Note Added in Proof. A preliminary communication of a synthesis of *N*-acetylactinobolamine has appeared: Rahman, M. A.; Frasier-Reid, B. *J. Am. Chem. Soc.* **1985**, *107*, 5576.

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Registry No. (±)-**2a**, 98903-70-9; (±)-**3**, 93000-77-2; (±)-**4**, 98903-43-6; (±)-**5** (isomer 1), 98903-44-7; (±)-**5** (isomer 2), 98921-20-1; (±)-**6a**, 98903-45-8; (±)-**6b**, 98903-46-9; (±)-**7a**, 98903-47-0; (±)-**7b**, 98903-48-1; (±)-**8** (isomer 1), 98903-49-2; (±)-**8** (isomer 2), 98974-82-4; (±)-**9** (isomer 1), 98903-50-5; (±)-**9** (isomer 2), 98974-83-5; (±)-**10**, 98903-51-6; (±)-**10** (methylene isomer), 98903-52-7; **11**, 98903-53-8; **12a**, 98903-54-9; **12b**, 98903-55-0; (±)-**13**, 98903-56-1; (±)-**14a** (isomer 1), 98903-57-2; (±)-**14a** (isomer 2), 98903-58-3; (±)-**14b** (isomer 1), 98903-59-4; (±)-**14b** (isomer 2), 98903-60-7; (±)-**15** (isomer 1), 98903-61-8; (±)-**15** (isomer 2), 98903-62-9; (±)-**16** (isomer 1), 98903-63-0; (±)-**16** (isomer 2), 98974-84-6; (±)-**16** (lactone), 98903-64-1; (±)-**17**, 98903-65-2; (±)-**17** (X = NH_2), 98903-66-3; (±)-**18**, 98903-67-4; (±)-**19**, 98903-68-5; (±)-**20**, 98903-69-6; (±)-6-oxabicyclo[3.2.1]oct-3-en-7-one, 68217-48-1; methoxypropyne lithium acetylide, 73390-08-6.

Supplementary Material Available: Copies of NMR spectra of advanced synthetic intermediates (6 pages). Ordering information is given on any current masthead page.

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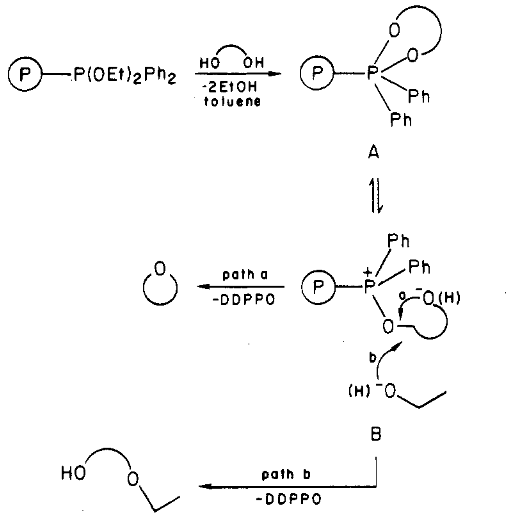
Diethoxydiphenylpolystyrylphosphorane: A New Polymeric Reagent for the Efficient Cyclodehydration of Simple Diols

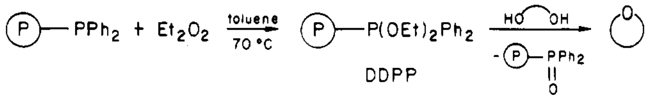
Summary: Diethoxydiphenylpolystyrylphosphorane, prepared by oxidative addition of diphenylpolystyrylphosphine with diethyl peroxide, is a heterogeneous, effectively neutral cyclodehydrating reagent which readily converts diols to cyclic ethers in excellent yields and allows for rapid and efficient product isolation.

Sir: Quite recently, we completed a comprehensive evaluation detailing the synthetic utility of diethoxytriphenylphosphorane, $Ph_3P(OEt)_2$ (DTPP), an effective reagent for promoting the cyclodehydration[1] and rearrangement[2] of an array of diols. On the basis of the current success of solid-phase methodology,[3] we envisioned that a cross-linked, polymer-supported dioxyphosphorane (i.e., diethoxydiphenylpolystyrylphosphorane; DDPP) might possibly allow for expeditious product isolation while simultaneously incorporating the characteristically mild cyclodehydration properties of DTPP. As a bonus, it seemed reasonable to expect the steric bulk and rigidity of the polymeric backbone to favorably influence regioselective phosphoranylation and subsequent cyclodehydration of unsymmetrical diols. In this preliminary account, we describe the preparation of DDPP and its successful application in the conversion of selected diols to cyclic ethers.

