Kamiya and Dr. Yoshikazu Wada (Takeda Chemical Industries Ltd.) for help with the X-ray structural analysis and Dr. Noriyuki Yonezawa and Taro Tsubomura for the ORTEP drawing.

Registry No. 1, 97350-55-5; **1**-C_6H_6, 97350-56-6; **1**-$CHCl_3$, 100813-06-7; **1**-*o*-$CH_3C_6H_4CH_3$, 100813-07-8; **1**-*m*-$CH_3C_6H_4CH_3$, 100813-08-9; **1**-*p*-$CH_3C_6H_4CH_3$, 100813-09-0; **1**-1,3,5-$(CH_3)_3C_6H_3$, 100813-10-3; **1**-PhCOOMe, 100813-11-4; **1**-MePh, 100813-12-5; **2**, 51760-20-4; **3**, 80-05-7; **4**, 97345-97-6.

Supplementary Material Available: A list of potential parameters, bond distances, and bond angles with their estimated standard deviations (6 pages). Ordering information is given on any current masthead page.

S–C–P Anomeric Interactions. 4. Conformational Analysis of 2-(Diphenylphosphinoyl)-1,3-dithiane[1,2]

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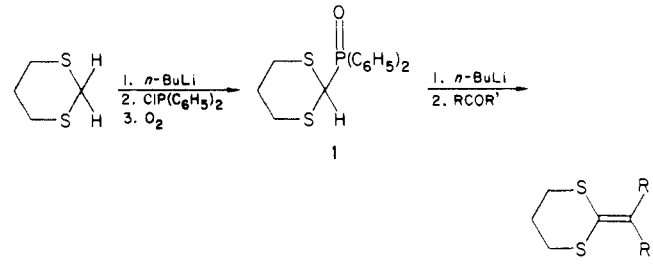
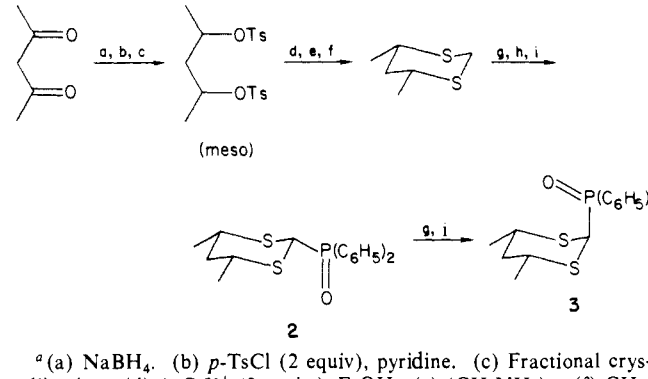
Abstract: Proton NMR spectroscopy and X-ray crystallographic studies demonstrate the predominance of the axial conformer of 2-(diphenylphosphinoyl)-1,3-dithiane (**1**). Chemical equilibration of anancomeric models (**2** ⇌ **3**) allows quantitative determination of the conformational free energy in **1**, 1.0 kcal/mol, which corresponds to an anomeric effect of 3.74 kcal/mol, the largest yet measured. Comparison of the structural data for **1**-ax and **2** (equatorial) provides information contrary to what would be expected if an $n_S \rightarrow \sigma^*_{C-P}$ interaction were responsible for the preferred axial conformation in **1**. Also, solvent effects do not show the trend to be expected if dipole/dipole interactions dominated the conformational behavior in **1**. Alternative rationalizations of the phenomenon are discussed. In particular, the possible importance of electrostatic, attractive interactions between the phosphoryl oxygen and the axial hydrogens at C(4,6) is suggested.

2-[1,3]Dithianyldiphenylphosphine oxide (**1**) has been studied in our laboratory as a potential precursor of ketene dithioketals (i.e., as a new Wittig–Horner/Corey–Seebach reagent[3,4] (Scheme I). It soon became obvious that the conformational behavior of **1** could provide useful information concerning the nature of the anomeric effect,[5,6] a phenomenon whose general chemical implications have recently been reviewed.[7,8] While much work has been dedicated to studies of the effect involving first-row elements, much less effort has been devoted to systems containing second-row elements.[9-11] The present work constitutes the first quantitative evaluation of a S–C–P anomeric interaction[2,12,13]

Scheme I



Scheme II[a]



[a] (a) $NaBH_4$. (b) *p*-TsCl (2 equiv), pyridine. (c) Fractional crystallization. (d) AcS^-K^+ (2 equiv.), EtOH. (e) $(CH_2NH_2)_2$. (f) $CH_2(OCH_3)_2$, $BF_3{\cdot}Et_2O$. (g) *n*-BuLi, THF-TMEDA. (h) $ClP(C_6H_5)_2$. (i) Air oxidation. (j) NH_4Cl, H_2O.

