of the triplet analogue of **21**, but without the *tert*-butyl substituent, requires a permutation of substituents for conversion to diradical **16** prior to intersystem crossing and β scission to form the phosphonate corresponding to **7**. The preparative-scale SET-induced photorearrangement of the thymidine-based 2-phenylallyl 3′,5′-phosphite **10** gave both diastereomers of phosphonate **11** that were separated by HPLC. The 2-phenylallyl functionality provides an opportunity for further functionalization. As reported elsewhere, **11** was not formed in useful amounts via triplet-sensitized reaction of **10**.

Introduction

Induction of the rearrangement of dimethyl 2-phenylallyl phosphite, **1**, to the corresponding 2-phenylallylphosphonate, **6**, by electron transfer to excited singlet 9,10-dicyanoanthracene (^{1}DCA*) was recently reported.[1] The experimentally determined regiochemistry and two potential mechanisms for the process are depicted in Scheme 1. (In Scheme 1, photo-SET oxidant 1,4-dicyanonaphthalene, DCN, employed in the present study, is depicted instead of DCA.) Although relative oxidation potentials for removal of an electron from phosphorus[2] and from the styryl[3] system are too close to permit the assignment of the position of the charge in cation radical **2**, it was proposed that **2** cyclizes rapidly to generate the distonic cyclic 1,3-cation radical **3**. Product formation may involve donation of an electron from the DCA radical anion to **3** to afford 1,3-diradical **4** from which product phosphonate **6** arises via C−O β scission to introduce the two π bonds in **6**. An alternative route to **6**, set forth in Scheme 1, is the ring opening of radical **3** to the styryl radical cation, **5**, prior to its reduction to **6** by electron capture. In addition to unusual mechanistic considerations, these photorearrangements are of interest for the formation of allylphosphonates that can be further functionalized and/or used in Horner−Emmons chemistry.

The same overall rearrangement including regiochemistry is effected by triplet sensitization[4] of the styryl functionality of **1** by benzophenone or triphenylene, as previously reported.[5] A *triplet* 1,3-diradical (triplet **4**) was invoked as the key intermediate. Product **6** presumably arises from singlet **4** following triplet−singlet intersystem crossing. The quantum yield for triplet-sensitized phosphonate **6** formation (ϕ_P) from **1** is relatively high (0.2−0.3).[5a,b] Strikingly, when phosphorus is part of a six-membered ring (**7**), the triplet-sensitized photorearrangement is very inefficient (ϕ_P = 0.002−0.003).[5a,b] A requisite

(1) Ganapathy, S.; Dockery, K. P.; Sopchik, A. E.; Bentrude, W. G. *J. Am. Chem. Soc.* **1993**, *115*, 8863.

(2) (a) Oxidation potential vs SCE for $(MeO)_3P$, 1.64 eV (Ohmori, H.; Nakai, S.; Masui, M. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2023). (b) Reduction potention for DCA, −0.89 eV (Darmanyan, A. P. *Chem. Phys. Lett.* **1984**, *110*, 89)

(3) Oxidation potential for α-methylstyrene vs SCE, is 1.76 eV (Katz, M.; Riemenschneider, P.; Wendt, H. *Electrochim. Acta* **1972**, *17*, 1595).

(4) Measured triplet energies, E_T, for: (a) α-Methylstyrene: 62 kcal/mol (Crosby, P. M.; Dyke, J. M.; Metcalfe, J.; Rest, A. J.; Salisbury, K.; Sodeau, J. R. *J. Chem. Soc., Perkin Trans. 2* **1977**, 182. Tuqlang, N. I.; Caldwell, R. A.; Melton, L. S. *J. Am. Chem. Soc.* **1989**, *111*, 457.) (b) Benzophenone: 69.2 kcal/mol; triphenylene 67.0 kcal/mol (both values from Murov, S. L.; Carmichael, I.; Hug, G. L. *Handbook of Photochemistry*; Marcel Dekker: New York, NY, 1993.)

(5) (a) Bentrude, W. G.; Dockery, K. P.; Ganapathy, S.; Lee, S.-G.; Tabet, M.; Wu, Y. W.; Cambron, R. T.; Harris, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 6192. (b) Ganapathy, S.; Cambron, R. T.; Dockery, K. P.; Wu, Y. W.; *Tetrahedron Lett.* **1993**, *34*, 5987. (c) Bentrude, W. G.; Lee, S.-G. *J. Am. Chem. Soc.* **1987**, *109*, 1577. (d) Bentrude, W. G.; Lee, S.-G.; Akutagawa, K.; Ye, W.; Charbonnel, Y.; Omelanczuk, J. *Phosphorus Sulfur* **1987**, *30*, 105.

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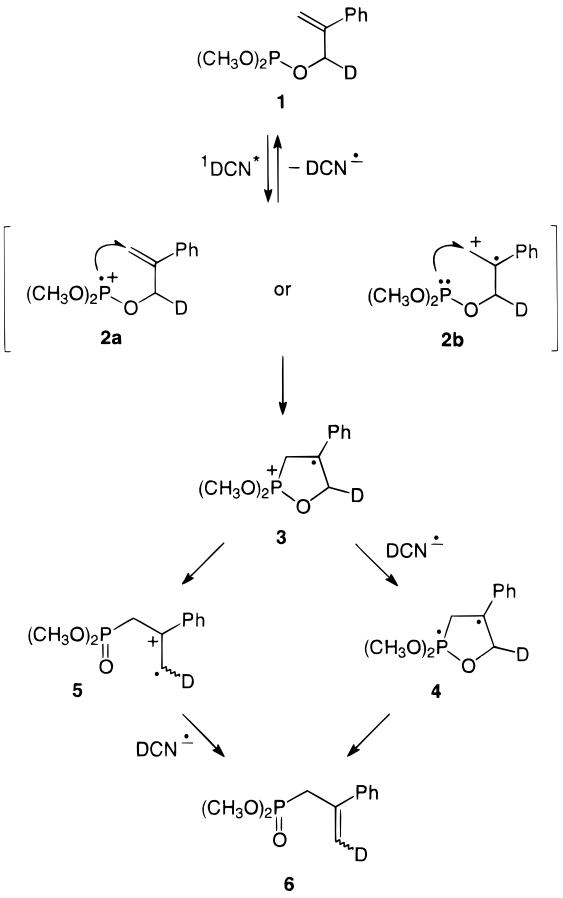
Scheme 1



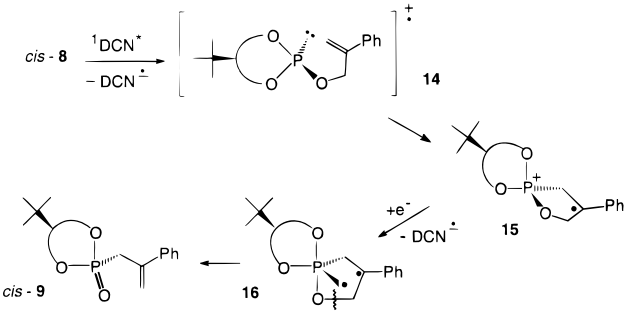
permutation of the positions of the substituents on phosphorus in the initial phosphoranyl 1,3-diradical, **22**, formed from triplet **1**, to generate a *thermodynamically*

more stable structure, **23**, has been proposed (eq 3).[5a,b] For **22** this process is fast and competes readily with reversal of 1,3-diradical formation back to triplet or ground state of **1**, and ϕ_P is relatively high. However, this permutation is proposed to be slow for the 1,3-diradical from **7** (analogous to **21**) leading to inefficient phosphonate formation and low ϕ_P.[5a,b] (For *tert*-butyl-substituted **7**, see **21** → **16**, Scheme 3.)