Scheme I. Phosphoranylation and Cyclodehydration of Diols with Diethoxydiphenylpolystyrylphosphorane (DDPP)



A typical experimental procedure involves the addition (via an airtight syringe) of diethyl peroxide (0.307 mL, 2.75 mmol)[4] to 2% divinylbenzene cross-linked diphenylpolystyrylphosphine (1.19 g, 4.5 mmol)[5] in anhydrous toluene solvent (5.0 mL) under nitrogen or argon. This mixture was heated (70 °C) with magnetic stirring for 48 h prior to addition of anhydrous 1,4-butanediol (1) (0.221 mL, 2.5 mmol). After being heated for 24 h (70 °C), the reaction mixture was filtered through a glass wool plug. ^{13}C NMR analysis of the resulting solution revealed >99% tetrahydrofuran (2). Confirmation of sample composition was accomplished by GLC analysis.[6]



^{31}P NMR analysis[7] of the reaction between diphenylpolystyrylphosphine (DDP; 595 mg) and diethyl peroxide (1.37 mmol) [3:1 toluene/benzene-d_6] after 48 h indicated resonances at δ 24.4 (10%), -6.5 (45%), and -55.3 (45%) for diethoxydiphenylpolystyrylphosphine oxide (DDPPO), DDP, and DDPP, respectively. The resonance at δ -55.3 is similar to that observed for DTPP (δ -55.0)[1] where the trigonal bipyramidal conformer having both ethoxy groups in the apical array is preferred.

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[1] Robinson, P. L.; Barry, C. N.; Kelly, J. W.; Evans, S. A., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 5210–5219.

[2] Robinson, P. L; Evans, S. A., Jr. *J. Org. Chem.* **1985**, *50*, 3860–3863.

[3] (a) Hodge, P., Sherrington, D. C., Eds. "Polymer Supported Reactions"; Wiley: London, 1980. (b) Mathur, N. K.; Narang, C. K.; Williams, R. E. "Polymers as Aids in Organic Chemistry"; Academic Press: New York, 1980. (c) Frechet, J. M. *Tetrahedron* **1981**, *37*, 663–683. (d) Lieto, J.; Milstein, D.; Albrilght, R. L.; Minkiewicz, J. V.; Gates, B. C. *CHEMTECH* **1983**, 46–53. (e) Balakrishnan, T.; Ford, W. T. *J. Appl. Polym. Sci.* **1982**, *27*, 133–138.

[4] *Diethoxy peroxide*: See ref 1 for full experimental details on the preparation and purification of diethyl peroxide. After crude diethyl peroxide has been prepared, *we recommend that purification by distillation should be done at temperatures of 25–28 °C and pressures between 70–80 torr.* It is best to store diethyl peroxide over 4-Å molecular sieves at -20 °C. Under these conditions it is stable indefinitely. We have consistently avoided the use of ground glass syringes in our transfers of homogeneous diethyl peroxide. See also for early preparative information: Chang, B. C.; Conrad, W. E.; Denney, D. B.; Denney, D. Z.; Edelman, R.; Powell, R. L.; White, D. W. *J. Am. Chem. Soc.* **1971**, *93*, 4004.

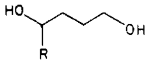
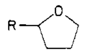
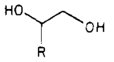
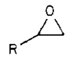
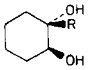
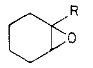
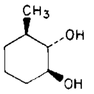
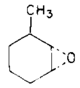
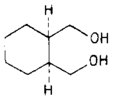
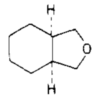
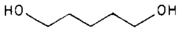
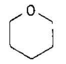
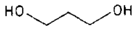
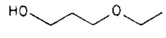
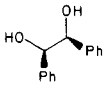
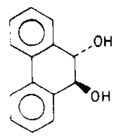
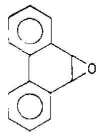
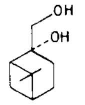
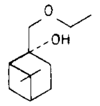
[5] Amos, R. A.; Emblidge, R. W.; Havens, N. *J. Org. Chem.* **1983**, *48*, 3598–3600. Also available from Aldrich Chemical Co. (24.3 mmol of phosphine/gram assuming complete reaction with a specified quantity of EtOOEt after 48 h at 70 °C.