Results and Discussion

Discovery of a Strong S–C–P Anomeric Interaction in 1. 2-[1,3]Dithianyldiphenylphosphine oxide (**1**) was prepared from 1,3-dithiane, *n*-butyllithium, and chlorodiphenylphosphine; the phosphine intermediate oxidized spontaneously to **1** during workup (Scheme I). Assignment of the proton NMR spectrum of **1**

(1) For part 3, see: Juaristi, E; López-Núñez, N. A.; Glass, R. S.; Petsom, A.; Hutchins, R. O.; Stercho, Y. accepted for publication in *J. Org. Chem.*

(2) A preliminary report on this work has appeared: Juaristi, E.; Valle, L.; Mora-Uzeta, C.; Valenzuela, B. A.; Joseph-Nathan, P.; Fredrich, M. F. *J. Org. Chem.* **1982**, *47*, 5038–5039.

(3) Juaristi, E.; Valle, L.; Mora, C. "Abstracts of Papers", 183rd National Meeting of the American Chemical Society; American Chemical Society: Washington, DC, 1982; ORGN 69. Juaristi, E.; Gordillo, B.; Valle, L. *Tetrahedron*, in press.

(4) For related examples, see inter alia: Corey, E. J.; Märkl, G. *Tetrahedron Lett.* **1967**, 3201–3204. Mikolajczyk, M.; Grzejszczak, S.; Zatorski, A.; Mlotkowska, B. *Ibid.* **1976**, 2731–2734.

(5) Szarek, W. A.; Horton, D. "The Anomeric Effect: Origin and Consequences"; American Chemical Society: Washington DC, 1979; ACS Symp. Ser. No. 87.

(6) Kirby, A. J. "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen"; Springer-Verlag: Berlin, 1983.

(7) Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry"; Pergamon Press: Oxford, 1983.

(8) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540–4552.

(9) For studies of the anomeric effect in thiane rings, see: Zefirov, N. S.; Blavoveshchenskii, V. S.; Kazimirchik, I. V.; Yakovleva, O. P. *J. Org. Chem. USSR (Engl. Transl.)* **1971**, *7*, 599–602. de Hoog, A. J. Ph.D. Thesis, University of Leiden, 1971, as cited in ref 6, p 24.

(10) For studies of the anomeric effect in 2-substituted 1,3-dithianes, see: (a) Juaristi, E.; Tapia, J.; Méndez, R. *Tetrahedron*, in press. (b) Hartmann, A. A. Ph.D. Thesis, University of Notre Dame, IN, 1971. (c) Pinto, B. M.; Sandoval-Ramirez, J.; Dev Sharma, R. *Tetrahedron Lett.* **1985**, *26*, 5235–5238.

(11) For studies of the anomeric effect in 2-substituted 1,3,5-trithianes, see: (a) Arai, K.; Iwamura, H.; Ōki, M. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3319–3323. (b) Ōki, M.; Sugawara, T.; Iwamura, H. *Ibid.* **1974**, *47*, 2457–2462. (c) Ōki, M.; Endo, T.; Sugawara, T. *Ibid.* **1975**, *48*, 2496–2501. (d) Sugawara, T.; Iwamura, H.; Ōki, M. *Ibid.* **1974**, *47*, 1496–1499.

(12) Mikolajczyk et al.[13] have recently found that the structurally related 2-(dimethoxyphosphoryl)-1,3-dithiane and 2-(dimethoxyphosphoryl)-1,3,5-trithiane exist largely in the axial conformation.

(13) Mikolajczyk, M.; Balczewski, P.; Wroblewski, K.; Karolak-Wojciechowska, J.; Miller, A.; Wieczorek, M.; Antipin, M. Y.; Struchkov, Y. T. *Tetrahedron* **1984**, *40*, 4885–4892.

