Diethoxytriphenylphosphorane: A Mild, Regioselective Cyclodehydrating Reagent for Conversion of Diols to Cyclic Ethers. Stereochemistry, Synthetic Utility, and Scope

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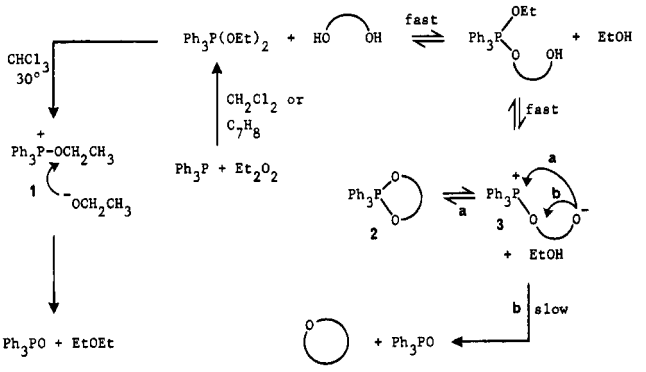
Abstract: Diethoxytriphenylphosphorane, $Ph_3P(OEt)_2$, prepared by reaction of triphenylphosphine and diethyl peroxide, is a "hydrolytically active" dioxyphosphorane which promotes mild cyclodehydration (40–110 °C) of diols to cyclic ethers in neutral media. The regioselectivity in the closure of (*S*)-(+)-propane-1,2-diol and (*R*)-(−)-pentane-1,4-diol with $Ph_3P(OEt)_2$ is high (81–82%) while the cyclodehydration of (*S*)-(+)-phenylethane-1,2-diol gives racemized (±)-styrene oxide. Simple 1,2-, 1,4-, and 1,5-diols afford good yields of the cyclic ethers but 1,3-propanediol and 1,6-hexanediol give mainly 3-ethoxy-1-propanol and 6-ethoxy-1-hexanol, respectively, with $Ph_3P(OEt)_2$. Tri- and tetra-substituted 1,2-diols afford the relatively stable 1,3,2-dioxaphospholanes (or σ-dioxyphosphoranes) in the presence of $Ph_3P(OEt)_2$, and, depending on conditions, the 1,3,2-dioxaphospholanes are selectively converted to epoxides, ketones or allylic alcohols. The carbonyl compounds arise from 1,2-hydride and 1,2-methyl migrations; the allylic alcohols are derived from thermolytic eliminations. *trans*-1,2-Cyclohexanediols afford essentially quantitative yields (>95%) of the cyclohexene oxides while *cis*-1,2-cyclohexanediol gives the stable 1,3,2-dioxaphospholane with $Ph_3P(OEt)_2$ which decomposes under thermal conditions to cyclohexanone (90%). $Ph_3P(OEt)_2$ is extremely useful for conversion of "sensitive" 1,2-diols to acidic and/or thermally labile epoxides as demonstrated by the quantitative conversion of 9,10-dihydro-*trans*-9,10-phenanthrenediol to 9,10-dihydrophenanthrene oxide and 2α,10-pinanediol to 2α,10-epoxypinane.

A wide variety of alkyl and aryl phosphites and phosphines undergo "redox" reactions with compounds possessing weak heteroatom–heteroatom bonds (e.g., O–O,[1] S–O,[2] S–S[3] O–Cl,[4] S–N,[5] etc.) as well as carbon–halogen bonds[6] to afford hydrolytically labile phosphonium salts and σ-heterophosphoranes. These "organophosphorus reagents" including the Mitsunobu reagent[7] have been particularly valuable in promoting substitution and condensation reactions of substances having active hydrogens.[1-7]

Scheme I. Mechanistic Proposal for Cyclodehydration of Diols with $Ph_3P(OEt)_2$



The pioneering work of Denney and co-workers[1a-f] dealing with the preparation and characterization (^1H and ^{31}P NMR) of oxyphosphoranes has laid the ground work for potentially useful synthetic applications of oxyphosphoranes in the synthesis of heterocycles.[1c,e] In fact, Denney et al.[8] have recently demonstrated that pentaethoxyphosphorane [$P(OEt)_5$] is particularly effective in converting 1,4-diols to the respective tetrahydrofurans. The basic structures of pentacoordinate phosphorus compounds[9] and the apicophilicity demands[10] as well as "apical potentials"[11] of various ligands are the current focus of extensive research. However, studies concentrating on the synthetic utility of acyclic σ-oxyphosphoranes have not been as intense nor sustained.[12] Acyclic oxyphosphoranes, particularly diethoxytriphenylphosphorane (DTPP),[13] as cyclodehydrating reagents have remained essentially unexplored. Herein, we describe our efforts

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(5) (a) Mukaiyama, T.; Ueki, M.; Maruyama, H.; Matsueda, R. *J. Am. Chem. Soc.* **1968**, *90*, 4490.

(6) (a) For a recent review, see: Appel, R.; Halstenberg, M. In "Organophosphorus Reagents in Organic Synthesis"; Cadogen, J. I. G., Ed.; Academic Press: New York, 1979; pp 378–424. (b) Slagle, J. D.; Huang, T. T. S.; Franzus, B. *J. Org. Chem.* **1981**, *46*, 3526–3530. (c) Ramos, S.; Rosen, W. *J. Org. Chem.* **1981**, *46*, 3530–3533. (d) Brett, D.; Downie, I. M.; Lee, J. B.; Matough, M. F. S. *Chem. Ind. (London)* **1969**, 1017. (e) Appel, R.; Scholer, H. F. *Chem. Ber.* **1977**, *110*, 2382. (f) Erickson, G. W.; Fry, J. L. *J. Org. Chem.* **1980**, *45*, 970–972. (g) Barry, C. N.; Evans, S. A., Jr. *J. Org. Chem.* **1981**, *46*, 3361–3364. (h) Barry, C.N.; Baumrucker, S. J.; Andrews, R. C.; Evans, S. A.; Jr. *J. Org. Chem.* **1982**, *47*, 3980–3983. (i) Barry, C. N.; Evans, S. A.; Jr. *Tetrahedron Lett.* **1983**, *24*, 661–664. (j) Castro, B.; Selve, C. *Tetrahedron Lett.* **1973**, 4459–4460.

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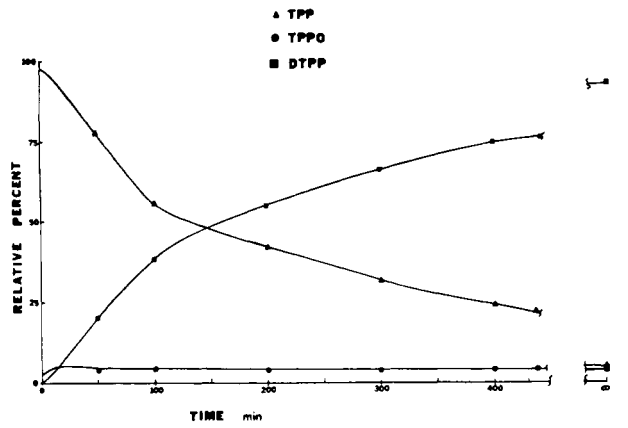


Figure 1. ^{31}P NMR results of triphenylphosphine–diethyl peroxide reaction vs. time.

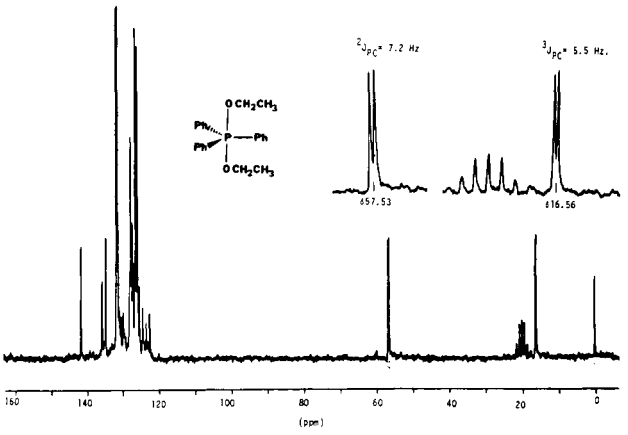


Figure 2. ^{13}C NMR spectrum of DTPP in toluene-d_8 at 25 °C.

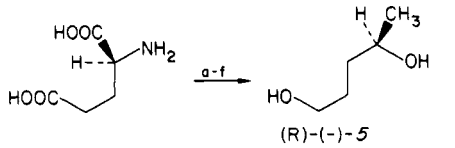
toward establishing the usefulness of DTPP for cyclodehydration of diols to cyclic ethers.

Results and Discussion

DTPP, prepared by a biphilic[1c,14] oxidative addition of triphenylphosphine (TPP) with diethyl peroxide (DEP), is isolable as a viscous oil by "flash distillation" (Kugelrohr apparatus) at 150–160 °C (0.05 torr). By careful monitoring of ^{31}P NMR data for disappearance of TPP and formation of DTPP, it is readily determined that 72% DTPP is formed after 8 h (>92%, 48 h at 70 °C) in toluene solvent (Figure 1). The initially rapid increase in the concentration of triphenylphosphine oxide (TPPO) is due to the fast reaction of TPP with a small quantity of ethyl hydroperoxide impurity. ^1H (see Experimental Section) and ^{31}P (δ −55.0) NMR parameters for DTPP are consistent with the pentacoordinated trigonal-bipyramidal conformer having apical ethoxy groups as previously proposed by Denney.[15] The ^{13}C NMR spectrum of DTPP (Figure 2) is also supportive of the assigned structure. Both geminal and vicinal phosphorus–carbon couplings *within* the ethyl group are observable and may have diagnostic significance (vide infra): $^2J_{POC}$ = 7.2 Hz (CH_2) and $^3J_{POCC}$ = 5.5 Hz (CH_3).

Homogeneous DTPP is stable indefinitely in anhydrous toluene solvent at 25 °C and shows no measurable decomposition even at 90 °C. However, it slowly decomposes in chloroform solvent presumably by irreversible Arbusov collapse of oxyphosphonium ion pair **1** to TPPO and diethyl ether (Scheme I).[16] DTPP also reacts with 1,1,2,2-tetrachloroethane solvent to give 1,1,2-trichloroethene, ethanol, and ethyl chloride.[13b] If a diol is added to DTPP, the rapid exchange of 2 equiv of ethanol by phosphoranylation of the diol commences, followed by equilibration of dioxyphosphorane **2** and oxyphosphonium betaine **3**[1d] (path a). Ultimately, slow formation of the cyclic ether by intramolecular displacement of TPPO from betaine **3** (path b) is achieved.[13b]

Scheme II[a]



[a] (a) $NaNO_2$, H_2SO_4; (b) $SOCl_2$; (c) $NaBH_4$, CH_3OH; (d) *p*-TsCl, pyr; (e) $LiAlH_4$, THF; (f) NaOH, H_2O.