The SET process gives phosphonate **6** from phosphite **1** relatively inefficiently ($\phi_P = 0.03$).[1] However, by contrast to the triplet-sensitized reactions of **1** and **7**, it has been reported that placement of phosphorus in a six membered ring *has little effect on* ϕ_P *for the SET-induced photorearrangement* ($\phi_P = 0.03$).[1] The low ϕ_P values measured for **1** and **7** are not surprising considering the typically observed predominance of back electron transfer in the initial radical ion pair formed in SET processes.

In this paper, we report that the SET-induced photorearrangement of cis/trans mixture of the cyclic phosphite **8** affords **9** in good yields with essentially complete *retention of configuration at phosphorus*. This stereochemistry is shown in Scheme 2 to be consistent with the acceptance of an electron by the distonic 1,3-radical cation intermediate **15** from **8** to give directly the

Scheme 2

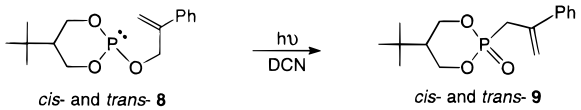


thermodynamically favored 1,3-diradical, **16**. Moreover, we will show this mechanism to be in accord with the constancy in the quantum yields for SET-induced rearrangements of **1** and **7**.

We also report the successful application of the photoinduced SET process for the preparation of cyclic phosphonate **11** from phosphite **10** in reasonable yields in a reaction that like **8** → **9** is retentive at phosphorus but to a slightly lower degree. The diastereomers of **11** are separable by chromatography. Phosphonates, phosphates, and phosphoramidates, as neutral analogues of cyclic 3′,5′-monophosphates, have been sought as potential agonists or antagonists of the action of the natural cyclic nucleotides, in the mapping enzyme active sites, and investigation of the potential chair-twist equilibrium of the six-membered phosphate ring.[6] The value of the SET process for preparation of **11** is accented by the reported[7] failure of the triplet-sensitized preparation of **11** from **10**.

Results

Stereochemistry of SET-Induced Photorearrangements of *cis*- and *trans*-8. Cyclic phosphites *cis*- and *trans*-**8** provide the opportunity to study the *stereochemistry at phosphorus* of the SET-induced photorearrangements of 2-phenylallyl phosphites (**8** → **9**). As reported elsewhere,[7] the diastereomeric phosphites, **8**, are easily prepared from the phosphorochloridites on reaction with 2-phenylallyl alcohol under conditions of kinetic control to give a configurationally stable, initial 8/92 cis/trans ratio of diastereomers (see also the Supporting Information). Two other ratios for stereochemical study were obtained by thermal equilibration.



The designation cis or trans for the diastereomers of *phosphite* **8** refers to the relationship of the *tert*-butyl and 2-phenylallyloxy groups. For *phosphonate* **9**, the *tert*-butyl and phosphoryl oxygen (P═O) are the priority groups. This convention for *phosphonates* is opposite to what we have used in other studies that involved closely related

(6) (a) Revenkar, G. R.; Robins, R. K. In *Handbook of Experimental Pharmacology*; Nathanson, J. A., Kebabian, J. W., Eds.; Springer-Verlag: Berlin and Heidelberg, West Germany, 1982; Vol. 58/I, pp 17−151. (b) Van Haastert, P. J. M.; Kien, E. *J. Biol. Chem.* **1983**, *258*, 9636. (c) Nelson, K. A.; Bentrude, W. G. *Carbohydr. Res.* **1992**, *234*, 141.

(7) Hager, D. C.; Bentrude, W. G. *J. Org. Chem.* **2000**, *65*, 2786−2791.

cyclic phosphonates,[8,9] but it follows the usual priority rules for the substituents on rings: O > C on phosphorus and C > H on carbon; i.e., the cis diastereomer of **9** has the *tert*-butyl and P═O cis to one another.

Assignments of absolute configuration to *cis*- and *trans*-**8** and -**9** were readily made on the basis of the well-established relationship between the ^{31}P chemical shift and the predominant axial or equatorial position of the RO on phosphorus in phosphites and the R substituent on phosphorus in phosphonates (δ^{31}P (equatorial) > δ^{31}P (axial)).[9] Previous work has shown the chair form **12** (2-phenylallyloxy axial) to be totally populated for phosphites such as **8**. Conformer **13** (P═O axial) is very predominantly populated for phosphonates similar to **9**.[9]

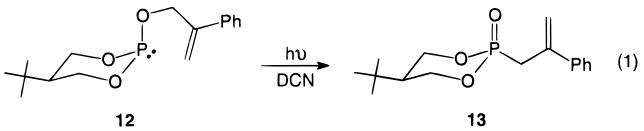
Deoxygenated methylene chloride solutions, 0.01 or 0.08 M in phosphite **8**, that contained approximately twice the concentration of 1,4-dicyanonaphthalene and a requisite amount of tri-*n*-propyl phosphate as internal standard, were irradiated in Pyrex tubes with UV light from a 450 W medium-pressure Hg lamp. Disappearance of phosphite **8** and formation of phosphonate **9** were monitored against the internal standard *(n*-PrO)$_3$PO by GC. Because the individual diastereomers of **8** are thermally equilibrated during GC analysis, only the total consumption of **8** can be determined in this way. The configurationally stable product phosphonate diastereomers, *cis*- and *trans*-**9**, could be readily quantitated by GC analysis. Consumption of the individual diastereomers of **8** was followed by two methods. Oxidation of residual phosphite **8** with *t*-BuOOH gives the corresponding phosphates that were quantitated by GC analysis. Significantly, this near-quantitative oxidation occurs with complete retention of configuration at phosphorus.[10] Alternatively, the amounts of individual diastereomers of both **8** and **9** were determined by ^{31}P NMR, very occasionally following careful concentration of the photolysate under argon. The GC and ^{31}P NMR methods gave closely similar results.

The results of these experiments using ^{31}P NMR to quantitate both disappearance of the diastereomers of **8** and formation of those of **9** are given in Table 1. Three initial cis/trans ratios of **8** were utilized. Each reaction was monitored at several conversions of phosphite. Notably, the thermodynamically less stable, higher energy *trans*-**8** is consumed more rapidly. Total yields of phosphonate (cis and trans) given are accountability yields based on phosphite converted and are seen to be quite good, especially at lower conversions. At each reaction time, the ratio (cis/trans) of phosphite **8** consumed is expressed in Table 1 as a ratio of percentages (cis + trans = 100%). The accountability yields of *cis*-**9** (based on converted *cis*-**8**) and of *trans*-**9** (based on converted *trans*-**8**) were calculated and also are recorded in the same manner (cis + trans = 100%). The agreement in ratios (cis/trans **8** consumed vs cis/trans **9** formed) in Table 1 is very good and leads to the conclusion that *the photorearrangement occurs with retention of configuration at phosphorus*. This stereochemistry is clearly shown in eq 1 for the cis diastereomers represented in their predominate chair conformations (**12** → **13**).