0002-7863/86/1508-2000$01.50/0

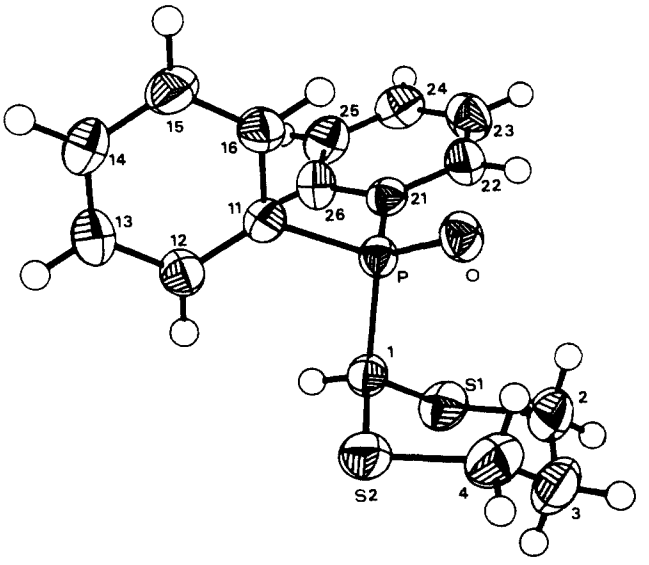
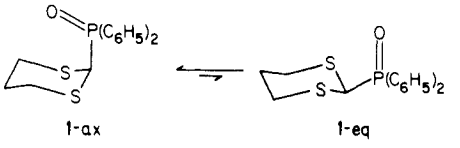


Figure 1. Perspective view of the molecular structure of **1**.

indicated a very large (ca. 1.2 ppm) chemical shift difference between axial and equatorial protons at C(4,6). [By comparison, $\Delta\delta_{ax/eq}$(H(4,6)) in 2-*tert*-butyl-1,3-dithiane[14] is ca. 0.09 ppm.] That the signals at 3.70 and 2.50 ppm correspond to the axial and equatorial protons, respectively, was confirmed by irradiation at 3.70 ppm causing the signal at 2.50 ppm to lose its geminal coupling, since it collapsed into a triplet (J_{gauche} = 4.5 Hz). Similarly, irradiation at 2.05 ppm changed the signals at 3.70 and 2.50 ppm to an AB quarter (J_{gem} = 14.4 Hz).

These spectroscopic observations are evidence for a deshielding effect of a *predominantly axial* phosphoryl group on the syn-axial H(4,6) (eq 1).



(1)

Support for this hypothesis comes from the observation that the downfield shift produced by the addition of Eu(fod)$_3$ is in the order H(4,6) (axial) > H(2) > H(4,6) (equatorial) > H(5). Observation of Dreiding models indicates that this result is reasonable only if one assumes the axial orientation for the phosphinoyl group, with the P–O bond above the dithianyl ring.[15]

There is, therefore, clear evidence for a strong anomeric interaction between the second-row elements sulfur and phosphorus (P=O). Definitive proof for the conformation of **1** was obtained by single-crystal X-ray diffraction.[2] A perspective view of the molecular structure is shown in Figure 1. The heterocyclic six-membered ring exists in a chair conformation with the substituent being axial.

Estimation of the Magnitude of the Anomeric Effect in 1. In order to quantitate the conformational effect present in **1**, the anancomeric derivatives **2** and **3** were prepared from *cis*-4,6-dimethyl-1,3-dithiane[14] by making use of the highly stereoselective reaction of 2-lithio-1,3-dithianes with electrophiles (Scheme II).[16] The proton NMR spectra of **2** and **3** were compared with that of **1** (all three in $CDCl_3$). Most interestingly, the coupling constants of H(2) to phosphorus in **1**, **2**, and **3** vary considerably: 6, 15, and 4.2 Hz, respectively (±0.2 Hz). On the assumption that $^2J_{H(2)/P}$ in the mobile dithiane (**1**) is the weighted average of those for the model diastereomers **2** and **3**,[17] then $K = (J_{eq} - J)/(J - J_{ax}) = 5.0$, which yields $\Delta G°_{39°C}$ = 1.0 kcal/mol for the free energy difference favoring **1**-ax over **1**-eq.

Scheme III

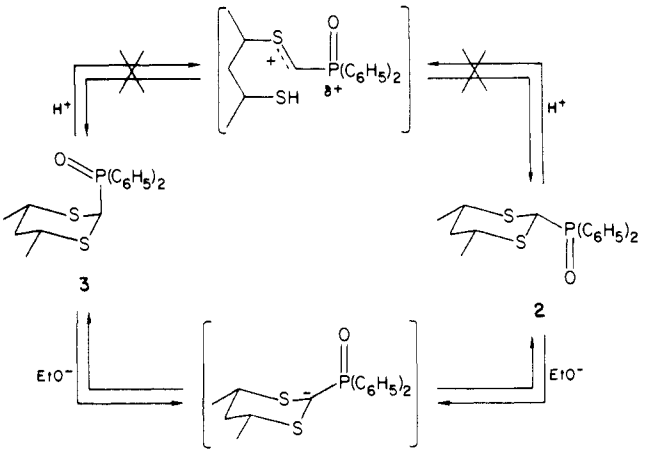
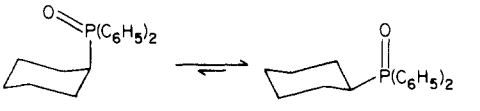


Table I. Chemical Equilibration of Anancomeric **2** and **3** with Ethanolic Sodium Ethoxide at 21 °C[a]

entry	starting diastereomer	3:2 ratio at equilibrium	K	$\Delta G°$, kcal/mol
1	**2**	84.82:15.18	5.59	1.005
2	**2**	85.12:14.88	5.72	1.019
3	**3**	83.86:16.14	5.20	0.963
4	**3**	84.25:15.75	5.35	0.980

[a] By integration of ^{1}H NMR signal areas; see text.