Although DTPP itself is stable in aromatic solvents,[16] the moderate yields obtained (42–61%) and the potential hazards[17] involved in the preparation and isolation of DEP prompted a search for other aliphatic peroxides capable of oxidative addition with phosphines enroute to useful, reactive dioxyphosphoranes. While our findings are the subject of a future publication,[18] we make only a brief comment here on the preparation and relative stability of bis(*n*-hexyloxy)triphenylphosphorane [$Ph_3P(OHex)_2$]. Di-*n*-hexyl peroxide [$(HexO)_2$], prepared by reaction of excess *n*-hexylmethanesulfonate with H_2O_2/KOH, reacts with TPP in toluene solvent (65 °C, 30 h). ^{31}P NMR examination of the reaction mixture indicates >95% $Ph_3P(OHex)_2$ (δ −56.2), 2% TPP (δ −5.6), and >2% TPPO (δ 27.3). The ^{31}P chemical shift of $Ph_3P(OHex)_2$ is consistent with a trigonal-bipyramidal conformation having the thermodynamically preferred apical hexyloxy groups. The geminal and vicinal phosphorus–carbon couplings, observable in the ^{13}C NMR [$^2J_{POC}$ = 7.8 Hz and $^3J_{POCC}$ = 5.5 Hz], are essentially identical with those observed for DTPP. $Ph_3P(OHex)_2$ in toluene solvent at 60 °C remained unchanged after 21 days as determined by ^{31}P NMR. By contrast, *n*-$Bu_3P(OHex)_2$ is apparently less stable than $Ph_3P(OHex)_2$. Holtz et al.[19] report that $(HexO)_2$ reacts with *n*-Bu_3P in dry benzene to afford Hex_2O; in acetone–water–benzene solvent, *n*-hexyl alcohol is formed.

Stereochemistry and Regioselection of the DTPP-Promoted Cyclodehydration of Diols. Regioselective cyclodehydrations of optically active, unsymmetrical diols could have important synthetic consequences by providing preparative routes to optically active ethers. However, information on one-step, regioselective cyclodehydration of optically active diols with oxyphosphoranes,[13] oxyphosphonium salts, or sulfuranes[20] is scarce.

We have prepared (*S*)-(+)-propane-1,2-diol [(+)-**4**, 71%, $[\alpha]^{18}_D$ + 14.20° (neat)][21] by lithium aluminum hydride reduction of (*S*)-(−)-ethyl lactate, (*S*)-(+)-phenylethane-1,2-diol [(+)-**5**, $[\alpha]^{18}_D$ +51.57° (*c* 0.785, benzene)][22] from borane reduction of (*S*)-

(14) (a) Denney, D. B.; Denney, D. Z.; Hall, C. D.; Marsi, K. L. *J. Am. Chem. Soc.* **1972**, *94*, 245–259. (b) Baumstark, A. M.; McCloskey, C. J.; Williams, T. E.; Chrisope, D. R. *J. Org. Chem.* **1980**, *46*, 3593–3597.

(15) (a) Denney, D. B.; Denney, D. Z.; Wilson, L. A. *Tetrahedron Lett.* **1968**, 85–89. (b) Kuboto et al. have similarly assigned the trigonal-bipyramidal conformation with apical CF_3CH_2O groups to $Ph_3P(OCH_3CF_3)_3$ based on ^1H NMR shifts and a ^{31}P NMR shift of −70.3 ppm. See: Kubota, T.; Miyashita, S.; Kitaxume, T.; Ishikawa, N. *J. Org. Chem.* **1980**, *45*, 5052–5057.

(16) DTPP also slowly reacts with $CHCl_3$ and $Cl_2CHCHCl_2$ by proton abstraction initiated by the low equilibrium concentration of ethoxide ion[1d] (e.g., $(CH_3CH_2O)_2PPh_3 \rightleftharpoons CH_3CH_2O^-Ph_3P^+OCH_2CH_3$) to afford ethanol and α- and β-elimination products. Since chloride ion results from the elimination processes, our ^{13}C NMR observations of CH_3CH_2Cl, arising undoubtedly from an Arbusov-type displacement of TPPO from Ph_3P^+OEt by Cl^- lends support to this hypothesis.

(17) (a) Magelli, O. L.; Sheppard, C. S. In "Organic Peroxides"; Swern, D., Ed.; Wiley-Interscience: New York, 1972; Chapter 1, Vol. I, pp 1–104. (b) Shanley, E. S. In "Organic Peroxides", Swern, D., Ed.; Wiley-Interscience: New York, 1972; Chapter 5, Vol. III, pp 341–364.

(18) Unpublished results from Jeffery W. Kelly, University of North Carolina.

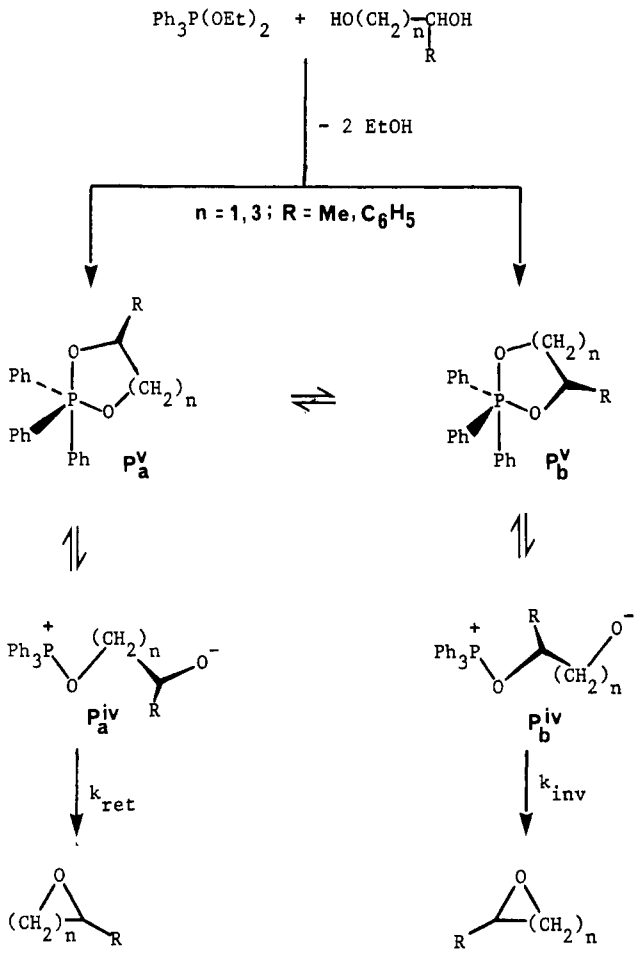
(19) Holtz, H. D.; Solomon, P. W.; Mahan, J. E. *J. Org. Chem.* **1973**, *38*, 3175–3179.

(20) Martin, J. C.; Franz, J. A.; Arhart, R. J. *J. Am. Chem. Soc.* **1974**, *96*, 4604–4611.

(21) (a) Jerina, D. M.; Ziffer, H.; Daly, J. W. *J. Am. Chem. Soc.* **1970**, *92*, 1056. (b) Winstein, S.; Heck, R. *Ibid.* **1952**, *74*, 5584. (c) Combas, J.; Haslinger, E.; Schmidt, V. *Chem. Ber.* **1976**, *109*, 2645.

(22) Fischer, E. *Chem. Ber.* **1912**, *63*, 2447.

Scheme III

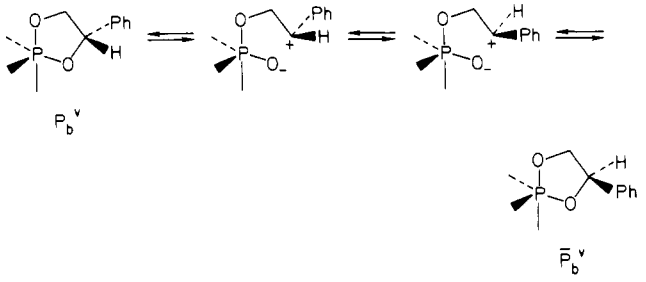


(+)-mandelic acid, and (4*R*)-(−)-pentane-1,4-diol [**6**, 11%, $[\alpha]^{21}_D$ −13.06° (neat)][23] from the series of reactions shown in Scheme II. Their regiochemical modes of cyclodehydration were examined using DTPP. The percent regioselection (82%) from cyclodehydration of (+)-diol **4** to mainly (*S*)-(+)-propylene oxide [(+)-**7**)] indicates predominant retention of configuration at C_2. This result is nearly identical with the results obtained when (+)-**4** undergoes cyclodehydration with TPP–diethyl azodicarboxylate[24] and TPP–CCl_4[25] demonstrating that displacement of the C_1 hydroxyl group (as TPPO) is preferred and that all *three* reactions are intimately related through presumably the same oxyphosphorane–oxyphosphonium intermediates.

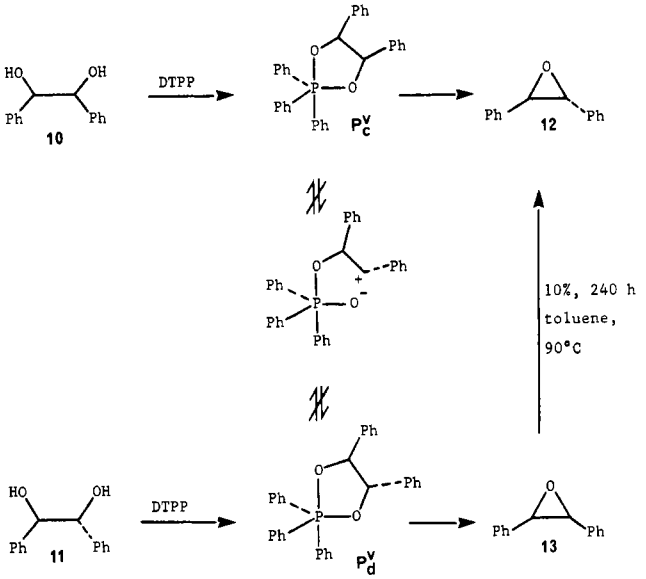
The reaction of (4*R*)-(−)-pentane-1,4-diol with DTPP gives (*R*)-(−)-2-methyltetrahydrofuran (**8**) as the predominant enantiomer reflecting largely retention (80.5%) of stereochemistry of C_2. On the basis of the similarlity in energetic considerations for closure of chains to three- and five- membered rings,[26] the similarity in percent regioselection for cyclodehydration of (+)-**4** and **6** is not too surprising.

These findings suggest that the regioselective distribution of stereoisomeric ethers arises from separate *stepwise* decompositions of oxyphosphonium betaines, P_a^{iv} and P_b^{iv}, with collapse of betaine P_a^{iv} being kinetically preferred because of favorable steric considerations (Scheme III). In fact, reaction of *d,l*-2,3-butanediol (**9**) with DTPP in CD_2Cl_2 (35 °C, 10 h) also demonstrates the stepwise nature of the cyclodehydration process giving exclusively *cis*-2,3-epoxybutane by ^{13}C NMR analysis [δ 12.9 (CH_3) and 52.4 (CHO)].[27] This latter result is consonant with the previous findings of Denney et al.[1b] where 88% *d,l*- and 12% *meso*-4,5-dimethyl-2,2,2-triethoxy-1,3,2-dioxaphospholanes gave 85% *cis*- and 15% *trans*-2,3-butene oxides, respectively, upon thermolysis (117 °C, 42 h).