Table 1. Stereochemistry of SET-Induced Photorearrangement of 8[a]

time, h	*cis*/*trans*-**8**	% **8** convn[f]	% **9** formed[g]	*cis*/*trans*-**8** consumed[h]	*cis*/*trans*-**9** formed[i]
0	20/80[b,e]	0	0		
2	28/72	35	81	3/97	3/97
4	43/57	61	74	5/95	6/95
6	63/37	80	67	8/92	11/89
0	55/45[c,e]	0	0		
2	61/39	48	80	49/51	47/53
4	72/23	73	73	48/52	46/54
6	83/17	91	72	50/50	48/52
0	82/18[d,e]	0	0		
2	77/23	37	76	89/11	91/9
4	81/19	56	64	80/20	80/20
6	83/17	78	64	83/17	79/21

[a] By ^{31}P NMR vs internal standard (*n*-PrO)$_3$P(O). [b] 0.42 mol of **8**, 0.008 M. [c] 0.13 mol of **8**, 0.001 M. [d] 0.10 mol of **8**, 0.008 M. [e] Each solution contained approximately 2 equiv of DCN relative to initial **8**. [f] Based on total moles of both cis and trans isomers of **8** consumed. [g] Accountability yield of total **9** formed, based on total moles of both cis and trans isomers of **8** consumed. [h] Based on moles of individual cis and trans isomers of **8** consumed. [i] Based on moles of individual cis and trans isomers of **9** formed.



(1)

However, the yields of these reactions are not quantitative. Hence, the conclusion that they are essentially stereospecific at phosphorus requires that the fraction of byproducts formed from each diastereomer of **8** is the same. That this requirement is met is supported by the excellent correspondence observed between cis/trans ratios of consumed **8** and cis/trans accountabilities of product **9** seen at three initial ratios of **8**, even with the two diastereomers being consumed at different rates. In addition, the results are internally consistent in each case at several conversions of phosphate. Finally, the essentially unchanged results noted over the period of the photoreactions that employed phosphate very rich in the thermodynamically less stable trans diastereomer (cis/trans = 8/92) is excellent evidence for the configurational stability of **8** at phosphorus under the reaction conditions (diastereomers of phosphate not interconverted). Furthermore, this ratio was unchanged in a control sample held at room temperature in the absence of UV light over the period of photolysis. Independent control reactions showed the phosphonate diastereomers to be configurationally stable and not consumed on photoirradiation. The conclusion concerning the retentive stereochemistry at phosphorus of the SET-induced photorearrangements of **8** to **9** clearly is soundly based.

SET-Initiated Photorearrangement of Thymidine 3′,5′-Cyclic 2-Phenylallyl Phosphite, 10. As reported elsewhere,[7] the known 3′,5′-*N*,*N*-dimethylphosphoramidite **10**,[11] derived from thymidine, is readily converted to

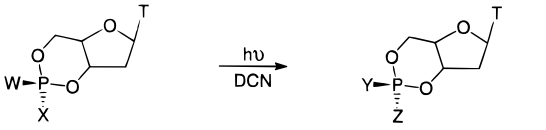
(8) Bhanthumnavin, W.; Arif, A.; Bentrude, W. G. *J. Org. Chem.* **1998**, *63*, 7753.

(9) Bentrude, W. G. In *Conformational Behavior of Six-Membered Rings*; Juaristi, E., Ed.; VCH: New York, NY, 1995; Chapter 7. Bentrude, W. G. In *Phosphorus-31 NMR Spectral Properties in Compound Characterization and Structural Analysis*; Quin, L. D., Verkade, J. G., Eds.; VCH Publishers: New York, NY, 1994; pp 41−53. Bentrude, W. G. In *^{31}P NMR Spectroscopy*; Verkade, J. G., Quin, L., Eds.; VCH Publishers: New York, NY, 1987; Chapter 11. Maryanoff, B. A.; Hutchins, R. O.; Maryanoff, C. A. *Top. Stereochem.* **1979**, *11*, 187.

(10) Bentrude, W. G.; Hargis, J. H. *J. Am. Chem. Soc.* **1970**, *92*, 7136.

(11) Bentrude, W. G.; Khan, M. H.; Saadein, M. R.; Sopchik, A. E. *Nucleosides Nucleotides* **1989**, *8*, 1359.

the 2-phenylallyl phosphite **10** and purified by chromatography in 66% isolated yield. In the present study, the thermodynamically less stable trans isomer predominated (cis/trans = 36/64; relationship of nucleobase and 2-phenylallyoxy groups) in this mixture which was configurationally stable at room temperature. The structure of phosphate **10** and the identity of its individual diastereomers were confirmed by comparison of ^{31}P, ^{1}H, and ^{13}C NMR spectra with those of the previously reported, well-characterized methyl and phenyl phosphites[12] analogous to **10**. Photoreaction of **10** on a small preparative scale (200−300 mg) in deoxygenated methylene chloride (250 mL) in an immersion well apparatus under SET conditions, with excited singlet 1,4-dicyanonaphthalene (^{1}DCN*) as the electron acceptor, was carried out with light from a 450 W medium-pressure UV lamp filtered through Pyrex.



cis-**10** W = $OCH_2CPh=CH_2$, X = lone pair
trans-**10** W = lone pair, X = $OCH_2CPh=CH_2$
cis-**11** Y = O, Z = $CH_2CPh=CH_2$
trans-**11** Y = $CH_2CPh=CH_2$, Z = O

After 8 h of irradiation, ^{31}P NMR analysis showed phosphite **10** to be 86% consumed. Phosphonate **11** was formed in 79% accountability yield, based on consumed **10** (68% yield, based on total **10**). ^{31}P NMR showed less than 5% of oxidation side product, the phosphate of **10**, to be present. Column chromatography afforded pure **11** as a mixture of cis and trans diastereomers in 63% overall yield (cis/trans = 33/67). The individual cis and trans diastereomers from another preparation of **11** starting with 120 mg of **10** were readily separated by HPLC (see the Experimental Section). This product mixture was considerably contaminated with the phosphate of **10**. Corrected for unreacted phosphite and phosphate byproduct, the total yield of isolated pure cis and trans diastereomers of **11** was 45%.

The identities of the individual cis and trans isomers of **11**, like those of **9**, were assigned from their relative ^{31}P NMR chemical shifts.[9] In addition the diagnostic ^{13}C NMR parameters of the diastereomers of **11** were compared to those known[6c] for the analogous phenyl- and methylphosphonates (phenyl or methyl in place of the 2-phenylallyl substituent on phosphorus of **10**). The structure of the *cis*-thymidine methylphosphonate analogous to **11** was determined by X-ray crystallography.[13]

The stereochemistry of the SET-initiated photorearrangement of **10**, followed quantitatively by ^{31}P NMR spectroscopy with $(n\text{-PrO})_3PO$ as internal standard, is revealed by the results recorded in Table 2. Reaction conditions were similar to those used for the stereochemical studies of **8**. As seen for the diastereomeric **8**, the configuration at phosphorus is largely *retained* in the product phosphonates, **11**, but with some increase in the cis/trans ratio of phosphonate **11** formed. The SET-induced photorearrangement of phosphite **10** is very sluggish beyond about 70% conversion (4 h), after which time the reaction is less stereochemically specific. Perhaps, side products absorb UV light or are themselves consumed by SET processes and interfere with the photoreaction of **10**. At higher conversions the yields in the stereochemical studies are somewhat lower than that in the preparative study.