Chemical equilibration of anancomeric **2** and **3** was initially attempted with acid catalysis.[18] However, only unchanged starting material was recovered, this being probably due to the high-energy content of the open-chain intermediate (Scheme III). Chemical equilibration **2** ⇄ **3** was, however, successfully effected with basic catalysis using ethanolic sodium ethoxide (Scheme III). Integration of the signals for H(2) in the proton NMR spectra served for the analysis of the diastereomeric ratios since these protons are sharp doublets and also provide an adequate spread of chemical shifts ($\delta_{eq} - \delta_{ax}$) so as to make calculations reliable. Table I summarizes the experimental equilibrium constants for equilibria initiated from both sides. An average value of 0.99 ± 0.03 kcal/mol for the conformational free energy difference of the 2-diphenylphosphinoyl group was calculated; this result is in full agreement with that obtained by the weighted-average coupling constant method (vide supra). The magnitude of the anomeric effect is usually defined as the difference of the free energy difference for the equilibrium studied and the conformational energy for the same substituent in cyclohexane.[19] The conformational preference of the diphenylphosphinoyl group in cyclohexane (eq 2) has recently been determined:[1] $\Delta G°[-P(O)(C_6H_5)_2]$



(2)

= −2.74 ± 0.08 kcal/mol. The calculated value of the anomeric

(14) Prepared according to: Eliel, E. L.; Hutchins, R. O. *J. Am. Chem. Soc.* **1969**, *91*, 2703–2715.

(15) (a) It is reasonable to assume that complexation of **1** with Eu(fod)$_3$ takes place on oxygen: Burdett, J. L.; Burger, L. L. *Can. J. Chem.* **1966**, *44*, 111–118. Goodman, S. C.; Verkade, J. G. *Inorg. Chem.* **1966**, *5*, 498–500. (b) See also: Hadzi, D. *J. Chem. Soc.* **1962**, 5128–5138. Maciel, G. E.; James, R. V. *Inorg. Chem.* **1964**, *3*, 1620–1651. We thank one of the reviewers for bringing these two references to our attention.

(16) Eliel, E. L.; Hartmann, A. A.; Abatjoglou, A. G. *J. Am. Chem. Soc.* **1974**, *96*, 1807–1816.

(17) Also, it has to be assumed that the methyl substituents at C(4,6) have a negligible effect on the value of the coupling constant between the nuclei at C(2).

(18) Cf.: Eliel, E. L.; Juaristi, E. *J. Am. Chem. Soc.* **1978**, *100*, 6114–6119.

(19) Reference 6, pp 7–11. There is, however, a well-recognized difficulty with evaluation in this fashion: the steric requirements of a group in the anomeric position of the heterocycle are different to those encountered in a cyclohexane. In the system at hand, because of the long C–S bonds, the steric congestion of an axial 2-substituent should be smaller to that of the same substituent in cyclohexane; therefore, the magnitude of the anomeric effect tends to be overestimated. See ref 1.

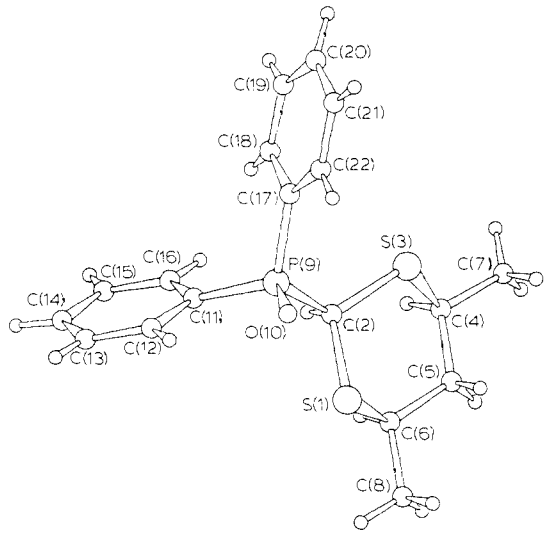


Figure 2. Perspective view of the molecular structure of **2**.