Scheme IV



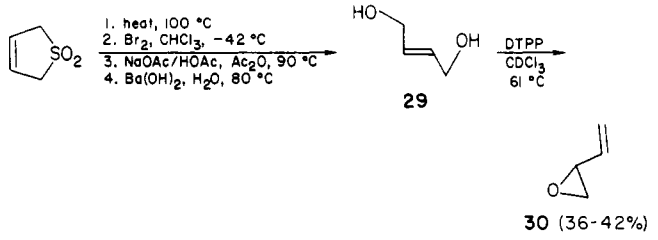
Scheme V



Steric considerations would predict that the percent regioselection should increase as the steric bulk of the attached R group at C_2 increases (Scheme III), and with this in mind, we examined the reaction between (+)-**5** and DTPP. Racemic (±)-styrene oxide was obtained (82%); the enantiomeric composition was assessed from ^1H NMR analysis using the chiral shift reagent Eu(hfc)$_3$.[28] We have prepared[29] and independently demonstrated[30] that (*S*)-(+)-styrene oxide (>95% ee) is configurationally stable under the reaction conditions, and, thus, reaction of optically active epoxide with TPP[31] or TPPO[32] does not occur nor compromise the configurational stability of optically active styrene oxide. We had previously suggested several possibilities for racemization[25] including (a) $k_{ret} = k_{inv}$, (b) formation of $PhC^+HCH_2O^-(H)$ through ionization of TPPO, and (c) ionization *within* the cyclic dioxyphosphorane (Scheme IV). This latter possibility seemed attractive because the propensity for carbon–oxygen ionization would be facilitated by (i) favorable 2p–3d π bonding between

(23) Egushik, C.; Kawata, A. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1704.
(24) Schurig, V.; Koppenhoefer, B.; Buerkle, W. *J. Org. Chem.* **1980**, *45*, 538–541.
(25) Robinson, P. L.; Barry, C. N.; Bass, S. W.; Jarvis, S. E.; Evans, S. A., Jr. *J. Org. Chem.* **1983**, *48*, 5396–5398.
(26) Stirling, C. J. M. *J. Chem. Educ.* **1973**, *50*, 844–845.
(27) A concerted decomposition pathway for phosphoranes is, in fact, symmetry allowed for some equatorial–equatorial or apical–apical substitutents, but numerous, if not all, phosphoranes with alkoxy substitutents prefer the stepwise route. See: Emsley, J.; Hall, D. "The Chemistry of Phosphorus"; Wiley: New York, 1976.
(28) Tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III) was obtained from the Aldrich Chemical Co.
(29) Dupin, E.; Dupin, J. F. *Bull. Soc. Chim. Fr.* **1970**, *249*–251.
(30) A control experiment using a sample of (*S*)-(+)-styrene oxide (>95% ee)[29] in CH_2Cl_2 solution containing TPP, ethanol, and TPPO was refluxed for 48 h at 40–45 °C. Isolation of the styrene oxide followed by ^1H NMR examination using Eu(hfc)$_3$ indicated no racemization.
(31) Richards, E. J.; Tebby, J. C. *J. Chem. Soc.* **1971**, 1059.
(32) Bissing, D. E.; Speziale, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 1405–1406.

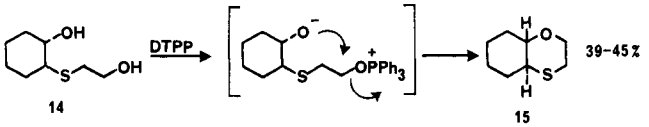
Scheme VI



the equatorial phosphoryl oxygen and the phosphorus atom in the trigonal-bipyramidal conformer[33] and (ii) the potential for stabilization of the incipient carbocation by the phenyl group. Certainly, extensive rotational freedom of the carbocation would racemize dioxyphosphorane P_b^v ($P_b^v \rightleftharpoons \bar{P}_b^v$), and through pseudorotation, the conformational isomeric phosphorane P_a^v would also be racemized; therefore, the requisite oxyphosphonium betaines P_a^{IV} and P_b^{IV} (R = Ph, Scheme III) would be without stereochemical integrity as would the final product, styrene oxide. Assuming the existence of an electron-deficient species is required to adequately rationalize formation of (±)-styrene oxide, it is conceivable that under similar conditions an analogous intermediate may permit facile equilibration of the *cis*- and *trans*-1,3,2-dioxaphospholanes (P_c^v and P_d^v, Scheme V) resulting from condensation of DTPP with either *meso*- or *d,l*-1,2-diphenylethane-1,2-diol (**10**, **11**). In principle, if equilibration of the diastereomeric 1,3,2-dioxaphospholanes is considerably faster than formation of configurationally stable epoxides, the extent of diastereoselection of epoxides starting from either diol should be essentially identical.[34] The benzylic positions in both dioxaphospholanes will benefit from resonance stabilization. An examination of molecular models also suggest that dioxaphospholane P_c^v may possess an inherent driving force for cleavage of the PO–CHPh bond as a way of relaxing the repulsive steric interactions between the *cis*-1,2-phenyls and the *syn*-phenyl group attached to the phosphorus atom.

The actual results of the experiment show that DTPP-promoted cyclodehydrations of *meso* diol **10** and *d,l* diol **11** are, in fact, *stereospecific*, affording *trans*- and *cis*-stilbene oxides (**12** and **13**), respectively. For example, a solution containing 84% *d,l*- and 16% *meso*-1,2-diphenylethanediols was refluxed with DTPP in CH_2Cl_2 until the combined yield of **12** and **13** was greater than 95% (ca. 3 weeks). ^1H NMR analysis showed the epoxide composition as 76% *cis*-stilbene oxide and 24% **12**. Similarly when a solution containing 15% *d,l*- and 85% *meso*-1,2-diphenylethanediols was reacted with DTPP in toluene at 90 °C (ca. 1 week), the epoxide composition was found to be 5% *cis*- and 95% *trans*-stilbene oxide. [An independent experiment also demonstrated that on prolonged heating of the *cis*-epoxide **13** (10 days, 90 °C in toluene), ca. 10% isomerization to *trans*-epoxide **12** occurred.] Homogeneous meso diol **10** reacts with DTPP in dry toluene (100 °C, 18 h) to afford >95% *trans*-oxide **12** by ^1H NMR analysis.[35] These results corroborate the findings of Boigegrain and Castro[36a] as well as those of Bartlett et al.[36b] and cast doubt on the importance of proposals b and c. Kinetic studies currently under way on the cyclodehydration of para-substituted phenylethane-1,2-diols will, perhaps, provide useful results to help solve this problem.

Cyclodehydration of Diols with DTPP. Synthetic Utility. The reaction of *trans*-2-[(2-hydroxyethyl)thio]cyclohexanol (**14**) with DTPP gives 39–45% of *trans*-1,4-oxathiadecalin (**15**) by GLC



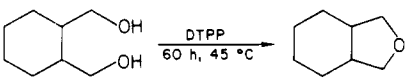
indicating that formation of oxathiadecalin **15** arises from initial phosphoranylation of the more sterically accessible 2-hydroxyethyl group followed by intramolecular displacement of TPPO by the C_1 alkoxide group. The reaction of diol **14** with TPP–CCl_4 also regioselectively phosphoranylates the 2-hydroxyethyl group but intramolecular cyclization only affords 6–13% oxathiadecalin **15** depending on the ratio of TPP to diol **14**.[6h] The major product of the TPP–CCl_4-mediated reaction is *trans*-2-[(2-chloroethyl)-thio]cyclohexanol.[6h]

We have systematically examined the facility with which DTPP promotes the cyclodehydration of simple diols to cyclic ethers. For example, 1,3-propanediol (**16**) reacts with DTPP in CH_2Cl_2 (45 °C) to give <3% oxetane and mainly 3-ethoxy-1-propanol (>97%) by GLC. These results indicate that while phosphoranylation of the hydroxyl group does occur, subsequent closure to the four-membered oxetane is thermodynamically disfavored relative to either ethoxide or 3-hydroxy-1-propoxide displacement of TPPO. These results are in direct contrast with the reports of Carlock and Mack[37] where it is indicated that reaction between TPP–diethyl azodicarboxylate and diol **16** afford near quantitative yield (98%) of oxetane.

While diol **16** resists cyclodehydration with DTPP, 2-ethyl-2-phenyl-1,3-propanediol (**17**) is readily converted to 3-ethyl-3-phenyloxetane (**18**) in 78%. Castro and Selve[6j] also indicate that diol **17** can be converted to oxetane **18** (60%) by initial phosphorylation with $P(NMe_2)_3$–CCl_4 followed by sodium methoxide initiated cyclization. Apparently, the geminal dialkyl effect (i.e., Thorpe–Ingold effect[38]) is responsible for the high efficiency of cyclodehydration evidenced here.

1,4-Butanediol (**19**) and 1,5-pentanediol (**20**) are smoothly converted to tetrahdyrofuran (85%) and tetrahydropyran (72%), respectively, with DTPP;[39] however, reaction of DTPP with 1,6-hexanediol (**21**) affords, as expected, essentially no oxepane (<6%) but mainly 6-ethoxy-1-hexanol (50%)[40] and starting diol **21** (44%) by GLC and ^{13}C NMR.

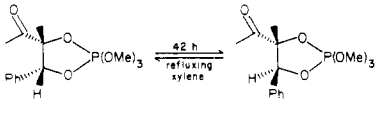
The reaction of *cis*-1,2-bis(hydroxymethyl)cyclohexane (**22**) with DTPP (60 h, 45 °C, CH_2Cl_2) gives 76% *cis*-8-oxabicyclo-[4.3.0]nonane (**23**)[41] which is similar to the result obtained when TPP–CCl_4 is used as a cyclodehydrating agent.[6g]



Attempted cyclodehydration of *cis*-(2-hydroxymethyl)cyclohexanol (**24**) with DTPP actually affords *cis*-2-[(ethyloxy)-

(33) Some oxyphosphoranes possessing equatorial PO^- groups may be "conformationally demanding" due to the strong p–d π interactions between oxygen and phosphorus. See: Luckenbach, R. "Dynamic Stereochemistry of Pentacoordinated Phosphorus and Related Elements"; Georg Thieme: Stuttgart, Germany, 1973.

(34) Ramirez et al. have also observed equilibration of diastereoisomeric 1,3,2-oxaphosphoanes, i and ii, in refluxing xylene solvent. Interestingly, they



i ii

suggest that isomerization may result from dissociation of the oxaphospholanes to the original reactants followed by recombination. See: Ramirez, F.; Bhatia, S. B.; Patwardhan, A. V.; Smith, C. P. *J. Org. Chem.* **1967**, *32*, 3547–3553.

(35) It is noteworthy that $Ph_3P(OHex)_2$ also stereospecifically converts meso diol **10** to epoxide **12** in 80% yield after 72 h in toluene solvent (65 °C).

(36) (a) Boigegrain, R.; Castro, B. *Tetrahedron* **1976**, *32*, 1283–1288. (b) Bartlett, P. D.; Landis, M. E.; Shapiro, M. J. *J. Org. Chem.* **1977**, *42*, 1661–1662.

(37) Carlock, J. T.; Mack, M. P. *Tetrahedron Lett.* **1978**, 5153.

(38) Searles, S.; Nickerson, R. G. Witsiepe, W. K. *J. Org. Chem.* **1959**, *24*, 1839.

(39) These results are consistent with the previous findings of Chang et al.[1c] where 1,4-butanediol reacts with $P(OEt)_5$ to give tetrahydrofuran (87%) and 1,5-pentanediol reacts with DTPP to afford tetrahydrofuran (81%).

(40) Diol **15** was treated with 1 equiv of NaH in THF (25 °C, 24 h); the suspension was treated with EtI in THF (60 °C, 48 h) to afford 65% of 6-ethoxy-1-hexanol by GLC analysis.

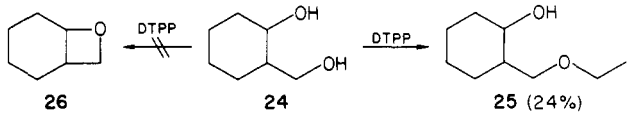
(41) Gillis, B. T.; Beck, P. E. *J. Org. Chem.* **1963**, *28*, 1388.