Table 2. Stereochemistry of SET-Induced Photorearrangement of 10[a] in Methylene Chloride

time, h	*cis*/*trans*-**10**	% **10** convn[e]	%**11** formed[f]	*cis*/*trans*-**10** consumed[g]	*cis*/*trans*-**11** formed[h]
0	35/65[b,d]	0	0		
1	40/60	27	83	22/78	16/84
4	55/45	59	60	28/72	26/74
6	61/39	67	63	18/82	27/73
0	36/64[c,d]	0	0		
1	41/59	23	88	19/81	23/77
4	55/45	58	68	19/81	24/76
6	65/35	70	70	21/79	27/73

[a] By ^{31}P NMR vs internal standard $(n\text{-PrO})_3PO$. [b] 0.218 mol of **10**, 0.009 M. [c] 0.318 mol of **10**, 0.012 M. [d] Both reactions contained approximately 1 equiv of DCN relative to initial **10**. [e] Based on total moles of both isomers of **10** consumed. [f] Accountability yield of total **11**, based on total moles of both isomers of **10** consumed. [g] Based on moles of individual cis and trans isomers of **10** consumed. [h] Based on moles of individual cis and trans isomers of **11** formed.

Discussion

Quantum Yields and Stereochemistry of Photorearrangement: 1,3-Cation Radical Scission Mechanism, Direct Ring Opening of 3 and 15. The energetics of electron acceptance from phosphorus or the 2-phenylallyl moiety of **8** and **10** is about 4 kcal/mol more favorable for excited singlet 1,4-dicyanonaphthalene than it is for 9,10-dicyanoanthracene.[14] Thus, the Weller equation[14b] estimates electron removal from phosphorus to be 14 kcal exergonic and from the π bond favorable by 11 kcal/mol. Nonetheless, the site of removal of the electron cannot be predicted.

A very straightforward way to understand the essential constancy of ϕ_P values for **1** and **7** (0.03[5a,b]) is to propose that the cyclic 1,3-cation radicals from both phosphites ring open directly to yield a phosphonate styryl cation radical (**5** of Scheme 1 or the species from the ring opening of the 1,3-cation radical analogous to **15** of Scheme 2 but without the *tert*-butyl substituent). This step is followed by electron transfer from the 1,4-dicyanonaphthalene radical anion ($DCN^{\cdot-}$) to give the product phosphonates (**6** of Scheme 1 and the analogue of **9**, Scheme 2, without the *tert*-butyl substituent). The cyclic 1,3-cation radical (**3** of Scheme 1 or its spiro counterpart, such as **15** of Scheme 2) is most likely formed irreversibly and most certainly in competition with back-electron transfer in the initial radical ion pair (e.g., **2**/$DCN^{\cdot-}$). Whether the phosphorus atom is part of a spiro system should have little effect on this competition leading to comparable values of ϕ_P for **1** and **7**.

(12) Nelson, K. A.; Sopchik, A. E.; Bentrude, W. G. *J. Am. Chem. Soc.* **1983**, *105*, 7752 and unpublished results.

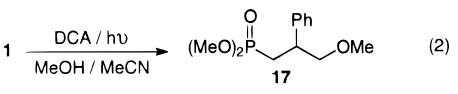
(13) Bentrude, W. G.; Sopchik, A. E.; Bajwa, G. S.; Setzer, W. N.; Sheldrick, W. S. *Acta Crystallogr.* **1986**, *C42*, 1027.

(14) (a) The reduction potential for DCN vs SCE is −1.28 eV while that for DCA is −0.89 eV. The singlet energies, E_S, for DCN and DCA are 3.45 and 2.88 eV, respectively (Darmanyan, A. P. *Chem. Phys. Lett.* **1984**, *110*, 89). All oxidation and reduction potentials, unless otherwise noted, are from Table 2 of: P*hotoinduced Electron Transfer*; Fox, M. A., Chanon, M., Eds.; Elsevier: New York, 1988; Part C, Chapter 4.1. (b) For the Weller equation, see: Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259.

The *stereochemistry* of rearrangement by this mechanism would clearly proceed with retention of configuration at phosphorus on formation from *cis*-**8**, via **14**, of the phosphonium ion-like 1,3-cation radical (distonic) intermediate **15** (Scheme 2). (See more detailed discussion in the next section.) There should be a favorable thermodynamic driving force for cleavage to the styryl cation radical precursor of *cis*-**9**, analogous to **5** of Scheme 1, as two π bonds are simultaneously introduced. Final reduction of the styryl-like radical cation analogous to **5**, formed from β scission of **15**, is favorable energetically by 11 kcal/mol, based on predictions of the Weller equation and the measured oxidation potential for α-methyl styrene (1.76 eV [14]), the singlet energy of ^{1}DCN* (3.45 kcal/mol[14]), and oxidation potential of DCN$^{\cdot-}$ (−1.28 eV[14]). Nonetheless, as set forth later, experimental evidence against a mechanism involving intermediates such as **5** exists.

In the *alternative mechanism* that we favor, depicted in Scheme 2, the intermediate cyclic 1,3-cation radical (**3** in Scheme 1 and **15** in Scheme 2) is reduced by DCN$^{\cdot-}$ to the singlet diradical (**4** in Scheme 1 and **16** in Scheme 3). The energetics of reduction of **3** or **15** by DCN$^{\cdot-}$, if the parallel reduction by DCN$^{\cdot-}$ of phosphonium salts $[RPPh_3]^+$ is a good model, is calculated from redox potentials to be *endergonic* by about 2 kcal/mol.[15] However, within experimental error, this number may well be energetically somewhat exergonic, allowing the reduction of **15** to **16** to occur readily.[14b] Nonetheless, DCA also brings about these reactions, though the $[RPPh_3]^+$ model predicts the trapping of **3** and **15** by DCA$^{\cdot-}$ to be endergonic by 11 kcal/mol.[16] These estimates appear to disfavor reaction via reduction of intermediates **3** and **15**. It should be noted, however, that other key reductions in photoinduced SET reactions that involve ^{1}DCA*/DCA$^{\cdot-}$ and that are estimated from redox potentials to be energetically unfavorable, nonetheless, occur readily.[17]

Important experimental evidence *against* the formation of **6** via **3** → **5** → **6** comes from unpublished results from this group of attempted trapping of **3** by methanol in the SET rearrangement of phosphite **1** photoinduced by DCA.[18] The addition of methanol in significant amounts to the DCA/SET-induced photorearrangement reaction of **1** via **5** in the presence of MeOH should yield adduct **17** (eq 2). Indeed, adduct **17** is generated along with large



(2)

amounts of **6**, but *its formation lags behind that of phosphonate* ***6***. By contrast, the methyl ether, MeOCH$_2$-CPh=CH$_2$,[18,19] is formed from the outset of the reaction in about 8% yield based on converted **1**. Evidently, **17** results from SET-induced reaction of phosphonate **6** with MeOH, rather than by trapping of **5**. The conversion of **6** to **17** under the SET conditions with DCA was independently verified.

It indeed seems quite probable that the reduction potentials for intermediates such as **3** and **15** are more favorable than predicted by the $[RPPh_3]^+$ model. Thus, the one-electron reduction potential for $[(RO)_4P]^+$, a closer model for **3** and **15**, should be less negative as a result of the electronegative alkoxy substituents on phosphorus. Furthermore, there may be a stabilizing interaction between the single-electron-containing orbitals on phosphorus and carbon in **4** and **16**. In fact, cyclopentane 1,3-diradicals (diyls), though clearly different from **4** and **16**, are comparatively long-lived when their odd electron bearing orbitals are properly oriented.[20] In addition ring opening of **3** and **15** to the styrene-like cation radicals may involve unforeseen, relatively high activation barriers such that reduction to the 1,3-diradical predominates.