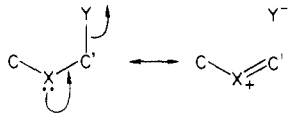
Table II. Selected Interatomic Distances and Angles in **1**-ax and **2** (Equatorial) with Standard Deviations in Parentheses

	1-ax[a]	**2** (equatorial)[b,c]
	Bond Lengths, Å	
S(1)-C(2)	1.809 (3)[d]	1.810 (4), 1.808 (4)
S(1)-C(6)[e]	1.810 (3)[d]	1.818 (5), 1.835 (5)
C(2)-P	1.825 (3)	1.840 (4)
C(5)-C(6)	1.517 (5)[d]	1.520 (7), 1.506 (7)
P-O	1.486 (2)	1.481 (3)
	Bond Angles, (deg)	
C(2)-S(1)-C(6)	101.3 (1)[d]	97.9 (2), 97.3 (2)
S(1)-C(2)-S(3)	114.5 (1)	113.1 (2)
S(1)-C(2)-P	110.4 (1)[d]	106.4 (2), 112.5 (2)
S(1)-C(6)-C(5)	113.9 (2)[d]	112.7 (4), 113.3 (4)
C(4)-C(5)-C(6)	113.3 (3)	115.6 (4)

[a] Reference 2. [b] Reference 23. [c] Since this molecule deviates significantly from C_s symmetry the bond lengths and angles of each half are listed separately. [d] Mean values, averaged assuming C_s ring symmetry. [e] The mean distance in **2** is slightly longer than that in **1**-ax due to the introduction of the methyl substituents into the 1,3-dithiane ring.[23,24]

effect operative in **1** (in solvent $CDCl_3$, vide infra) is therefore 3.74 kcal/mol, which appears to be *the largest* yet recorded.[19]

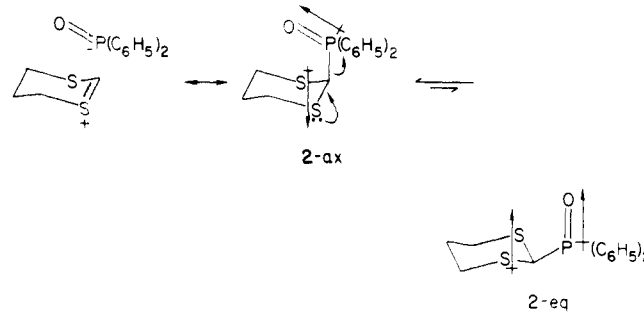
Interpretation of the S–C–P Anomeric Effect Operative in 2-(Diphenylphosphinoyl)-1,3-dithiane. Most commonly, the anomeric effect has been rationalized in terms of stabilization by (1) dipole–dipole interaction[20,21] and (2) delocalization of the lone pair on the endocyclic heteroatom into the antiperiplanar (axial) adjacent polar bonds.[22] According to the second interpretation, in gauche (axial) C–X–C′–Y systems the C′–X distances are significantly shorter than normal while the C′–Y bond lengths are longer than normal (eq 3).



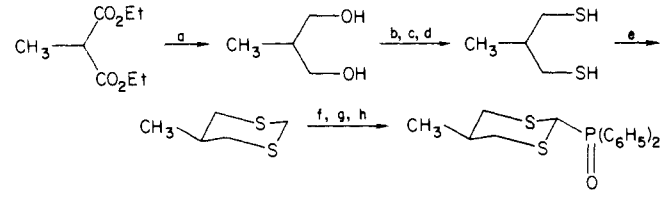
(3)

Comparison of the structural data of **1** (axial)[2] and **2** (equatorial, Figure 2) was made in order to examine the possible importance of $n_S \rightarrow \sigma^*_{C-P}$ interactions which, if significant, would be manifested in shortened C–S and elongated C–P distances in the axial vs. equatorial isomer. Selected bond lengths and angles for **1** and **2** are given in Table II. Comparison of these values

Scheme IV



Scheme V[a]



[a] (a) $LiAlH_4$, Et_2O. (b) *p*-TsCl (2 equiv), pyridine. (c) AcS^-K^+ (2 equiv), EtOH. (d) $(CH_2NH_2)_2$. (e) $CH_2(OCH_3)_2$, $BF_3{\cdot}OEt_2$. (f) *n*-BuLi, THF–TMEDA, −78 °C. (g) ClP $(C_6H_5)_2$. (h) Air oxidation.