Table I. Cyclodehydration of Optically Active Diols with DTPP in Dichloromethane Solvent at 40–50 °C[a]

diol	ether (%)	% ret[b,c]
(*S*)-(+)-propane-1,2-diol [(+)-**4**]	2-methyloxirane (85)	81.7
(*S*)-(+)-phenylethane-1,2-diol [(+)-**5**]	2-phenyloxirane (82)	50
(*R*)-(−)-pentane-1,4-diol (**6**)	2-methyloxolane (82)	80.5

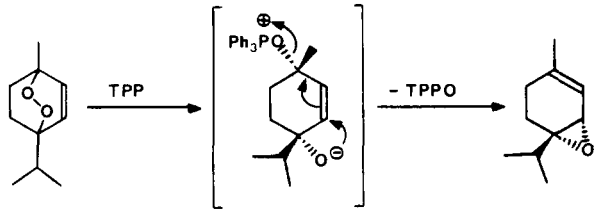
[a] The values for percent retention (% ret) reported here are determined by chiral shift reagent studies (vide infra). Our previous[13] preliminary results were based on optical rotations and are in error. An authentic sample of (*S*)-(+)-2-methyloxirane was prepared by a known method. A homogeneous sample of 2-methyloxolane was isolated by preparative GLC and its rotation was negative indicating predominant retention of stereochemistry. [b] Percent retention (% ret) equals percent regioselectivity. [c] Determined by ^{1}H NMR analysis of the enantiomeric mixture of cyclic ethers using added chiral shift reagent Eu(hfc)$_3$.

methyl]cyclohexanol (**25**, 24%) instead of *cis*-7-oxabicyclo-[4.2.0]octane (**26**), in keeping with the severe energetic requirements and high activation energy anticipated during formation of simple oxetanes (vide supra).[38]



26 **24** **25** (24%)

Generally, the cyclodehydration of (*Z*)-2-butene-1,4-diol (**27**) to 2,5-dihydrofuran (**28**), depending on the choice of catalyst,[42] is complicated by rearrangement to crotonaldehyde and gives variable yields (35–75%). Reaction of diol **27** with DTPP affords 2,5-dihydrofuran in excellent yield (95% by GLC; 57–70% isolated). The geometric constraints imposed by the C=C bond in diol **27** (compared to 1,4-butanediol) encourage favorable promixity for cyclodehydration. On the other hand, treatment of the diastereoisomeric (*E*)-2-butene-1,4-diol (**29**), prepared by the sequence of reactions shown in Scheme VI,[43] with DTPP in $CDCl_3$ (61 °C, 18 h) gives a distilled (70 °C) material (35–42%) whose ^{1}H NMR spectrum is completely superimposable on the ^{1}H NMR spectrum of an authentic sample of 3,4-epoxy-1-butene (**30**). Although gratifying, this finding is not totally unexpected since ascaridole (**31**), when treated with TPP, apparently affords a zwitterionic intermediate which decomposes to the unsaturated epoxide **32**.[44] These latter results are, of course, consonant with



31 **32**

the ring closure predictions of Baldwin[45] where the "3-exo-trig" cyclization is predicted to be favored.

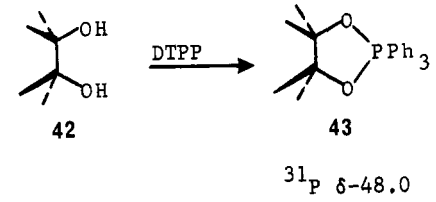
The yields of epoxides from the cyclodehydration of 1,2-diols promoted by DTPP are generally high in refluxing CH_2Cl_2 (Table II). For example, 1,2-propanediol (**4**) reacts with DTPP to afford 83% propylene oxide (**7**) while 1-phenylethane-1,2-diol (**5**) and decane-1,2-diol (**33**) both give near quantitative yield (>99%) of styrene oxide and 1,2-epoxydecane, respectively.

Other monosubstituted diols having primary and secondary hydroxyl groups react with DTPP. 4-Methyl-1,2-pentanediol (**34**) gives 83% 4-methyl-1,2-epoxypentane (**35**) after 72 h reflux and 3-phenyl-1,2-propanediol (**36**) reacts with DTPP to give >99% 3-phenyl-1,2-epoxypropane (**37**).

2,2-Disubstituted-1,2-diols also give good-to-excellent yields of epoxides. 2-Methyl-1,2-pentanediol (**38**) reacts with DTPP to afford 66% 2-methyl-1,2-epoxypentane (**39**) after 116 h in refluxing CH_2Cl_2. We have also prepared acid-sensitive 2α,10-epoxypinane (**40**)[46] in >99% (^{1}H and ^{13}C NMR and GLC analyses) from the cyclodehydration of 2α,10-pinanediol (**41**)[47] with DTPP (40 °C, CH_2Cl_2, 68 h).

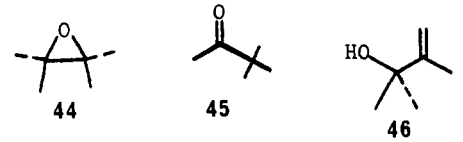
The reactions of tri- and tetra-substituted 1,2-diols with DTPP afford stable 1,3,2-dioxaphospholanes which selectively decompose to epoxides, ketones, or allylic alochols depending on the reaction conditions. For example 2,3-dimethylbutane-2,3-diol (pinacol, **42**) reacts with DTPP in C_6D_6 (60 °C, 24 h) to afford σ-phosphorane **43** conveniently identified by ^{31}P NMR analysis (δ −48.0). Vacuum thermolysis (200 °C, 15 torr) of σ-dioxyphosphorane **43** gives a 2:2:1 ratio of 2,3-dimethyl-2,3-epoxybutane (**44**), 3,3-dimethylbutanone **45**, and 3-hydroxy-2,3-dimethyl-1-butene **46**, respectively (Scheme VII). Decomposition of the oxyphosphorane **43** by heating in toluene (110 °C, 24 h) selectively affords allylic alcohol **46** (60%) and the oxirane **44** (10%). Amberlyst-15, a beaded polystyrene sulfonic acid,[48] initiates the rearrangement of oxyphosphorane **43** (65 °C, 24 h) characterized by a 1,2-methyl

Scheme VII



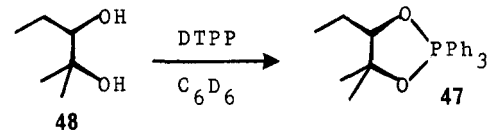
42 **43**

^{31}P δ-48.0



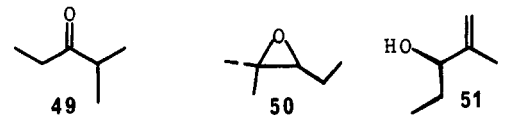
44 **45** **46**

Scheme VIII



48 **47**

^{31}P δ-48.3



49 **50** **51**

(42) (a) Paul, R.; Fluchaire, M.; Collardeau, G. *Bull. Soc. Chim. Fr.* **1950**, 668. (b) Anhydrous hydrobromic acid: Weinheimer, A. J.; Kantor, S. W.; Hauser, C. R. *J. Org. Chem.* **1953**, *18*, 801. (c) Alcoa "Activated Alumina H-41" and iodine: Brace, N. O. *J. Am. Chem. Soc.* **1955**, *77*, 4157.

(43) (a) Monson, R. S. "Advanced Organic Synthesis"; Academic Press: New York, 1971; p 72. (b) V'yunova, N. S. *Bull Acad. Sic. USSR, Div. Chem. Sic.* (*Engl. transl.*) **1964**, 528.

(44) (a) Pierson, G. O.; Runquist, O. S. *J. Org. Chem.* **1969**, *34*, 3654. (b) Herz, W.; Ligon, R. C.; Kanno, H.; Schuller, W. H.; Lawrence, R. V. *J. Org. Chem.* **1970**, *35*, 3338.

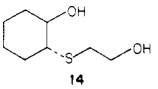
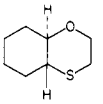
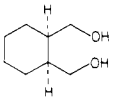
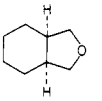
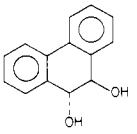
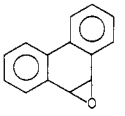
(45) Baldwin, J. E. *J. Chem. Soc. Chem. Commun.* **1976**, 734.

(46) (a) Blackett, B. N.; Coxon, J. M.; Hartshorn, M. P.; Jackson, B. L. J.; Muir, C. N. *Tetrahedron* **1969**, *25*, 1479. (b) Coxon, J. M.; Dansted, E.; Hartshorn, M. P.; Richards, K. E. *Tetrahedron* **1969**, *25*, 3307–3312.

(47) Coxon, J. M.; Dansted, E.; Hartshorn, M. P.; Richards, K. E. *Tetrahedron* **1968**, *24*, 1193–1197.

(48) Polystyrenesulfonic acid is available in bead form from Rohm & Haas Co.

Table II. Summary of the Cyclodehydration of Diols with $Ph_3P(OEt)_2$

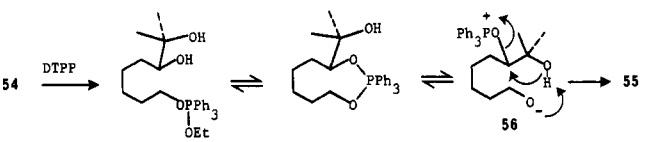
diol	ether (yield, %)
1,2-propanediol (**4**)	1,2-epoxypropane (**7**) (83)
1-phenyl-1,2-ethanediol (**5**)	1,2-epoxyethylbenzene (82–99)
(4*R*)-(−)-1,4-pentanediol (**6**)	(*R*)-(−)-2-methyltetrahydrofuran (**8**) (82)
d,l-2,3-butanediol (**9**)	*cis*-2,3-epoxybutane
84% *d,l*- (**11**) and 14% *meso*-1,2-diphenylethanediol (**10**)	76% *cis*- (**13**) and 24% *trans*-stilbene oxide (**12**) in 95% combined yield
 14	 15 (39-45)
1,3-propanediol (**16**)	oxetane (<3)
1-ethyl-2-phenyl-1,3-propanediol (**17**)	3-ethyl-3-phenyloxetane (**18**) (78)
1,4-butanediol (**19**)	tetrahydrofuran (85)
1,5-pentanediol (**20**)	tetrahydropyran (72)
1,6-hexanediol (**21**)	oxepane (<6)
 22	 23 (76)
(*Z*)-2-butene-1,4-diol (**27**)	2,5-dihydrofuran (**28**) (95)
(*E*)-2-butene-1,4-diol (**29**)	3,4-epoxy-1-butene (**30**) (35–42)
1,2-decanediol (**33**)	1,2-epoxydecane (99)
4-methyl-1,2-pentanediol (**34**)	4-methyl-1,2-epoxypentane (**35**) (83)
3-phenyl-1,2-propanediol (**36**)	3-phenyl-1,2-epoxypropane (**37**) (99)
2-methyl-1,2-pentanediol (**38**)	2-methyl-1,2-epoxypentane (**39**) (66)
 41	 40 (99)
3,7-dimethyl-1,6,7-octanetriol (**54**)	3,7-dimethyl-6,7-epoxyoctan-1-ol (**55**) (85%)
trans-1,2-cyclohexanediol (**57**)	cyclohexene oxide (**59**) (99)
1-methyl-*trans*-1,2-cyclohexanediol (**58**)	1-methylcyclohexene oxide (**60**) (99)
cis-1,2-cyclohexanediol (**61**)	cyclohexanone (**63**) (90)
 66	 65 (99)

migration to 3,3-dimethylbutanone **45** as the only product. Lithium bromide, on the other hand, reacts with oxyphosphorane **43** affording a 1:1 mixture of ketone **45** and epoxide **44**. Finally, if oxyphosphorane **43** is allowed to stand in $CDCl_3$ at ambient temperature for 10 days, a 90% yield of epoxide **44** is realized.