Stereochemistry at Phosphorus: 1,3-Diradical Mechanism. The stereochemistry of the SET-induced photorearrangements of phosphites **8** and **10** is readily understood in terms of the 1,3-diradical mechanism for the photorearrangement process. This is shown for *cis*-**8** in Scheme 2 presented earlier. The initial radical cation **14**, formed by SET to ^{1}DCN*, undergoes cyclization to the distonic 1,3-radical cation **15**. As stated previously, the stereochemistry at phosphorus is fixed initially by formation of **15**. Reduction of **15** by electron transfer from the DCN radical anion affords the phosphoranyl 1,3-diradical, **16**, that undergoes β scission to yield product **9** with predictably cis stereochemistry.

If **14** is in fact a styryl cation radical like **2b**, formation of **15** essentially involves the attack of the nucleophilic, three-coordinate phosphorus lone pair on the electrophilic carbon of **14**. The anticipated charge/electron distribution shown for **15** was demonstrated in the ESR spectrum of the closely related adduct from reaction of the radical cation of $(MeO)_3P$ with 1,1-di-*tert*-butylethene.[21] The formation of **15** then finds direct stereochemical analogy in the retentive stereochemistry at phosphorus noted in the formation of phosphonium salts from reaction of optically active phosphines with benzyl bromide.[22] Similarly, the thermal Arbuzov reaction of phosphite **18** with methyl iodide yields methylphosphonate **20** with retention of configuration at phosphorus.[23] This process is depicted in the sequence **18** → **19** → **20** in which **19** is analogous to **15**.

If instead **15** is the product of cyclization of a phosphorus cation radical ion, it is very significant that the analogous radical cations derived from $(MeO)_3P$ and

(15) Based on the average of the one-electron reduction potentials of $[PhCMe_2PPh_3]^+$ (−1.51 eV) and $[MeCPh_2PPh_3]^+$ (−1.24 eV) which undergo rapid cleavage to Ph_3P and the free radicals $PhCMe_2$ and $MeCPh_2$, respectively (Saveant, J. M.; Binh, S. K. *J. Org. Chem.* **1977**, *42*, 1242 and the reduction potential for DCN (−1.28 eV[15]).

(16) Based on the averaged phosphonium salt reduction potential of ref 16 and the reduction potential for DCA (−0.89 eV[15]).

(17) An example is found in the well-known DCA-promoted, anti-Markovnikov addition of methanol to 1,1-diphenylethylene. The reaction proceeds via the 1,1-diphenylethylene cation radical to give high yields of methanol adduct, although the necessary reduction of intermediate 1,1-diphenyl-2-methoxy radical is estimated from oxidation half-wave potentials to be endergonic by about 9 kcal/mol. Thus, for diphenylethyl radical, a valid model, the reduction potential vs SCE is −1.34 eV (Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132) while that for DCA is only −0.89 eV.[15]

(18) Dockery, K. P. Ph.D. Thesis, University of Utah, 1995.

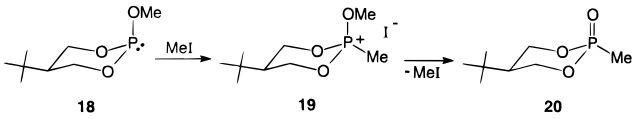
(19) This ether could result from trapping of 2-phenylallyl cations formed on cleavage of the initial radical cation (**2b**) or by addition of MeOH to **2b** followed by scission to yield **17** and the radical $(MeO)_2P(O)^{\cdot}$. Studies with deuterium-labeled **1** indicate the latter process dominates.

(20) Adam, W.; Hoessel, P.; Huemmer, W.; Platsch, H.; Wilson, R. M. *J. Am. Chem. Soc.* **1986**, *108*, 929.

(21) Gara, W. B.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1978**, 150.

(22) Horner, L.; Fuchs, H.; Winkler, H.; Rapp, A. *Tetrahedron Lett.* **1963**, 965.

(23) Bentrude, W. G.; Hargis, J. H. *J. Am. Chem. Soc.* **1970**, *92*, 7136. Haque, M. U.; Caughlan, C. N.; Hargis, J. H.; Bentrude, W. G. *J. Chem. Soc. A* **1970**, 1786.



18 19 20

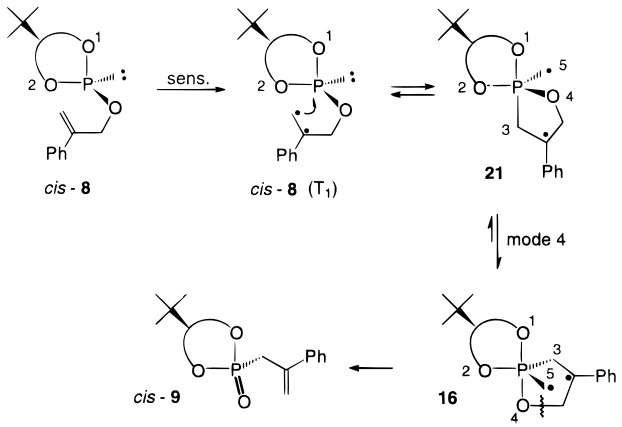
$(EtO)_3P$ are known from ESR measurements to be *highly pyramidal* with a *p*/*s* ratio for the SOMO spin density on phosphorus of approximately 3/1.[24] The barrier to inversion, though to our knowledge not measured, will be relatively high because of the electronegativity of the alkoxy groups attached to phosphorus.[24] Sufficiently rapid formation of **15**, in competition with inversion of cation radical **14** at phosphorus, would retain configuration at phosphorus. By contrast, the stereochemistry of oxidation of phosphorus-centered cation radicals from Ph_3P occurs with random stereochemistry.[24]

It should be noted that the *triplet-sensitized photorearrangement* of **8** to **9** also takes place with retention of configuration at phosphorus.[7] As shown in Scheme 3, the proposed initial 1,3-diradical intermediate **21** isomerizes to the same intermediate **16** that is postulated to be formed *directly* by reduction of **15**. The significance of the *initial* formation of **16** rather than **21** in the SET processes (Scheme 2) will be set forth in detail in the next section. β scission of either **16** or **21** would afford phosphonate **9** with the correct stereochemistry (*cis*-**9** in Scheme 3).

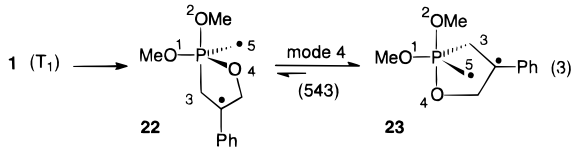
Quantum Yields for SET-Induced Photorearrangements of 1 and 7: 1,3-Diradical Mechanism. The following arguments, set forth elsewhere,[5] apply to the formation, relative energies, and interconversions of permutamers of the phosphoranyl 1,3-diradicals assumed to be formed in the *triplet-sensitized* rearrangement of phosphites **1**, **7**, and *cis*- and *trans*-**8**. (Phosphites **7** and **8** differ only in the presence of the *tert*-butyl substituent on the six-membered ring). They serve as a necessary background for understanding the consistency between the stereochemistry of the SET-induced rearrangement of **8**, the constancy of quantum yields for the SET rearrangement processes for **1** and **7** ($\phi_P = 0.03$), and the quantum yields and stereochemistry of the *triplet-sensitized* photorearrangements of **1**, **7**, and *cis*-**8**.