Table III. Solvent Effect on the Chemical Shift Difference ($\Delta\delta_{ax/eq}$) for the C(4,6) Methylene Protons in **1** and on the Conformational Energies ($\Delta G°$) of the Diphenylphosphinoyl Group in **4**

solvent	ϵ[a]	$\Delta\delta$, ppm	$\Delta G°_{39°C}$, kcal/mol[b]
$CDCl_3$	4.7	1.19	1.07
CD_3CO_2D	6.2	1.05[c]	*d*
CF_3CO_2D	8.2	0.15	0.30
CD_2Cl_2	8.9	1.13	1.12
CD_3COCD_3	20.7	1.36[c]	1.74
CD_3OD	32.6	0.94[c]	*d*
DMF-d_7	36.7	1.22	*d*
CD_3CN	37.5	1.04	1.06
Me_2SO-d_6	48.9	*d*	1.78

[a] Dielectric constant for protiated solvents. [b] Estimated standard deviation: ±0.1 kcal/mol. $\Delta G°(CH_3)$ = 1.07 kcal/mol.[29] [c] Due to low solubility in this solvent, the measurement was performed by pulse FT NMR at 100.1 MHz by using a (PD, 180°, τ, 90°, AT)$_n$ sequence to eliminate the solvent signal. [d] Not determined.

reveals that the C–P distance in **2** (equatorial) may actually be significantly longer than that in **1** (axial). This observation, as well as the lack of any significant difference in the mean S(1)–C(2) lengths, is *contrary* to expectations if an $n_S \rightarrow \sigma^*_{C-P}$ interaction makes an important contribution to the preferred axial conformation in **1** (or in **2** $\rightleftarrows$ **3**).[23,24]

According to the interpretation of the anomeric effect given by Edward,[20] electrostatic dipole/dipole repulsion disfavors the equatorial conformer while dipole/dipole attraction should favor the axial conformer in the equilibrium such as that depicted in Scheme IV.[25,26] Thus, if dipole/dipole interactions were dominant in the conformational equilibria of **1** (and **2** $\rightleftarrows$ **3**), it would be expected that the contribution of the equatorial form should increase with increasing dielectric constant of the medium.[27]

(20) Edward, J. T. *Chem. Ind. (London)*, **1955**, 1102–1104. See also ref 21.
(21) Jeffrey, G. A.; Pople, J. A.; Radom, L. *Carbohydr. Res.* **1972**, *25*, 117–131.
(22) Romers, C.; Altona, C.; Buys, H. R.; Havinga, E. *Top. Stereochem.* **1969**, *4*, 39–97. See also ref 21.
(23) Juaristi, E.; Valenzuela, B. A.; Valle, L.; McPhail, A. T. *J. Org. Chem.* **1984**, *49*, 3026–3027.
(24) McPhail, A. T.; Onan, K. D.; Koskimies, J. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1004–1008.
(25) The ring dipole in 1,3-dithiane has been determined by Havinga et al.[26] Despite some uncertainty as to the precise orientation of the phosphinoyl group in **1**–**3**, the disposition of the dipoles in Scheme IV should be approximately correct.
(26) Kalff, H. T.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1966**, *85*, 467–484.
(27) See, for example: Eliel, E. L.; Giza, C. A. *J. Org. Chem.* **1968**, *33*, 3754–3758.

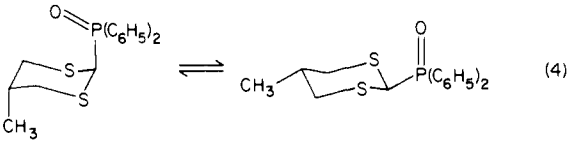
Table IV. Room Temperature ^{13}C NMR Signal Assignments in Compounds **1-3** (ppm from Me_4Si, $CDCl_3$)[a]

compd	C(2)	C(4,6)	C(5)	C_{ipso}	C_o	C_m	C_p	other
1	37.15 (69.6)	26.97	24.91	132.17 (100)	131.07 (8.6)	128.30 (11.7)	131.69 (2.5)	
2	48.49 (64.3)	41.34 (7.3)	43.35	*b*	131.83 (9.8)	128.16 (12.6)	132.25 (2.6)	Me, 21.49
3	39.41 (71.9)	35.36	43.28 (2.3)	*b*	130.94 (8.7)	128.28 (11.4)	131.49 (2.4)	Me, 21.79

[a] C/P coupling constants in parentheses. [b] Obscured by baseline noise.

Since, from the assignment of the ^1H NMR spectrum of **1** (vide supra), it appeared that the magnitude of the chemical shift difference between axial and equatorial protons at C(4,6) increases with increasing population of the axial conformer, the solvent effect on the chemical shift difference [$\Delta\delta_{ax/eq}(4,6)$] was measured (Table III). The results *do not* show the expected[27] solvent effect, i.e., a stronger anomeric effect in the less polar media.