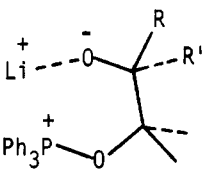
The product trends as a function of reaction conditions are nearly identical for σ-dioxyphosphorane **47** (^{31}P NMR δ −48.3), obtained from DTPP and 2-methylpentane-2,3-diol (**48**), with the exception of LiBr. At 60 °C for 3 days, LiBr reacts with phosphorane **47** in C_6D_6 to afford only the rearranged product 2-methyl-3-pentanone **49**. Phosphorane **47** decomposes (i) in $CDCl_3$ solvent at 60 °C to afford 2-methyl-2,3-epoxypentane (**50**, 60% after 3 days), (ii) in toluene solvent at 110 °C to give 3-hydroxy-2-methyl-1-pentene (**51**, 31% after 24 h), and (iii) in the presence of Amberlyst-15 to afford >95% ketone **49**.

The allylic alcohols **46** and **51** are probably formed by an intramolecular proton abstraction within the appropriate betaine followed by elimination of TPPO. It is expected that the sulfonic acid[49] will initiate Wagner–Meerwein rearrangement of phosphoranes **43** and **47** or epoxides **44** and **50**. We have independently demonstrated that LiBr[50] does not promote rearrangement of an authentic sample of either epoxide **44** or **50** when reaction conditions are simulated. Thus, it seems reasonable to conclude that

Scheme IX



Li^+ initiates hydride or methyl migration by complexation with the apical phosphoryl oxygen atom in phosphoranes **43** and **47** or the respective betaines (e.g., **52** and **53**).



52 (R=R'=Me)

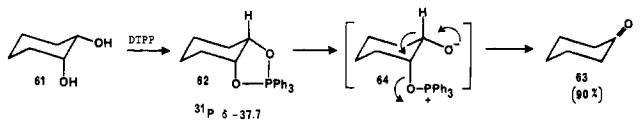
53 (R=H, R'=Et)

3,7-Dimethyl-1,6,7-octanetriol (**54**) reacts with DTPP to afford 85% 3,7-dimethyl-6,7-epoxyoctan-1-ol (**55**) and only 15% of a three-component unidentifiable mixture (GLC). The relatively high yield of epoxide **55** obtained from this reaction is a bit surprising in light of the results for the cyclodehydration of structurally similar diol **48**. It seems evident that the primary hydroxyl group must facilitate formation of the requisite oxy-

(49) The pK_a's of most sulfonic acids lie in the range 1.20 to −1.79. See: Albert, A.; Sergeant, E. P. "The Determination of Ionization Constants"; Chapman and Hall: London, 1984; A Laboratory Manual pp 144–146.

(50) (a) Rickborn, B.; Gerkin, R. M. *J. Am. Chem. Soc.* **1968**, *90*, 4193–4194. (b) Rickborn, B.; Gerkin, R. M. *Ibid.* **1971**, *93*, 1693–1700.

Scheme X



phosphonium betaine. That is, phosphoranylation of the $-CH_2OH$ should be kinetically favorable, followed by rapid intramolecular exchange of Ph_3P to give the appropriate betaine **56** (Scheme VIII), which could undergo cyclodehydration to the observed epoxide. Thus, the intramolecular incorporation of Ph_3P and subsequent activation of the secondary hydroxyl group may account for the relative ease of cyclodehdyration of **54** compared to **48**.

trans-1,2-Cyclohexanediol (**57**) and 1-methyl-*trans*-1,2-cyclohexanediol (**58**) react smoothly with DTPP to afford essentially quantitative yields (>98%) of the corresponding epoxides **59** and **60**. On the other hand, *cis*-1,2-cyclohexanediol (**61**) under identical reaction conditions gives initially σ-dioxyphosphorane **62** (^{31}P NMR δ −37.7), which is decomposed under vacuum thermolysis conditions (180 °C, 10 torr) to cyclohexanone (**63**, 90%). This result is consistent with an interpretation involving formation of betaine **64** with subsequent loss of TPPO via a 1,2-hydride shift (Scheme IX). This result also parallels the findings of Denney et al.[1c] where the reaction of diol **61** with $P(OEt)_5$ also gives a σ-dioxyphosphorane and eventually ketone **63** during thermolysis.

Despite their immense biological significance, only a few synthetic routes to arene oxides are currently available.[51] As a demonstration of the potential synthetic utility of DTPP as a mild cyclodehydrating reagent for conversion of "sensitive" 1,2-diols to reactive epoxides[52] in neutral media, we have prepared 9,10-epoxy-9,10-dihydrophenanthrene (**65**)[53] (>99% by ^1H and ^{13}C NMR) by cyclodeydration of 9,10-dihydro-*trans*-9,10-phenanthrenediol (**66**)[58] with DTPP (CH_2Cl_2–CH_3CN, 1:1, 40 °C, 48 h).

As a final note, DTPP can now be prepared as a 1.0 M solution in toluene and stored under N_2 indefinitely (see Experimental Section). The utilization of this standard solution of DTPP shortens the reaction times considerably. Phenylethane-1,2-diol (racemic **5e**, *cis*-1,2-bis(hydroxymethyl)cyclohexane (**22**), and 1,5-pentanediol (**20**) are converted to the corresponding cyclic ethers in ≥90% yield in ≤24 h (70 °C).

Conclusions

The DTPP-promoted cyclodehydration of diols to cyclic ethers has several unique advantages over existing synthetic methods: (a) the "active" phosphorane is isolable, easy to prepare, and stable in nonprotic anhydrous solvents; (b) reaction conditions are mild (40–100 °C) and effectively *neutral*; (c) regioselectivity in the closure of unsymmetrical diols to cyclic ethers is relatively high; (d) the isolation of the product(s) from triphenylphosphine oxide is conveniently accomplished by distillation or "rapid" column chromatography.

Experimental Section

Several simple diols and their corresponding cyclic ethers are commercially available from Aldrich Chemical Co. *trans*-2-[(2-Hydroxyethyl)thio]cyclohexanol,[6h] *trans*-1,4-oxathiadecalin,[60] 1,2-decanediol,[4c] 1,2-epoxydecane,[4c] 4-methylpentane-1,2-diol,[4c] and 4-methyl-1,2-epoxypentane[4c] have previously been reported. 2,5-Dihydrofuran was obtained from the iodine-catalyzed cyclodehydration of (*Z*)-2-butene-1,4-diol.[42c] *cis*-Hexahydrophthalyl alcohol was prepared in the following manner: cyclohexanecarboxylic anhydride was converted to the diethyl ester,[61] followed by reduction to the *cis*-diol (mp 42–43 °C) with $LiAlH_4$.[62] *cis*-Hexahydrophthalan was prepared by heating *cis*-hexahydrophthalyl alcohol at 159–161 °C for 14 h in Me_2SO.[41]

General Procedure for the Cyclodehydration Reaction with DTPP. The identity and yields of the various product components of the cyclodehydration reactions were determined using ^1H, ^{13}C, and ^{31}P NMR and GLC analyses. Comparison of the NMR spectra and GLC retention times of the various components of the reactions with authentic samples of the reactants and products secured the structural assignments. All the cyclodehydrations were performed in essentially the same manner with some minor variations in reaction time and solvent; the procedures described for the conversion of 1,2-propanediol to propylene oxide should be considered illustrative for the cyclodehydration reactions involving "in situ" generation of DTPP. The reaction times can be decreased if one uses a standard 1.0 M solution of DTPP in toluene. The procedure described for the conversion of phenylethane-1,2-diol to styrene oxide should be considered as representative. The summary of the experimental results is presented in Table II.

Propylene Oxide (**7**). Diethyl peroxide (0.99 g, 0.011 mol) in dichloromethane solvent (5 mL) was mixed with TPP (2.88 g, 0.011 mol) and the resulting solution was refluxed (42 °C) for 0.5 h. A solution of 1,2-propanediol (761 mg, 10 mmol) in 7 mL of dry CH_2Cl_2 was added and the resulting solution was refluxed for 90 h. The reaction progress was monitored by GLC analyses and after ca. 90 h; 82% propylene oxide was realized.

Styrene Oxide. The standard solution of DTPP (3.1 mL, 1.0 M in toluene, 3.1 mmol) was added to a 10-mm NMR tube containing phenylethane-1,2-diol (314 mg, 3.0 mmol) via syringe. To this was added C_6D_6 (1 mL, NMR lock solvent) and the mixture cooled to −78 °C, sealed under vacuum, and then slowly warmed to 70 °C for 24 h. ^{13}C NMR indicates formation of styrene oxide (>90%).

Reaction of Diethyl Peroxide and TPP. Diethyl peroxide (0.99 g, 0.011 mol) was added to triphenylphosphine (2.88 g, 0.011 mol) in dry toluene (5 mL) and the mixture was kept at 75 °C for 48 h. ^{31}P NMR analysis (C_6D_6) showed >92% conversion to the dioxyphosphorane (δ −55.0);[1a] for ^{13}C NMR (C_6D_6) analysis see Figure 2. Reduced-pressure distillation [Kugelrohr apparatus, 150–160 °C (0.1 torr)] afforded diethoxytriphenylphosphorane as a viscous oil in >92% purity: ^1H NMR ($CDCl_3$) δ 0.75 (t, 6 H, J = 7 Hz, CH_3), 2.56 (p, 4 H, $^3J_{HCCH} = {}^3J_{POCH}$ = 7 Hz, CH_2), 7.24–7.54 (m, 15 H, meta and para phenyl CH's), 7.90–8.24 (*m*, 6 H, ortho phenyl CH's). This material can be stored for several months in toluene solvent (N_2), but will slowly decompose in chloroform solvent.

Preparation of ≈1.0 M DTPP. Diethyl peroxide (27 g, 0.30 mol) was added to triphenylphosphine (78.6 g, 0.3 mol) dissolved in toluene (195

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mL) at 0 °C under N_2. The mixture was then heated at 70 °C for 48 h to form DTPP. The final concentration of the standard solution was determined from the initial amount of triphenylphosphine and the total volume of toluene solution. The composition of the solution was ascertained by an inversed gated decoupling ^{31}P NMR experiment.

Diethyl Peroxide. Diethyl sulfate (308 g, 2 0 mol) and hydrogen peroxide (240 mL, 30% solution, 2.11 mol) were mixed at 10 °C (ice bath) in a three-neck, 1-L round-bottom flask equipped with overhead stirrer, dropping funnel, and condenser. Potassium hydroxide (112 g, 2.0 mol) in 100 mL of water was added dropwise (1.5 h) while maintaining a 15–20 °C temperature range (ice bath). The solution was allowed to stir for an additional 3 h (20–25 °C) and then overnight at ambient temperature. The organic layer was separated, washed with water (100 mL), and dried ($MgSO_4$). The magnesium sulfate was removed by filtration and while the crude diethyl peroxide *may be* distilled at atmospheric pressure, bp 60–63 °C (lit.[1c] bp 60–64 °C) with considerable care, *distillation at 25–28 °C (50–70 torr) is preferred*! The diethyl peroxide (21–45 g, up to 61%) was stored at −20 °C–over 4 Å molecular sieves. ^1H NMR ($CDCl_3$) δ 1.20 (t, 3 H, J = 6.5 Hz, CH_3), 3.95 (q, 2 H, J = 6.5 Hz, CH_2); ^{13}C NMR ($CDCl_3$) δ 13.4 (CH_3), 69.4 (CH_2O).