[6] The ethereal products were identified in the reaction mixture by comparing their ^{13}C NMR spectral properties with those obtained from authentic materials. Their presence and relative composition was obtained by GLC analysis. Gas chromatographic analyses were obtained with a stainless steel column (0.125 in. i.d. × 10 ft packed with 20% Carbowax 20 M on Chromosorb W-HP-AW-DMCS, 100–200 mesh).

[7] Ford, W. T.; Mohanraj, S.; Periyasamy, M. *Br. Polym. J.* **1984**, *16*, 179–187.

0022-3263/85/1950-5007$01.50/0

Table I. Cyclodehydration and *O*-Ethylation of Diols Using Diethoxydiphenylpolystyrylphosphorane in Toluene[a]

entry	diol		ether (%)	
1		**1**, R = H		**2**, R = H (99)
2		**3**, R = Me		**4**, R = Me (90)
3		**5**, R = Me		**6**, R = Me (96)
4		**7**, R = Ph		**8**, R = Ph (98)
5		**9**, R = H		**10**, R = H (93)
6		**11**, R = Me		**12**, R = Me (70)
7		**13**		*cis*-**14** (18) *trans*-**14** (82)
8		**15**		**16** (95)
9		**17**		**18** (85)
10		**19**		**20** (90)
11		**21**		**22** (99)
12		**23**		**24** (70)[b]
13		**25**		**26** (83)

[a] The etheral products are identified in the reaction mixture from their ^{13}C NMR spectra. Their presence and relative compositions were confirmed by comparing their GLC retention times with authentic samples. [b] 9,10-Dihydro-*trans*-9,10-phenanthrenediol is sparingly soluble in toluene solvent. Addition of acetonitrile is required for complete solubilization of **23**.

A schematic rationale for the conversion of diols to cyclic ethers using DDPP is described in Scheme I. Exchange of the ethoxy ligands in DDPP with a diol could afford 1,3,2-dioxaphospholane A which would be in dynamic equilibrium with betaine B, the quintessential intermediate for cyclic ether formation (path a). However, if the free energy of activation is unfavorable for chain closure, displacement of Ⓟ-P(O)Ph$_2$ (DDPPO) by ethoxide ion becomes competitive and, in some cases, the dominant pathway (path b; cf. Table I, entries 10 and 13).

Generally, the yields for conversion of diols to cyclic ethers using DDPP are high (70–99%) and in most cases rival those obtained employing the *homogeneous* dioxyphosphorane DTPP[1] (Table I). DDPP is particularly effective in converting unhindered 1,2-, 1,4-, and 1,5-diols to epoxides, tetrahydrofurans, and tetrahydropyrans, respectively (cf. entries 1–9, 11–12). However, attempted cyclodehydration of 1,3-propanediol (**19**) to oxetane gave only 3-ethoxy-1-propanol (**20**) consistent with the unfavorable free energy associated with four-membered ring formation.[8]

The stereospecific conversion of *meso*-1,2-diphenylethane-1,2-diol (**21**)[9] to *trans*-stilbene oxide (**22**)[10] is in accord with the energetically favorable "3-exo-tet"[11] cyclization from betaine B with inversion of stereochemistry at the displacement terminus. Interestingly, the regioselective cyclodehydration of (*S*)-(+)-phenylethane-1,2-diol[12] [(*S*)-**7**] with DDPP is evident from examination of the enantiomeric mixture of styrene oxides which is rich in the (*S*)-(+)-1-phenyl-1,2-epoxyethane[13] [(*S*)-**8**] enantiomer (68% ee). This % ee translates into 84% retention of stereochemistry at C2. By contrast, DTPP converts (*S*)-**7** to racemized (±)-styrene oxide.[1,14]

trans-2-Hydroxy-*cis*-3-methylcyclohexene (**13**)[15] undergoes cyclodehydration with DDPP (38 °C, toluene solvent) to afford a mixture containing *trans*-2-methylcyclohexene oxide (*trans*-**14**; 82%)[16] and *cis*-2-methylcyclohexene oxide (*cis*-**14**; 18%).[16] This finding is significant because it indicates that the C2 hydroxyl group proximal to the methyl group occupies the more sterically congested environment and is unable to easily undergo phosphoranylation and subsequent displacement. It seems unlikely that suitable betaine intermediates necessary for epoxide formation will exist in chair conformations due to the severe steric demands caused by the axial substituents in betaines C and D.[2] It may be more reasonable

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(8) Searles, S.; Nickerson, R. G.; Witsiepe, W. K. *J. Org. Chem.* **1959**, *24*, 1839–1844.