Diradical **21** (Scheme 3) has been proposed to be formed kinetically via apical introduction of the terminal (primary) end of the 1,2-diradical-like styryl unit of triplet *cis*-**8**.[5,7] The apical introduction of the methylene to yield **21** is in accord with conclusions from ESR work concerning the formation of phosphoranyl monoradicals by *reversible* oxidative addition of alkyl radicals to trialkyl phosphites via the apical position.[25] It has been proposed[5,7] that formation of **21** is highly reversible by analogy to alkyl radical attack on phosphites.[25] Phosphoranyl 1,3-diradical **21** is thermodynamically less stable than its permutational isomer **16**, which results from a single mode 4 permutation of **21** (Scheme 3).

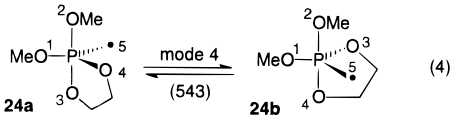
Scheme 3



Similarly, **22** (eq 3) is the presumed initial 1,3-diradical intermediate in the triplet-sensitized photorearrangement of **1**.[5] To explain the efficient formation of phosphonate **2** ($\phi_P = 0.2-0.3$) from phosphate **1**, it has been postulated that there is *rapid*, though perhaps reversible, conversion (eq 3) of the kinetically formed 1,3-diradical **22** to the thermodynamically more stable form, **23**, from which *equatorial* α-scission to reform phosphite **1** does not occur. On β scission, **23** gives **6**. Such an isomerization



is of mode 4, and has been established by kinetic ESR work to be relatively fast for phosphoranyl *monoradicals* analogous to **22**, e.g., **24** (**24a** ⇆ **24b**), eq 4.[26] The mode 4 permutation is operative rather than the mode 1 permutation defined for truly pentacovalent phosphorus molecules. The isomerization **22** → **23**, followed by β scission to give **6**, essentially traps **22** and prevents reformation of triplet phosphite or, following intersystem crossing, regeneration of ground state phosphate. The result is a comparatively large value for ϕ_P (0.2−0.3).[5a,b]



By contrast, the analogous permutation process for *spiro phosphoranyl monoradicals* is known to be unusually slow.[27] Therefore, 1,3-diradical **21** (Scheme 3) from *cis*-**8** (and its analogue from **7**) is presumed to isomerize to **16** only *very slowly* leading to a low ϕ_P (for **7**, ϕ_P = 0.003), because **21** reopens primarily to the ground or triplet state **7**.[5]

Totally consistent with the above views and Schemes 2 and 3 is the fact that for SET-initiated photorearrangement the quantum yields for phosphonate formation from **1** and **7**, though inefficient, are the same (ϕ_P = 0.03),[1]

(24) For the characterization of radical cations of phosphines (Ar_3P and R_3P) and phosphites ($(RO)_3P$, R = Me, Et), see: (a) Tordo, P. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; Wiley and Sons: Chichester, 1990; Chapter 6. (b) Hasegawa, A.; McConnachie, G. D. G.; Symons, M. C. R. *J. Chem. Soc., Faraday Trans. 1* **1984**, *80*, 1005. (For effects of substituent electronegativity on the pyramidal nature of these and related radicals, see: Symons, M. C. R. *Chemical and Biochemical Aspects of Electron Spin Resonance Spectroscopy*; Van Nostrand Reinhold: Wokingham, 1978.)

(25) Cooper, J. W.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1976**, 808. Baban, J. A.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1980**, 876. Dockery, K. P.; Bentrude, W.G. *J. Am. Chem. Soc.* **1994**, *116*, 10332. Dockery, K. P.; Bentrude, W.G. *J. Am. Chem. Soc.* **1997**, *119*, 1388.

(26) Cooper, J. W.; Parrot, M. J.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1977**, 730. Five-coordinate phosphorus modes of permutation, applicable to trigonal bipyramidal phosphoranyl radicals, have been defined (Musher, J. I. *J. Chem. Educ.* **1974**, *51*, 94).

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

unlike those for the triplet-sensitized photorearrangements of the same phosphites (0.3 and 0.003).[5a,b] As shown in Scheme 2, reduction of the distonic cyclic 1,3-radical cation **15**, formed from *cis*-**8**, gives directly the *thermodynamically stable* 1,3-diradical **16**, which β scissions to form product phosphonate *cis*-**9** rather than undergo *equatorial* P−CH_2 α scission to triplet or ground state *cis*-**7**. The opportunity for facile ring opening to regenerate phosphate **8** is precluded because the thermodynamically less stable form **21**, initially formed in reversible fashion in the triplet-sensitized rearrangement of **7**, would have to be formed from the thermodynamically more stable, directly formed **16**. As discussed earlier in this paper, closure to **3**, **15**, and the 1,3-cation radical analogue from **7** without *tert*-butyl substitution should occur with the same efficiency. Likewise, their trapping by electron donation by $DCN^{\cdot-}$ to give **4** and **16** should not be perturbed by phosphorus being part of a spiro system (**15** and its analogue from **7**). The overall quantum yield for phosphonate formation, ϕ_P, is then predicted to be similar for **1** and **7**, as is found experimentally.[1]

Preparation of Cyclic Nucleotide-Based Phosphonates, 11. Phosphorothioate, methylphosphonate, and phenyl and methyl phosphate analogues of nucleoside cyclic 3′,5′-monophosphates have been prepared as potential mimics or antagonists of the interactions of the natural cyclic nucleotides, cAMP and cGMP, with protein kinases and phosphodiesterases.[6] The photorearrangement product phosphonate **11**, isolated as the diastereomeric mixture in 63% yield, was separable into the individual diastereomers. The SET-initiated process is expected to be superior to the more classical alternative, the Arbuzov reaction of the methyl phosphite analogous to **10** with 2-phenyl-3-bromopropene. Thus, with 3′,5′-cyclic methyl phosphites derived from nucleosides, e.g., adenosine and guanosine, featuring nucleobases with strongly nucleophilic sites, alkylation at nitrogen is a likely side reaction. Indeed, methyl iodide, utilized to alkylate the phosphate oxygen of the salt of c-AMP to form the methyl phosphate, was reported to also alkylate the nucleobase.[28] High concentrations of 2-phenyl-3-bromopropene would be needed to alkylate phosphorus in competition with product methyl bromide that will be formed increasingly as the reaction progresses.

The 2-phenylstyryl moiety of phosphonate **11** is subject to further chemical modification making it a potential precursor to hitherto unknown cyclic nucleotide derivatives. This lends further significance to the preparation of these new cyclic nucleotide derivatives.

Conclusions

The SET-initiated photorearrangements of the *cis*- and *trans*-2-phenylallyl phosphites, **8**, to the corresponding phosphonates, **9**, take place with *retention* of configuration at phosphorus. This result is consistent with, though not proof of, the previously postulated rearrangement mechanism for these processes illustrated for *cis*-**8** in Scheme 2. Electron donation to the stereospecifically formed, cyclic, distonic 1,3-cation radical intermediate **15** gives rise directly to 1,3-phosphoranyl diradical **16** that generates phosphonate *cis*-**9** with retention of configuration at phosphorus. Very significantly, in Scheme 2 the thermodynamically stable 1,3-diradical **16**, which has the methylene carbon *equatorial* and ring oxygen *apical* on trigonal bipyramidal phosphorus, is formed directly. By analogy to what is known about phosphoranyl *monoradicals*, the equatorial position of the methylene precludes facile P−CH_2 scission to reform *cis*-**8** and reduce the quantum yield for formation of phosphonate **9**. The rates of presumably irreversible formation of 1,3-cation radicals **3** and **15** (and the non-*tert*-butyl-substituted analogue from **7**) should be similar and equally competitive with back-electron transfer within the initial radical-ion pair. The result is the experimentally observed essentially identical quantum yields for phosphonate formation (ϕ_P) for **1** and **7** (ϕ_P = 0.03). By contrast, electron donation to **15** (or its non-*tert*-butyl analogue from **7**) to give **21** (or the non-*tert*-butyl analog) directly would lead to ring opening to reform the starting phosphite, *cis*-**8**, by α-scission of the apical CH_2 (Scheme 3) in competition with relatively slow rearrangement to *cis*-**9** (**21** → **16** → *cis*-**9**). The result would be a decreased quantum yield for phosphonate formation (ϕ_P) from **7** relative to that for **1**, contrary to experimental observation. (The stereochemistry of the conversion of **8** to **9** would be unchanged by formation of **21** followed by its β scission to afford **9**.) An alternative mechanism, ring cleavage of **3** to give styryl cation radical **5**, is discounted by the failure in an unpublished study[18] of MeOH to trap **5**.