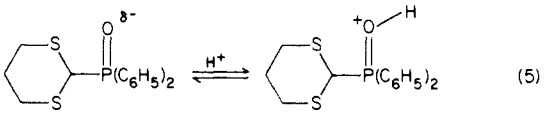
The lack of correlation of $\Delta G°$ with the dielectric constant of the solvent was confirmed when quantitative solvent effects on the magnitude of the anomeric effect for the 2-phosphinoyl group in 1,3-dithiane were determined by proton NMR spectroscopic application of the equation $K = (J_{eq} - J_{mobile})/(J_{mobile} - J_{ax})$ to the mobile *trans*-5-methyl-2-(diphenylphosphinoyl)-1,3-dithiane (**4**, eq 4) and the anancomeric models **2** and **3**. The methyl group



(4)

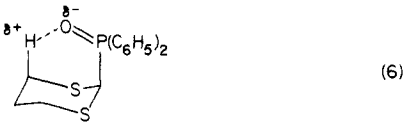
in **4** serves as a counterpoise,[28] so that the equilibrium constant is close to unity, permitting a more precise calculation of $\Delta G°$ than would be possible in **1**. Scheme V shows the method of preparation of **4** from 2-methyl-1,3-propanediol, and Table III summarizes the results in nine solvents of different polarity. Although the precision of these $\Delta G°$ values is only of the order of ±0.1 kcal/mol, the observed trend clearly confirms the proposed correlation between $\Delta\delta_{ax/eq}(4,6)$ and $\Delta G°$.[30]

It is remarkable, however, that the axial preference of the 2-diphenylphosphinoyl group decreases substantially in trifluoroacetic acid (Table III). This very acidic solvent is likely to transfer a proton to the phosphoryl oxygen (eq 5),[15,31] and in



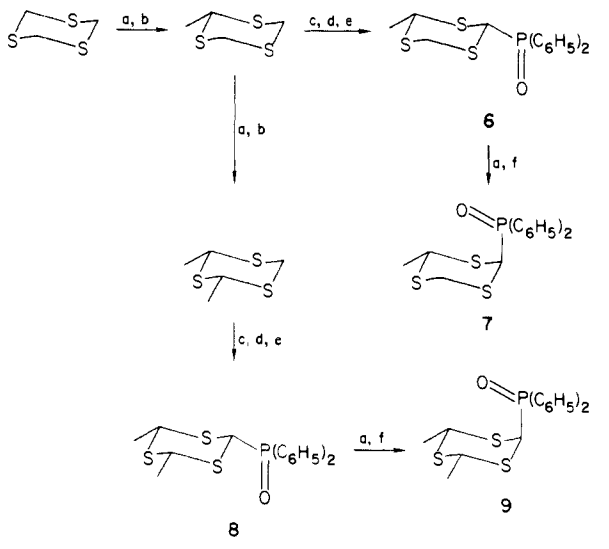
(5)

this event the stability present in **1**-ax is evidently lost. It seems possible that protonation (or at least the formation of hydrogen-bonded complexes[15b]) neutralizes some electrostatic, attractive interaction between the phosphoryl oxygen and the axial hydrogens in **1**-ax (eq 6).[13]



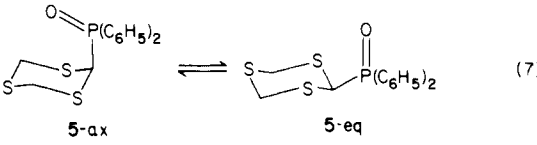
(6)

Scheme VI[a]



[a] (a) *n*-BuLi, THF, −20 °C. (b) CH_3I. (c) *n*-BuLi, THF, −50 °C. (d) $ClP(C_6H_5)_2$. (e) Air oxidation. (f) NH_4Cl, H_2O.

Support for this hypothesis comes from the conformational behavior of 2-(diphenylphosphinoyl)-1,3,5-trithiane (**5**), which shows an even higher predominance of the axial conformer (eq 7). Compound **5** was prepared from 1,3,5-trithiane[34] and chlo-



(7)

rodiphenylphosphine via *n*-butyllithium; the phosphine intermediate oxidized spontaneously to **5** during workup. The proton NMR spectrum of **5** shows an even larger (1.36 ppm) chemical shift difference between axial and equatorial protons at C(4,6) than that observed in **1** (1.20 ppm).