Reaction of Di-*n*-hexyl Peroxide and TPP. Di-*n*-Hexyl peroxide (500 mg, 2.5 mmol) in dry toluene (5 mL) was added to triphenylphosphine (570 mg, 2.2 mol) and the resulting solution was allowed to stand at 65 °C. ^{13}C and ^{31}P NMR analysis after 30 h indicated ca. 95% bis(*n*-hexyloxy)triphenylphosphorane: ^{31}P NMR (toluene d_8) δ −56.2; ^{13}C NMR (toluene d_8) δ 62.2 (d, $^2J_{POC}$ = 7.8 Hz, CH_2O), 31.4 (d, $^3J_{POCC}$ = 5.5 Hz, CH_2CH_2O), 32.1, 26.3, 23.0 (CH_2)$_3$, 14.2 (CH_3).

Di-*n*-hexyl Peroxide (38% yield) was prepared from the reaction of *n*-hexyl methanesulfonate (54 g, 0.30 mol)[63] with potassium hydroxide (29.4 g, 0.53 mol) and 30% hydrogen peroxide (30 mL): bp 56–58 °C (0.5 torr) [lit.[63] bp 58 °C (0.5 torr)]; ^1H NMR ($CDCl_3$) δ 0.7–1.1 (m, 3 H, CH_3), 1.1–1.7 [m, 8 H, $(CH_2)_4$], 3.95 (t, 2H, CH_2O); ^{13}C NMR ($CDCl_3$) δ 74.2 (OCH_2), 31.7, 27.9, 25.8, 22.6 (CH_2's), 14.0 (CH_3).

***n*-Hexyl methanesulfonate**[64] was prepared (99% yield) from the reaction of 1-hexanol (30.6 g, 0.30 mol), triethylamine (45.5 g, 0.450 mol), and methanesulfonyl chloride (38.2 g, 0.330 mol): ^1H NMR ($CDCl_3$) δ 0.7–1.1 (m, 3 H, CH_3), 1.1–1.7 [m, 8 H, $(CH_2)_4$], 2.95 (s, 3 H, OSO_2CH_3), and 4.18 (t, 2 H, CH_2OMs).

(*S*)-(+)-Propane-1,2-diol [(+)-4]: bp 80–81 °C (10 torr) [lit.[21] bp 82–83 °C (10 torr)]; ^1H NMR ($CDCl_3$) δ 1.13 (d, 3 H, J = 6.5 Hz, CH_3), 3.2–4.0 (m, 3 H, $CHCH_2$), 4.52 (s, 2 H, OH). A sample of this material was purified by preparative GLC: $[\alpha]^{20}_D$ +14.2° (neat) [lit.[21] $[\alpha]^{20}_D$ +16.6° (neat)]. On the basis of rotation this sample has 85.5% ee of (*S*)-(+)-propane-1,2-diol.

(*S*)-(+)-Phenyl-1,2-ethanediol [(+)-5]: mp 65.0–66.0 °C (lit.[22] mp 66 °C); ^1H NMR ($CDCl_3$) δ 2.52 (brs, 2 H, OH), 3.70 (m, 2 H, CH_2OH), 4.84 (dd, 1 H, $CHOH$), 7.36 (s, 5 H, C_6H_5); $[\alpha]^{18}_D$ +51.57° (*c* 0.785, benzene) [lit.[22] (*R*)-(−)-phenyl-1,2-ethanediol, $[\alpha]^{18}_D$ −51.9° (*c* 0.77, benzene)].

(4*R*)-(−)-1,4-Pentanediol [(−)-6]: bp 99–101 °C (3 torr) [lit.[65] bp 95–96 °C (1.5 torr)]; ^1H NMR ($CDCl_3$) δ 1.18 (d, 3 H, J = 6 Hz, CH_3), 1.38–1.58 (m, 4 H, $CH_2CH_2CH_2OH$), 3.61 (t, 2 H, J = 5 Hz, CH_2OH), 3.64–3.96 (m, 1 H, $CHOH$), 4.39 (s, 2 H, OH). A sample of this material was purified by preparative GLC $[\alpha]^{22}_D$ −13.06° (neat) [lit.[66] $[\alpha]^{22}_D$ −13.4° (neat)].

(*S*)-(+)-γ-[(Tosyloxy)methyl]-γ-butyrolactone: mp 85–86 °C (lit.[67] mp 85–86 °C); $[\alpha]^{23}_D$ +46.64° (*c* 1.40, $CHCl_3$) [lit.[67] (*R*)-(−)-γ-[(tosyloxy)methyl]-γ-butyrolactone, $[\alpha]^{23}_D$ −46.3° (*c* 1.33, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 1.47 (s, 3 H, CH_3), 1.68–1.95 (m, 4 H, CH_2CH_2), 4.07–4.25 (m, 2 H, CH_2OTs), 4.56–4.83 (m, 1 H, C_γ-H), 7.37 (d, 2 H, J = 8 Hz, meta H's), and 7.79 (d, 2 H, J = 8 Hz, ortho H's).

(*S*)-(+)-γ-(Hydroxymethyl)-γ-butyrolactone: ^1H NMR ($CDCl_3$) δ 1.94–2.78 (m, 4 H, ring CH_2), 3.42–4.05 (m, 3 H, CH_2OH), 4.49–4.81 (m, 1 H, C_γ-H) [lit.[23] ^1H NMR ($CDCl_3$) δ 1.95–2.75 (4 H, CH_2CH_2), 3.80 (2 H, CH_2OH), 4.63 (1 H, C_γ-H)].

(*S*)-(+)-γ-Butyrolactone-γ-carboxyl chloride: bp 103 °C (2–4 torr) [lit.[23] bp 117.1 °C (4.5 torr)]; ^1H NMR ($CDCl_3$) δ 2.32–2.92 (m, 4 H, ring CH_2), 5.15–5.37 (m, 1 H, CHCOCl).

Control Test Conditions for Racemization of (*S*)-(+)-1-Phenyl-1,2-epoxyethane. (*S*)-(+)-1-Phenyl-1,2-epoxyethane (100 mg), prepared by procedures described by Dupin and Dupin,[29] was admixed with dichloromethane (5 mL), ethanol (100 mg), TPP (100 mg), and TPPO (100 mg). after 48 h at reflux, the volatile materials were removed under reduced pressure (ca. 26–29 °C). *n*-Hexane (100 mL) was added to the residue and stirred for 24 h at ambient temperature. The hexane solution was separated and concentrated to dryness (25 °C). Examination of the recovered (*S*)-(+)-1-phenyl-1,2-epoxyethane using Eu(hfc)$_3$ in a ^1H NMR study revealed no racemization.

(*S*)-(+)-1-Phenyl-1,2-epoxyethane.[29] (*S*)-(+)-Phenylethane-1,2-diol (2.7 g, 0.0196 mol) was allowed to react with *p*-toluenesulfonyl chloride (3.62 g 0.019 mol) in anhydrous pyridine solvent (22 mL) (0–5 °C, 24 h) to afford the tosylate (31%). Treatment of the tosylate (1.79 g, 0.006 mmol) with sodium methoxide (0.324 g, 0.006 mol) in methanol gave (*S*)-(+)-1-phenyl-1,2-epoxyethane. The ^1H NMR spectrum of epoxide was identical with commercial (±)-1-phenyl-1,2-epoxyethane. A chiral shift ^1H NMR study using Eu(hfc)$_3$ indicated that the (*S*)-(+)-epoxide is in >95% ee.

***d,l*-2,3-Butanediol (9).** A sample of commercial 2,3-butanediol (Aldrich Chemical Co.) was separated into the *d,l* and meso isomers by preparative GLC (12-ft column containing Carbowax 20M on Chromosorb W; column temperature = 200 °C; injection port temperature = 250 °C). The fractions were analyzed by ^1H and ^{13}C NMR and gave the following results. *d,l*-2,3-Butanediol: ^1H and NMR ($CDCl_3$) δ 1.15 (d, 6 H, CH_3), 3.5 (7, 2 H, CH), 3.93 (s, 2 H, OH); ^{13}C NMR ($CDCl_3$) δ 19.27 (CH_3) and 72.45 (CH). *meso*-2,3-Butanediol: ^1H NMR ($CDCl_3$) δ 1.14 (d, 6 H, CH_3), 3.7 (m, 2 H, CH), 3.93 (s, 2 H, OH); ^{13}C NMR ($CDCl_3$) δ 16.94 (CH_3), 70.93 (CH).

Reaction of *d,l*-2,3-Butanediol and DTPP. A mixture containing 1.56 mmol each of *d,l*-2,3-butanediol, TPP, and diethyl peroxide in dichloromethane-d_2 solvent was heated in a sealed 5-mm NMR tube (35 °C, 10 h). The sample was analyzed by ^{13}C NMR and absorptions were observed for ethanol [δ 17.9 (CH_3), 57.3 (CH_2)], diethyl ether [δ 17.1 (CH_3), 67.4 (CH_2)], and *d,l*-2,3-butanediol, as well as the carbons for the phenyls in TPP and TPPO. In addition, two absorptions were observed for *cis*-2,3-epoxybutane (δ 12.9 (CH_3), 52.4 (CHO)] but *none* for *trans*-2,3-epoxybutane [δ 17.6 (CH_3), 55.2 (CHO)].[68]

Reaction of *d,l*-1,2-Diphenylethane-1,2-diol with DTPP. Diethyl peroxide (0.495 g, 0.055 mol) in dichloromethane (3 mL) was added to triphenylphosphine (1.44 g, 0.055 mol) and the resulting solution was allowed to reflux for 18 h. A mixture containing 84% *d,l*- and 16% *meso*-1,2-diphenylethane-1,2-diol (1.07 g, 0.050 mol) was added and the mixture was kept at reflux until the combined epoxide yield was >95% (this required 3 weeks). ^1H NMR analysis revealed that the epoxide composition was 76% *cis*-stilbene oxide and 24% *trans*-stilbene oxide indicating that 8% *cis*-stilbene oxide had *isomerized* during the course of the reaction.

Reaction of meso-1,2-Diphenylethane-1,2-diol with DTPP. Diethyl peroxide (0.99 g, 0.011 mol) in dry toluene (5 mL) was added to triphenylphosphine (2.88 g, 0.011 mol) and the resulting solution was kept at 90 °C for 1 h prior to the addition of *meso*-1,2-diphenylethane-1,2-diol (2.14 g, 0.010 mol). The mixture was kept at 100 °C (18 h) and then concentrated (rotary evaporator). ^1H NMR analysis of the residue revealed >95% conversion to *trans*-stilbene oxide.

***d,l*-1,2-Diphenylethane-1,2-diol (11).**[69] Silver acetate (56.8 g, 0.34 mol) was added to *trans*-stilbene (16.3 g, 0.151 mol) in glacial acetic acid (275 mL). To this was added finely ground iodine (40.3 g, 0.158 mol) over 0.5 h. The mixture was stirred vigorously for 45 min, then wet acetic acid (164 mL of HOAc, 6.8 g of H_2O) was added. The mixture was kept at 90–95 °C for 3 h; then sodium chloride (60 g) was added and the mixture was stirred an additional 45 min. It was filtered, washed with warm toluene (275 mL), and concentrated under reduced pressure affording a residue which was dissolved in methanol (180 mL) under N_2. Methanolic KOH (18.5 g of KOH in 135 mL of methanol) was added and the resulting solution was stirred at ambient temperature under N_2 for 36 h. The basic solution was neutralized (10% aqueous HCl) at 0 °C and the mixture was concentrated. The product was extracted with ether (5 × 250 mL), dried ($MgSO_4$), and concentrated (rotary evaporator) to afford 16.21 g (75.6%) of substances identified as 77% *d,l*- and 23% *meso*-hydrobenzoin. Two recrystallization ($CHCl_3$) afforded 84% *d,l*- and 16% *meso*-hydrobenzoin. This material was used without further purification: ^1H NMR ($CDCl_3$) δ 3.00 (brs, 2 H, OH), 4.64 (s, 2 H, $CHOH$), 6.98–7.30 (m, 10 H, Ar CH).