(9) Pohorles, L. A.; Sarel, S.; Ben-Shoshan, R. *J. Org. Chem.* **1959**, *24*, 1878–1881.

(10) **22**: mp 68–70 °C; ^{1}H NMR (CDCl$_3$) δ 3.85 (s, 2 H, HCOC) and 7.40 (s, 10 H, Ar CH).

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

(12) Comparison of the optical rotation of the *R* enantiomer, $[\alpha]^{18}{}_{\rm D}$ −51.9° (*c* 0.77, benzene), indicates that our sample of the *S* enantiomer, $[\alpha]^{18}{}_{\rm D}$ +51.57° (*c* 0.785, benzene), is 99.4% optically pure. See: Fischer, E. *Chem. Ber.* **1912**, *63*, 2447.

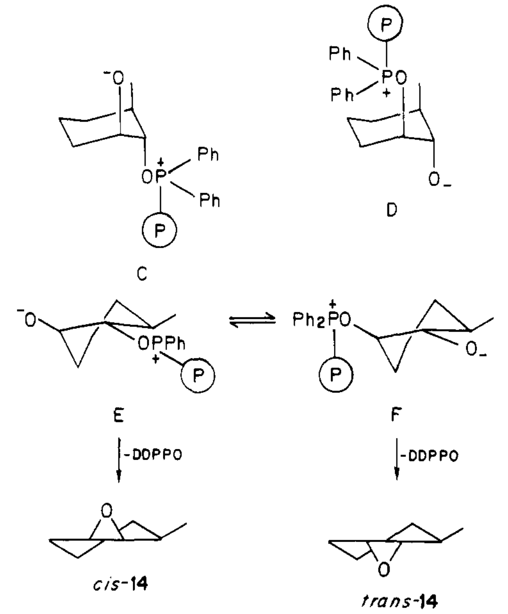
(13) Dupin, C.; Dupin, J. F. *Bull. Soc. Chim. Fr.* **1970**, 249–251. A chiral shift ^{1}H NMR study using Eu(Hfc)$_3$ was employed to assess the enantiomeric purity of **8**.

(14) Robinson, P. L.; Barry, C. N.; Bass, S. W.; Jarvis, S. E.; Evans, S. A., Jr. *J. Org. Chem.* **1983**, *48*, 5396–5398.

(15) Klein, J.; Dunkelblum, E. *Tetrahedron* **1968**, *24*, 5701–5710.

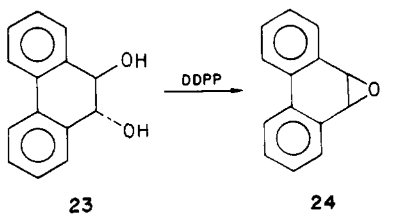
(16) See Paquette, L. A.; Barrett, J. H. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. 5, pp 467–71.

Scheme II. Preferred Betaines for Cyclodehydration of 1,2-Cyclohexanediols



to assume that the diastereoselectivity favoring *trans*-**14** arises from the differences in steric interactions within the two twist-boat betaine intermediates, E and F. The pictorial representations in Scheme II may be useful in helping to rationalize the diastereoselectivity in the cyclodehydration of **13**.

As a demonstration of the potential synthetic utility of DDPP for conversion of acid-sensitive 1,2-diols to epoxides in neutral media, we have prepared 9,10-epoxy-9,10-dihydrophenanthrene (**24**; 70%) by cyclodehydration of 9,10-dihydro-*trans*-9,10-phenanthrenediol (**23**)[17] with DDPP.



23 **24**

Sterically hindered 1,2-diols may be especially susceptible to the bulk and/or rigid backbone of the polymeric dioxyphosphorane DDPP. For example, phosphoranylation of 2α,10-pinanediol (**25**)[18] presumably occurs at the sterically more accessible primary hydroxy group resulting in exclusive ethoxide substitution (i.e., **26**). Formation of 1,3,2-dioxaphosphorane A or, more importantly, the prerequisite betaine B are apparently prevented and subsequent cyclodehydration to 2α,10-epoxypinane does not occur.