Photoinduced SET rearrangement of the thymidine cyclic 3′,5′-phosphite **10** gives reasonable yields of the 2-phenylallylphosphonate diastereomers of **11** that are separable by HPLC. Chemical modification of the alkene functionality of **11** may lead to increased bioapplications.

Experimental Section

Preparation of Compounds. Methylene chloride was distilled from calcium hydride under argon. Reagents are from Aldrich Chemical Co. Tri-*n*-propyl phosphate was distilled prior to use. Thymidine (Sigma) was used as received. DCN (1,4-dicyanonaphthalene) was prepared by standard procedures.[29] 2-Phenylallyloxy 5-*tert*-butyl 1,3,2-dioxaphosphorinane, **8**,[7] 2-oxo-2-phenylallyl-5-*tert*-butyl 1,3,2-dioxaphosphorinane, **9**,[7] and the thymidine 3′,5′-cyclic 2-phenylallyl phosphite, **10**,[7] were made by procedures published elsewhere and also are available in the Supporting Information.

Photochemical Reactions. The study of the stereochemistry of rearrangement of **8** with DCN as SET agent utilized light from a 450-W medium-pressure Hg lamp, equipped with a Pyrex glass sleeve in a water-cooled immersion photochemical apparatus. Samples were prepared in Pyrex tubes by glovebox techniques under an argon atmosphere and placed about 2.5 cm from the immersion tube apparatus. Preparative-scale irradiations of **10** were carried out on argon-purged solutions in a photochemical reaction vessel, fitted with a quartz immersion tube, with Pyrex-filtered light from a 450-W medium-pressure Hg lamp.

Physical Methods. Melting points are uncorrected. *J* values given in the ^{1}H NMR spectral data refer to proton−proton coupling unless otherwise stated. A 60 s repetition rate was employed when the photoreactions were monitored by ^{31}P NMR to ensure the accuracy of the integration. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, GA. GC−EIMS (70 eV) analyses utilized a 30 m × 0.25 mm fused silica capillary column. Reported intensities are percentages of the base peak intensity. Other low resolution EIMS (70 eV) as well as HRMS (EI, 70 eV) measurements utilized a standard inlet

(28) Attempted alkylation of both the potassium and silver salts of cAMP with alkyl iodides led to alkylation at N1 of the nucleobase. Jarvest, R. L.; Lowe, G.; Potter, B. V. L.; *J. Chem. Soc., Perkin Trans. 2* **1981**, 186. Beres, J.; Sandor, P.; Kalman, A.; Koritansnsky, T.; Otvos, L. *Tetrahedron* **1984**, *40*, 2405.

(29) Kleigman, J. M.; Barnes, R. K. *Tetrahedron* **1970**, *26*, 2555. Heiss, L.; Paulus, E. F.; Rehling, H. *Leibigs Ann. Chem.* **1980**, 1583.

system. FABMS(LSIMS) spectra were obtained using a cesium ion gun. The GLC yields were determined with a flame ionization detector on a 20 m × 0.25 mm fused silica capillary column (DB-1) with tri-*n*-propyl phosphate as internal standard.

Stereochemistry of the Photoinduced Single-Electron Transfer Initiated Rearrangement of 5-*tert*-Butyl-2-(2-phenylallyloxy)-1,3,2-dioxaphosphorinane (8). The following sample preparation procedure is typical. In a glovebag under an argon atmosphere was added tri-*n*-propyl phosphate to a preweighed 25.0 mL volumetric flask that contained 1,4-dicyanonaphthalene (48.1 mg, 0.270 mmol). The flask was removed from the glovebag and reweighed (tri-*n*-propyl phosphate, 73.9 mg, 0.330 mmol). In the glovebag, the contents were dissolved and diluted to 25.0 mL with dry methylene chloride. Similarly, 5-*tert*-butyl-2-(2-phenylallyloxy)-1,3,2-dioxaphosphorinane, **8** (37.6 mg, 0.128 mmol), was placed under argon in a 10.0-mL volumetric flask and then diluted to 10.0 mL with the solution of internal standard. Three quartz test tubes (13 mm × 80 mm) were flushed with argon, capped with rubber septa, and transferred to the glovebag. To each tube was transferred 2.5 mL of the reaction solution via syringe. The samples were irradiated with light from a medium pressure 450-W Hg lamp, filtered through a Pyrex glass sleeve. The photolysis solutions were sampled at 0, 2, 4, and 6 h. At each conversion, the moles of each diastereomer of unreacted **8** were determined by ^{31}P NMR, by reference to the internal standard, on aliquots of reaction solution transferred to an NMR tube in a glovebag under argon. Moles of the individual diastereomers of **9** formed were determined in the same way. Very rarely, it was necessary to concentrate the samples under a slow stream of argon prior to quantitation by ^{31}P NMR. The yields of the individual diastereomers of **9** (tri-*n*-propyl phosphate internal standard) also could be determined by GLC on a sample carefully concentrated under argon, using a 20 m × 0.32 mm RSL-150 capillary column. The individual diastereomers of remaining phosphite **8** were quantitated by GC in those cases by slow syringe addition under argon to the concentrate of approximately 1.1 equiv of a *t*-BuOOH in an organic solvent to convert **8** to the phosphate. The data of Table 1 are based on the ^{31}P NMR method. Yields of **9** at t = 6 h, based on converted starting dioxaphosphorinane, were in the range of 64−72%. Product phosphonate structures were confirmed by ^{31}P NMR and GC−EIMS comparisons to authentic phosphonates prepared independently.

Stereochemistry of Photoinduced Single-Electron Transfer Initiated Rearrangement of Thymidine 3′,5′-Cyclic 2-Phenylallyl Phosphite (10). Via the above glovebag techniques, preweighed phosphite (88.9 mg, 0.218 mmol) **10** in a 25.0-mL volumetric flask was diluted to volume with a 50.0-mL methylene chloride stock solution of 1,4-dicyanonaphthalene (43.7 mg, 0.245 mmol) and tri-*n*-propyl phosphate (88.7 mg, 0.396 mmol). To each of four rubber septa capped, argon-flushed NMR tubes (5 mm) that had been fitted with 10/30 ground glass joints was transferred 1.5 mL of the above solution via syringe. The tubes were degassed by four freeze−pump−thaw cycles on a vacuum line (0.02 mmHg) and flame sealed. The reaction mixture was checked by ^{31}P NMR at time zero. The tubes were irradiated with Pyrex sleeve filtered light from a medium-pressure 450-W Hg UV lamp. The photolysis solutions were monitored at periods over the time of the reaction by ^{31}P NMR without opening the tubes. The final yields (at t = 6 h) of phosphonate **11** ranged from 63 to 70%, based on converted starting phosphite (Table 2). By utilizing the ^{31}P NMR peak area of the internal standard, along with those of remaining phosphite and phosphonate diastereomers formed, the moles of consumption and formation of each was determined and reported on a percentage basis (Table 2). It was shown that the reactions also could be quantitated accurately to give comparable results by opening the tubes under argon, oxidizing the remaining phosphite to the phosphate with *tert*-butyl hydroperoxide and then concentrating the mixture under vacuum before ^{31}P NMR analysis. The results of Table 1 were obtained by the direct ^{31}P NMR procedures without invasion of the NMR tubes.