***meso*-1,2-Diphenylethane-1,2-diol (10).**[70] Benzoin (21.2 g, 0.15 mol) in dry ether/THF (200 mL of each) was added dropwise to a suspension of $LiAlH_4$ (5.0 g, 0.13 mol) in ether (100 mL) at 0 °C over 6 h under

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N_2. The mixture was kept at 0 °C for 18 h then at ambient temperature for 5 h. Water (5 mL) was cautiously added followed by phosphoric acid (25% aqueous, 15 g of 85% H_3PO_4 in 38 mL of H_2O). The product was continuously extracted into ether and this solution was separated, dried ($MgSO_4$), and concentrated to give an off-white solid (19.3 g, 90%). ^1H NMR evaluation of the sample indicated that the composition was 85:15 *meso*:*d*,*l*-hydrobenzoin. Two recrystallizations from chloroform afforded *meso*-hydrobenzoin homogeneous by ^1H NMR: ^1H NMR ($CDCl_3$) δ 2.38 (s, 2 H, OH), 4.76 (s, 2 H, C*H*OH), 7.02–7.32 (m, 10 H, Ar CH).

***trans*-2,3-Diphenyloxirane (12)** was prepared (90% yield) from the reaction of *trans*-stilbene (5.0 g, 0.028 mol) with *m*-CPBA (6.0 g, 0.028 mol) in hot chloroform: mp 68–70 °C (lit.[71] 68.6–69.8 °C); ^1H NMR ($CDCl_3$) δ 3.85 (s, 2 H, HCOC), 7.40 (s, 10 H, Ar CH).

***cis*-2,3-Diphenyloxirane (13)** was prepared (65% yield) from the reaction of *cis*-stilbene (4.0 g, 0.022 mol) with *m*-CPBA (4.8 g, 0.022 mol) below 30 °C: ^1H NMR ($CDCl_3$) δ 4.32 (s, 2 H, HCOC), 7.00–7.40 (m, 10 H, Ar CH).

Reaction of Bis(*n*-hexyloxy)triphenylphosphorane with *meso*-1,2-Diphenylethane-1,2-diol. Di-*n*-hexyl peroxide (500 mg, 2.5 mmol) in dry toluene (5 mL) was added to triphenylphosphine (650 mg, 2.5 mmol) and *meso*-1,2-diphenylethane-1,2-diol (480 mg, 2.5 mmol). The resulting solution was then allowed to stand at 65 °C for 72 h. ^1H NMR analysis indicated 80% conversion to *trans*-stilbene oxide with 20% unreacted diol remaining.

3-Phenylpropane-1,2-diol (36) was prepared (38%) from the reaction of allylbenzene (12.27 g, 0.104 mol) with formic acid solution). Basic hydrolysis of the hydroxyl formate and purification by rapid chromatograpy (silica; 50:50 hexanes/ethyl acetate) gave **36**: bp 90–94 °C (0.05 torr) [lit.[72] bp 124 °C (3 torr)]; ^1H NMR ($CDCl_3$) δ 2.68 (d, 2 H, $J_{DC} = J_{EC}$ 7.5 Hz, $C_6H_5CH_2$), 3.00–3.63 (brs, 2 H, OH), 3.39 (q, 1 H, J_{AC} = 7.5, J_{AB} = 11 Hz, CH_AH_BOH), 3.55 (q, 1 H, J_{BC} = 3, J_{AB} = 11 Hz, CH_AH_BOH), 3,84 (octet, 1 H, J_{CB} = 3 , $J_{AC} = J_{CD} = J_{CE}$ = 7.5 Hz, C*H*OH), 7.49–7.11 (*m*, 5 H, Ar CH).

3-Phenyl-1,2-epoxypropane (37) was prepared (45% yield) by the *m*-CPBA epoxidation of allylbenzene: bp 52–55 °C (0.5–1.5 torr) [lit.[73] bp 95 °C (12 torr)]; ^1H NMR ($CDCl_3$) δ 2.52 (q, 1 H, J_{AB} = 5.5, J_{BX} = 3 Hz, CH_AH_BO), 2.82 (d, 1 H, J_{AB} = 5.5, J_{AX} = 0 Hz, CH_AH_BO), 2.73 (d, 1 H, J_{BX} = 4 Hz, $C_6H_5CH_AH_B$), 2.86 (d, 1 H, J_{AX} = 5 Hz, $C_6H_5CH_AH_B$), 3.00–3.24 (m, 1 H, CH), 7.26 (s, 5 H, Ar CH).

2-Methylpentane-1,2-diol (48) was obtained by performic acid oxidation–base hydrolysis of 2-methyl-1-pentane (21.0 g, 0.250 mol) in 18% yield: bp 92–99 °C (25 torr) [lit.[74] bp 167–168 °C (760 torr)]; ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, J = 6 Hz, CH_2CH_3), 1.14 (s, 3 H, CH_3COH), 1.25–1.56 (m, 4 H, CH_2CH_2), 3.40 (s, 2 H, CH_2OH), 3.75 (brs, 2 H, OH); ^{13}C NMR ($CDCl_3$), δ 69.5 (C_1), 73.2 (C_2), 41.4 (C_3), 17.1 (C_4), 14.7 (C_5), 23.1 (C_6).

2-Methyl-1,2-epoxypentane (39). Dimethyl sulfoxide (550 mL) was added to a mixture of sodium hydride (13.2 g, 0.55 mol) and trimethylsulfoxonium iodide (121 g, 0.55 mol) under a nitrogen atmosphere. The mixture was kept at 20 °C with cooling (ice bath) until hydrogen evolution ceased and then stirred at ambient for 0.5 h. To this was added 2-pentanone (64 mL, 52 g, 0.60 mol) and the mixture was stirred at ambient temperature for 0.5 h then at 50 °C for 2h. Water (1.5 L) was added and the product was extracted with dichloromethane (5 × 250 mL). The combined dichloromethane extracts were dried (anhydrous $MgSO_4$), filtered, and concentrated (rotary evaporator), to an oily residue. Distillation (75–130 °C, 760 torr) [lit.[75] bp 111–113 °C (760 torr)] afforded a mixture of dichloromethane (8.3 g) and 2-methyl-1,2-epoxypentane (9.8 g, 15%): ^1H NMR ($CDCl_3$) δ 0.62–1.56 (m, 7 H, $CH_2CH_2CH_3$), 1.20 (s, 3 H, CH_3CO), 2.49 (s, 2 H, CH_2O); ^{13}C NMR ($CDCl_3$) δ 53.5 (C_1), 56.9 (C_2), 39.0 (C_3), 18.7 (C_4), 14.2 (C_5), 20.9 (C_6).

2β,10-Pinanediol (41) was obtained in 7% overall from potassium permanganate oxidation of β-pinene. HPLC facilitated isolation of **41** (silica; 50:50 ethyl acetate/hexanes): mp 84.0–85.5 °C (lit.[47] mp 85.0–86.0 °C).

Reactions of 2,3-Dimethylbutane-2,3-diol (42) with DTPP. (a) Vacuum Thermolysis: Diethyl peroxide (0.99 g, 0.011 mol) in dry C_6D_6 was added to triphenylphosphine (2.88 g, 0.011 mol) and the resulting solution was allowed to refluxed for 24 h. 2,3-Dimethylbutane-2,3-diol (1.18 g, 0.010 mol) was then added and the mixture was refluxed for 1 week. The mixture was then concentrated and thermolyzed using the Kugelrohr apparatus (ca. 200 °C, 15 torr). The distillate was analyzed by ^{13}C NMR and found to contain pinacolone (**45**, 40%), 2,3-dimethyl-2,3-epoxybutane (**44**, 40%), and 2,3-dimethylbut-1-en-3-ol (**46**, 20%).

(b) Chloroform-Promoted Phosphorane Decomposition. Diethyl peroxide (0.99 g, 0.011 mol) in dry C_6D_6 (3 mL) was added to triphenylphosphine (2.88 g, 0.011 mol) and the resulting solution was refluxed for 24 h. 2,3-Dimethylbutane-2,3-diol (1.18 g, 0.010 mol) was added and the resulting mixture was refluxed for 24 h. Crystals of the phosphorane (determined by ^{13}C NMR) formed on cooling; the solvent was removed and $CDCl_3$ (3 mL) was then added and the solution was kept at ambient temperature for 10 days. ^{13}C NMR analysis revealed the presence of 2,3-dimethyl-2,3-epoxybutane (**44**) in 90% yield.

(c) Thermolysis in Hot Toluene. Diethyl peroxide (0.99 g, 0.011 mol) in dry toluene (ca, 8 mL) was added to triphenylphosphine (2.88 g, 0.011 mol) and the resulting solution was kept at 100 °C for 24 h. 2,3-Dimethylbutane-2,3-diol (1.18 g, 0.010 mol) was added and the mixture was kept at 100 °C for 24 h. ^{13}C NMR analysis of the reaction mixture indicated that no phosphorane was left; a 60% yield of 2,3-dimethyl-1-buten-3-ol (**46**) was realized: ^{13}C NMR ($CDCl_3$) δ 152.0 (C_2), 108.4 (C_1), 28.9 (C_4 and C_3-methyl). This material was isolated by rapid chromatography (silica; 50:50 hexanes/ethyl acetate) and its ^1H NMR was identical with the published NMR spectrum.[76] A 10% yield of epoxide **44** was also formed in the thermolysis and 20% of starting diol **42** apparently formed during hydrolysis of the phosphorane.

(d) Reaction with Polystyrenesulfonic Acid and Lithium Bromide. Diethyl peroxide (0.950 g, 0.0104 mol) in dry toluene (8 mL) was added to triphenylphosphine (2.75 g, 0.0104 mol) and the resulting solution was kept at 75 °C for 24 h. 2,3-Dimethylbutane-2,3-diol (1.09 g, 0.0094 mol) in dry toluene (5 mL) was added and the mixture was kept at 60 °C for 24 h. One-half of the mixture was added to dry lithium bromide (ca. 0.5 g) while the other half was added to polystyrenesulfonic acid beads, both were kept at 65 °C for 3 days. ^{13}C NMR analysis of each revealed that reaction with lithium bromide gave a 1:1 mixture of pinacolone (**45**) and the epoxide **44** while the reaction with polystyrenesulfonic acid gave only **45**.

2,3-Dimethylbutane-2,3-diol (42) is available from Aldrich Chemical Co: ^{13}C NMR ($CDCl_3$) δ 74.9 (COH) and 24.8 (CH_3).

2,3-Dimethyl-2,3-epoxybutane (44) was prepared (31% yield) by the *m*-CPBA epoxidation of 2,3-dimethyl-2-butene (5.0 g, 0.059 mol): bp 82–84 °C (760 torr) [lit.[4c] bp 83–93 °C (760 torr)]; ^1H NMR ($CDCl_3$) δ 1.31 (s, 12 H, CH_3); ^{13}C NMR δ 61.9 (CCH_3), 21.1 (CCH_3).

3,3-Dimethyl-2-butanone (45) was available from Aldrich Chemical Co: ^{13}C NMR ($CDCl_3$) δ 210.3 (C=O), 44.0 [$C(CH_3)_3$], 26.4 ($COCH_3$), 24.1 [$C(CH_3)_3$].