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Received June 20, 1985

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[17] Cortez, C.; Harvey, R. G. *Org. Synth.* **1978**, *58*, 12–17.

[18] Coxon, J. M.; Dansted, E.; Hartshorn, M. P.; Richards, K. E. *Tetrahedron* **1968**, *24*, 1193–1197.

Upper Excited-State Reactions of α,β-Unsaturated Thiones: Photocycloaddition to Electron-Deficient Olefins

Summary: Thioenone 1 upon excitation to S_2 in presence of electron-deficient olefins yields thietanes and the cycloaddition is found to be stereospecific, regioselective, and site specific.

Sir: With mechanistic and synthetic studies continuing unabated, the photoannulation of enones has taken an important place among the best known and most reliable organic photochemical transformations.[1] In contrast to this state of affairs, little attention has been paid to thioenones. Considering the wealth of chemistry exhibited by enones, a systematic study of the photochemical behavior of thioenones should be of interest. However studies have been made only on systems distantly related to α,β-unsaturated thioenones. Photocycloaddition of 1,2-dithiole-3-thiones to olefins has been investigated.[2] The cycloadditions are suggested to originate from the lowest triplet state ($n\pi^*$), and the reactions are nonstereospecific. Several 4-thiouracil and 4-thiouridine derivatives have been irradiated in the presence of unsaturated nitriles.[3] The products are believed to derive from thietanes, although these have been isolated only in a few cases. However, details of the mechanism are not fully understood. Thus a systematic study on the photochemical behavior of a simple thioenone is lacking. Work in this area has been hindered significantly by the poor stability of monomeric thioenones.[4] After a careful scruitiny of a large number of thioenones,[5] we have initiated a systematic investigation on the photocycloaddition of 1,1,3-trimethyl-2-thioxo-1,2-dihydronaphthalene (**1**). The preliminary results presented here substantiate the general conclusion that while the ubiquitously studied carbonyl group can be considered a closely related system, the excited thione function has distinctive characteristics of its own.

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[1] Eaton, P. E. *Acc. Chem. Res.* **1968**, *1*, 50. de Mayo, P. *Acc. Chem. Res.* **1971**, *4*, 41. Bauslaugh, P. G. *Synthesis* **1970**, 287. Baldwin, S. W. *Org. Photochem.* **1981**, *5*, 123.

[2] de Mayo, P. *Tetrahedron Lett.* **1973**, 1561. Okazaki, R.; Ishii, F.; Ozawa, K.; Inamoto, N. *Chem. Lett.* **1972**, 9. Okazaki, R.; Ishii, F.; Okawa, K.; Ozawa, K.; Inamoto, N. *J. Chem. Soc., Perkin Trans. 1* **1975**, 270.

[3] Fourrey, J. L.; Jouin, P.; Moron, J. *Tetrahedron Lett.* **1974**, 3005. Fombert, C.; Fourrey, J. L.; Jouin, P.; Moron, J. *Tetrahedron Lett.* **1974**, 3007. Fourrey, J. L.; Jouin, P.; Moron, J. *Tetrahedron Lett.* **1973**, 3229.

[4] Thioenones generally undergo very facile thermal dimerization via a Diels–Alder process: Karakasa, T.; Yamaguchi, H.; Motoki, S. *J. Org. Chem.* **1980**, *45*, 927. Beslin, P.; Lagain, D.; Vialle, J. *Tetrahedron Lett.* **1979**, 2677. Karakasa, T.; Motoki, S. *J. Org. Chem.* **1978**, *43*, 4147. Pradere, J. P.; Bonet, G.; Quinon, H. *Tetrahedron Lett.* **1972**, 3471.

[5] Several cyclic thioenones possessing transoid geometry are reported to be stable. Metzner, P.; Vialle, J. *Bull. Soc. Chim. Fr.* **1972**, 3138. Barton, D. H. R.; Choi, L. S. L.; Hesse, R. H.; Pechet, M. M.; Wilshire, C. *J. Chem. Soc., Perkin Trans 1* **1979**, 1166. Schmuser, W.; Voss, J. *J. Chem. Res, Synop.* **1980**, 262; *J. Chem. Res., Miniprint* **1980**, 3361.

0022-3263/85/1950-5009$01.50/0