Preparative Scale Photoinduced Single-Electron Transfer Initiated Rearrangement of Thymidine Cyclic 2-Phenylallyl-3′,5′-phosphite (10). By glovebag techniques, a photoreaction vessel was charged with thymidine cyclic 2-phenylallyl-3,5-phosphite **9** (237 mg, 0.587 mmol; cis/trans = 34/66), 1,4-dicyanonaphthalene (112 mg, 0.49 mmol), and methylene chloride (250 mL). An immersion well containing a 450-W medium pressure Hg lamp (Pyrex sleeve) was fitted to the vessel. The reaction solution, continuously purged with a slow stream of argon, was irradiated for 8 h. The moles of the individual diastereomers of **9** and **10** were determined by ^{31}P NMR peak integration by reference to the internal standard. Samples for ^{31}P NMR work were prepared by carefully evaporating the solvent under argon and dissolving the residue in $CDCl_3$. The yield of **10** was determined to be 79%, based on an 86% conversion of starting phosphite (overall yield 68%). The crude product was purified by column chromatography (eluting with 50% ethyl acetate/hexane) to give 149 mg (63% isolated overall) yield of a mixture (cis/trans = 33/67) of solid phosphonate **10**.

A less pure 34/66 trans/cis mixture of diastereomers of **10** from another preparation, based on 120 mg of starting phosphite **9**, was chromatographed (HPLC) with 96:4 $CHCl_3$/MeOH on a Rainin Dynamax 21.4 mm i.d. silica gel column. By ^{31}P NMR peak area integration, 89% of the starting phosphite was accounted for in the product mixture as unreacted phosphite (7%), byproduct phosphate impurity (20%) from insufficient deoxygenation, and **10** (51%, cis plus trans). HPLC gave 15 mg trans (95% pure, ^{31}P NMR) and 27 mg cis (97% pure, ^{31}P NMR): trans/cis, 36/64 by weight. The accountability of phosphite converted (corrected for phosphate formation) in terms of the purified isomers of **10** was 45%. Further purification by HPLC ($CHCl_3$/MeOH) gave the individual isomers of **10** in >99% purity. *trans*-**10**: ^{31}P NMR (121.4 MHz C_6D_6) δ 22.5; ^{1}H NMR (499.8 MHz acetone-d_6) δ 1.83 (d, J = 1.3 Hz, 3 H, CH_3), 2.36 (ddd, J = 2.7, 8.3, 13.2 Hz, 1 H), 2.52 (ddd, J = 9.3, 9.6, 13.2 Hz, 1 H), 3.36 (d, $^2J_{HP}$ = 21.0 Hz, 1 H), 3.44 (d, $^2J_{HP}$ = 21.0 Hz, 1 H), 3.96 (dddd, J = 9.2, 5.0, 10.3 Hz, $^4J_{HP}$ = 0.4 Hz, 1 H), 4.39 (ddd, J = 5.0, 9.5 Hz, $^3J_{HP}$ = 14.9 Hz, 1 H), 4.56 (ddd, J = 10.3, 9.5 Hz, $^3J_{HP}$ = 4.0 Hz, 1 H), 4.79 (dddd, J = 9.6, 8.3, 9.2 Hz, $^3J_{HP}$ = 1.0 Hz, 1 H), 5.41 (d, ^2J = 5.5 Hz, 1 H), 5.54 (d, ^2J = 5.5 Hz, 1 H), 6.31 (dd, J = 9.3, 2.7 Hz, 1 H), 7.22−7.62 (m, 6 H), 10.0 (bs, 1 H, NH); ^{13}C NMR (125.7 MHz $CDCl_3$) δ 12.57, 33.14 (d, $^1J_{CP}$ = 134.8 Hz), 35.25 (d, $^3J_{CP}$ = 5.9 Hz), 70.18 (d, $^2J_{CP}$ = 10.4 Hz), 73.65 (d, $^3J_{CP}$ = 12.1 Hz), 76.47 (d, $^2J_{CP}$ = 5.4 Hz), 86.36, 111.77, 118.22 (d, $^3J_{CP}$ = 12.3 Hz), 126.32, 128.27, 128.60, 136.15, 138.02 (d, $^2J_{CP}$ = 11.3 Hz), 139.78 (d, ^{2} J_{CP} = 3.7, 149.40, 162.89 Hz). *cis*-**10**: ^{31}P NMR (121.4 MHz $CHCl_3$) δ 27.3; ^{1}H NMR (499.8 MHz acetone-d_6) δ 1.82 (d, J = 1.3 Hz, 3 H), 2.32 (ddd, J = 9.2, 10.3, 13.2 Hz), 2.49 (ddd, J = 2.6, 8.2, 13.2 Hz, 1 H), 3.26 (d, $^2J_{HP}$ = 22.2 Hz, 2 H), 3.70 (dddd, J = 9.2, 10.7, 5.2 Hz, $^4J_{HP}$ = 0.8 Hz, 1 H), 4.33 (ddd, J = 5.2, 9.2 Hz, $^3J_{HP}$ = 16.3 Hz, 1 H), 4.40 (ddd, J = 10.7, 9.2 Hz, $^3J_{HP}$ = 3.5 Hz, 1 H), 4.84 (dddd, J = 8.2, 10.3, 9.2 Hz, $^3J_{HP}$ = 1.6 Hz, 1 H), 5.36 (d, ^2J = 5.7 Hz, 1 H), 5.55 (d, ^2J = 5.7 Hz, 1 H), 6.29 (dd, J = 9.3, 2.6 Hz, 1 H), 7.22−7.62 (m, 6 H), 10.0 (bs, 1 H); ^{13}C NMR (125.7 MHz $CDCl_3$) δ 12.58 (CH_3), 32.58 (d, $^1J_{CP}$ = 137.5 Hz), 35.44 (d, $^3J_{CP}$ = 6.9 Hz), 68.56 (d, $^2J_{CP}$ = 9.6 Hz), 73.87 (d, $^3J_{CP}$ = 5.2 Hz), 74.07 (d, $^2J_{CP}$ = 5.0 Hz), 83.50, 112.51, 117.99 (d, $^3J_{CP}$ = 11.9 Hz), 126.28, 128.21, 128.43, 134.49, 137.85 (d, J_{CP} = 11.5 Hz), 139.64 (d, $^2J_{CP}$ = 3.5), 149.75, 162.73; FAB LRMS, m/z 405 (M^+). Anal. Calcd for $C_{19}H_{21}N_2O_6P$: C, 56.47; H, 5.23. Found: C, 56.45; H, 5.19. (Determined on a mixture of isomers, cis/trans = 33/67).

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Supporting Information Available: Procedures for preparation of **8**−**10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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