Reactions of 2-Methylpentane-2,3-diol with DTPP. Since these reaction conditions are similar to the reactions of DTPP and pinacol, only the results are presented.

(a) Reaction with Chloroform. ^{13}C NMR shows ca. 60% conversion to 2-methyl-2,3-epoxypentane (**50**) in $CDCl_3$ after 3 days at reflux. The other 40% was diol **48** probably from partial hydrolysis of the phosphorane **47**.

(b) Thermolysis in Hot Toluene. ^{13}C NMR indicates 31% 3-methyl-1-penten-3-ol (**51**), 26% 2-methyl-3-pentanone (**49**), and 43% diol **48**.

(c) Reaction with Polystyrenesulfonic Acid and Lithium Bromide. ^{13}C NMR of both reactions show near quantitative (>95%) conversion to 2-methyl-3-pentanone **49**.

2-Methylpentane-2,3-diol (48) was obtained in 23% yield from the performic acid oxidation–base hydrolysis of 2-methyl-2-pentene (8.7 g, 0.104 mol): bp 88–89 °C (25 torr) [lit.[74] bp 184–185 °C (760 torr)]; ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 6 Hz, CH_2CH_2), 1.36 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.2–1.8 (m, 2 H, CH_2CH_3), 2.86 [brs, 1 H, $(CH_3)_2COH$], 3.04 (brd, 1 H, CHO*H*), 3.26–3.36 (m, 1 H, C*H*OH); ^{13}C NMR ($CDCl_3$), δ 80.3 [$(CH_3)_2COH$], 73.3 (CHOH), 26.4, 24.6, 23.2 (C_1, C_4, and C_6), 11.5 (CH_2CH_3).

2-Methyl-2,3-epoxypentane (50) was prepared by *m*-CPBA oxidation of the olefin: bp 28–30 °C (65 torr) [lit.[77] bp 97–98 °C (760 torr)]; ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz, CH_2CH_3), 1.53 (p, 2 H, J = 7 Hz, CH_2), 1.30 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 2.72 (t, 1 H, J = 6 Hz, CH); ^{13}C NMR ($CDCl_3$) δ 65.1 (C_3), 57.6 (C_2), 24.9 (C_1), 22.4 (C_4), 18.5 (C_6), 10.6 (C_5).[69]

Test for Rearrangement of 2,3-Dimethyl-2,3-epoxybutane and 2-Methyl-2,3-epoxypentane. Each epoxide (500 mg, 5 mmol) was added

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to lithium bromide (ca. 500 mg) in dry toluene (3 mL). This mixture was kept at 70 °C for 48 h. ^{13}C NMR analysis of the filtered mixture revealed no reaction.

3,7-Dimethyl-1,6,7-octanetriol (54) was prepared (60% yield) from the reaction of citronellol (16.25 g, 0.104 mol) with formic acid (63 mL, 88%, 1.43 mol) and hydrogen peroxide (30%, 14.5 mL) followed with base hydrolysis: bp 145–150 °C (1.0 torr) [lit.[79] bp 160–161 °C (2 torr)]; ^1H NMR ($CDCl_3$) δ 0.92 (d, 3 H, J = 4.5 Hz, $CHCH_3$), 1.16 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 0.99–1.88 (m, 1 H, CH_2, $CHCH_3$), 2.66–3.44 (brs, 4 H, OH, $CHOH$), 3.68 (t, 2 H, J = 6 Hz, CH_2OH).

3,7-Dimethyl-6,7-epoxyoctan-1-ol (55) was prepared (30% yield) by oxidation of citronellol (5.0 g, 0.032 mol) with *m*-CPBA (6.88 g, 0.032 mol): bp 75 °C (0.05 torr) [lit.[80] bp 104–105 °C (2.5 torr)]; ^1H NMR ($CDCl_3$) δ 0.92 (d, 3 H, J = 5 Hz, $CHCH_3$), 1.25 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.40–1.90 (m, 7 H, CH_2, CH), 2.30–2.85 (m, 2 H, OH, CHO), 3.65 (t, 2 H, J = 6 Hz, CH_2OH).

1-Methylcyclohexane-*trans*-1,2-diol (58) was prepared (40% yield) from the oxidation of 1-methylcyclohexane (10.0 g, 0.104 mol) with formic acid (63 mL, 88%, 1.43 mol) and 30% H_2O_2 (10.0 g, 0.104 mol) followed with base hydrolysis: mp 83–85 °C [lit.[81] mp 83–84 °C]; ^1H NMR ($CDCl_3$) δ 1.20 (s, 3 H, CH_3), 1.22–2.00 (m, 8 H, CH_2), 2.80 (brs, 1 H, CH_3COH), 3.50 (brs, 1 H, $CHOH$).

1-Methylcyclohexene 1,2-oxide (58) was prepared (16% yield) by oxidation of 1-methylcyclohexene (5.0 g, 0.052 mol) with *m*-CPBA (11.18 g, 0.052 mol): bp 52 °C (35 torr) [lit.[82] bp 60–61 °C (40 torr)]; ^{13}C NMR ($CDCl_3$) δ 59.51 (C_1), 57.44 (C_2), 23.96 (C_3)*, 24.83 (CH_3)*, 20.10 (C_4), 19.68 (C_5), 29.93 (C_3). For procedures for assigning the ^{13}C NMR resonances, see ref 83. The asterisk (*) indicates that these assignments may be interchangeable.

9,10-Dihydrophenanthrene-9,10-diol (66) was prepared (19% yield) by reduction of phenanthrenequinone (12 g, 0.058 mol) with $LiAlH_4$ (6 g in 1 L of ether: mp 193–194 °C (lit.[58b] mp 185–190 °C); ^1H NMR ($CDCl_3$) δ 4.47 (brs, 2 H, OH), 5.64 (m, 2 H, $CHOH$), 7.27–7.58 (m, 4 H, Ar CH), 7.76 (dd, 2 H, J = 2.8 Hz, Ar CH), 7.79 (dd, 2 H, J = 2, 8 Hz, Ar CH); ^{13}C NMR ($CDCl_3$) δ 72.37 (CHOH), 123.39, 126.45, 127.95, 132.36, 138.19.

9,10-Epoxy-9,10-dihydrophenanthrene (65): ^1H NMR (Me_2SO-d_6) δ 4.66 (s, 2 H, CHO), 7.42 (t, 2 H, J = 8 Hz, Ar CH), 7.52 (t, 2 H, J = 2.8 Hz, Ar CH), 7.76 (d, 2 H, J = 2.8 Hz, Ar CH), 8.24 (d, 2 H, J = 8 Hz, Ar CH); ^{13}C NMR (Me_2SO-d_6) δ 55.69 (CHO), 123.96, 128.24, 129.50, 131.13, 131.79.

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Registry No. (+)-**4**, 4254-15-3; (+)-**5**, 25779-13-9; (−)-**6**, 56718-04-8; (+)-**7**, 16088-62-3; **5** (tosylate), 40435-14-1; (−)-**8**, 63798-13-0; *dl*-**9**, 6982-25-8; **10**, 579-43-1; *dl*-**11**, 655-48-1; *dl*-**12**, 38628-70-5; **13**, 1689-71-0; *dl*-**14**, 96455-82-2; *dl*-**15**, 96455-83-3; **16**, 504-63-2; **17**, 24765-56-8; **18**, 13912-01-1; **19**, 110-63-4; **20**, 111-29-5; **21**, 629-11-8; **22**, 15753-50-1; **23**, 13149-01-4; **24**, 96553-66-1; **25**, 96455-84-4; **27**, 6117-80-2; **28**, 1708-29-8; **29**, 821-11-4; *dl*-**30**, 22910-58-3; *dl*-**33**, 81096-87-9; *dl*-**34**, 91049-45-5; *dl*-**35**, 96553-67-2; *dl*-**36**, 19881-97-1; *dl*-**37**, 96553-68-3; *dl*-**38**, 89968-90-1; *dl*-**39**, 96481-54-8; **40**, 32162-29-1; **41**, 94480-84-9; **42**, 76-09-5; **43**, 49595-63-3; **44**, 5076-20-0; **45**, 75-97-8; **46**, 10473-13-9; **47**, 96455-85-5; **48**, 96553-69-4; **49**, 565-69-5; **50**, 96611-53-9; **51**, 96481-55-9; **54**, 31558-25-5; **55**, 1564-98-3; *dl*-**57**, 54383-22-1; *dl*-**58**, 96455-86-6; **59**, 286-20-4; *dl*-**60**, 60363-27-1; **61**, 1792-81-0; **62**, 96553-70-7; **63**, 108-94-1; **65**, 585-08-0; **66**, 25061-61-4; DEP, 628-37-5; DTPP, 86852-11-1; $(HexO)_2$, 3903-89-7; $Ph_3P(OHex)_2$, 96481-56-0; $HexOSO_2Me$, 16156-50-6; HexOH, 111-27-3; $MeSO_2Cl$, 124-63-0; $HO(H_2)_3OEt$, 111-35-3; $HO(CH_2)_6OEt$, 40868-73-3; *p*-$Me(C_6H_4SO_2Cl$, 98-59-9; *trans*-PhCH=CHPh, 103-30-0; *dl*-PhCOCHOHPh, 579-44-2; *m*-CPBA, 937-14-4; *cis*-PhCH=CHPh, 645-49-8; $PhCH_2CH=CH_2$, 300-57-2; HCO_2H, 64-18-6; HCO_3H, 107-32-4; $CH_2=C(CH_3)(CH_2)_2CH_3$, 763-29-1; $Me_3SO^+I^-$, 1774-47-6; $CH_3CO(CH_2)_2CH_3$, 107-87-9; $(CH_3)_2C=C(CH_3)_2$, 563-79-1; $(CH_3)_2C=CHCH_2CH_3$, 625-27-4; (*S*)-(−)-ethyl lactate, 687-47-8; (*S*)-(+)-mandelic acid, 17199-29-0; L-glutamic acid, 56-86-0; (*S*)-(+)-γ-[(tosyloxy)methyl]-γ-butyrolactone, 58879-34-8; (*S*)-(+)-γ-(hydroxymethyl)-γ-butyrolactone, 32780-06-6; (*S*)-(+)-γ-butyrolactone-γ-carbonyl chloride, 54848-33-8; β-pinene, 127-91-3; citronellol, 106-22-9; 1-methylcyclohexene, 591-49-1; phenanthrenequinone, 84-11-7; (*S*)-styrene oxide, 20780-54-5; *dl*-styrene oxide, 67253-49-0; *cis*-2,3-epoxybutane, 1758-33-4; oxetane, 503-30-0; tetrahydrofuran, 109-99-9; tetrahydropyran, 142-68-7; oxepane, 592-90-5; *dl*-1,2-epoxydecane, 67210-45-1.

Total Synthesis of (±)-Tirandamycin A

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Abstract: A convergent, 12-step synthesis of racemic tirandamycin A is described. The key features of the synthesis are preparation of the 2,9-dioxabicyclo[3.3.1]nonane system of the natural product by oxidation of furfuryl alcohol **8a** and attachment of the 3-acyl tetramic acid moiety via the dianion of phosphonate **4b**.

Tirandamycin A (**1**)[1] is a member of the 3-dienoyl tetramic acid family of antibiotics. This family of antibiotics includes several structurally similar substances such as tirandamycin B[2] (**2**), streptolydigin,[1a,3] nocamycin,[4] and Bu-2313 A and B.[5] These substances display a diversity of biological activities. For instance,

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