In order to quantitate the conformational equilibrium **5**-ax ⇄ **5**-eq, the anancomeric derivatives **6–9** were prepared according to Scheme VI.[35] Application of the weighted-average coupling constant method (vide supra) provided $K = [J(\mathbf{6}) - J(\mathbf{5})]/[J(\mathbf{5}) - J(\mathbf{7})] = (15.0 - 6.9)/(6.9 - 6.0) = 9$ and $K' = [J(\mathbf{8}) - J(\mathbf{5})]/[J(\mathbf{5}) - J(\mathbf{9})] = (17.1 - 6.9)/(6.9 - 6.0) = 11.33$, which yield $\Delta G°_{39°C} = 1.43 \pm 0.08$ kcal/mol for the free energy difference favoring **5**-ax over **5**-eq. This result is rather interesting in view of the fact that the anomeric effect observed in trithianes is generally smaller than that for dithianes.[10a,11] Here it could be rationalized in terms of a stronger electrostatic interaction in **5**-ax, with its more acidic H(4,6).

Considering that for aromatic systems the ring ^{13}C chemical shifts are a useful and sensitive probe in studies of the polar and resonance effects of substituents[36] and that $p_\pi - d_\pi$ interactions

(28) Eliel, E. L.; Della, E. W.; Williams, T. H. *Tetrahedron Lett.* **1963**, 831–835.

(29) Eliel, E. L.; Hutchins, R. O. *J. Am. Chem. Soc.* **1969**, *91*, 2703–2715.

(30) No simple rationalization can be advanced at the moment for the (greatest) anomeric effect observed in acetone and Me_2SO. These are solvents which could compete for the 4,6-hydrogens, disfavoring the axial $P(O)Ph_2$ conformation, contrary to observation. We thank one of the reviewers for pointing this out.

(31) The pK_a of trifluoroacetic acid is 0.2[32] and that of protonated **1** is probably lower;[33] therefore, even in trifluoroacetic acid as solvent, the equilibrium depicted in eq 5 may not be entirely displaced to the right. In our hands, the study of the conformational behavior of **1** in stronger acids was not possible due to extensive decomposition of the dithiane.

(32) Streitwieser, A., Jr.; Heathcock, C. H. "Introduction of Organic Chemistry", 2nd ed.; Macmillan: New York, 1981; p 1197.

(33) We are not aware of any pK_a determination of protonated phosphoryl acids. By comparison, protonated dimethylsulfoxide has $pK_a = 0$.[32]

(34) Prepared according to the method of: Bost, R. W.; Constable, E. W. *Org. Synth. Collect. Vol. II* **1943**, 610–611.

(35) Conformational inversion of the ring in **6**, **8**, and **9** leads to a highly unfavorable syn-diaxial disposition of 1,3 substituents. Inversion in **7** places the methyl group axial (unfavorable by ca. 1.8 kcal/mol[29]) and the diphenylphosphinoyl group equatorial (unfavorable by ca. 1.4 kcal/mol; vide infra); therefore, the energy content of this form exceeds 3.0 kcal/mol, which corresponds to a negligible contribution at room temperature (<1%).

(36) Levy, G. C.; Nelson, G. L. "Carbon-13 NMR for Organic Chemists"; Wiley-Interscience: New York, 1972; Chapter 4.

between the P^V atom and aromatic systems are quite sizable,[37] the analysis of the ^{13}C NMR spectra of **1–3** was undertaken (Table IV). A most interesting observation suggests some form of *electron transfer to the axial phosphinoyl group*. Indeed, the chemical shifts for the ortho and para carbons in the axial isomers **1** and **3** appear at significantly higher fields than those in equatorial **2**. By contrast, the signal for the meta carbons in **1**, **2**, and **3** is essentially constant. These results are indicative of increased electron density at phosphorus in the axial isomers. Because the crystallographic data are contrary to a $n_S \rightarrow \sigma^*_{C-P}$ mechanism (vide supra), an alternative explanation is called for.

In view of the importance of through-space 2p–3d overlap effects between methoxy or dimethylamino groups and phosphorus in various organophosphorus compounds,[38] through-space 3p–3d electron donation from sulfur to phosphorus might help to account for the preferred axial orientation of the phosphorus moiety in **1**.[39] The P–S distance of ca. 3.0 Å observed in **1**-ax is much less than the sum of the van der Waals radii (3.75 Å) of P and S, and therefore a bonding interaction may be operative. We are presently investigating other systems related to **1–3**, whose conformational behavior might establish this point.

Conclusion

The conformational behavior of **1** suggests that several factors may be responsible for the large predominance of **1**-ax over **1**-eq. In particular, the erratic response to solvent changes clearly indicates that a dipole/dipole interaction is not the sole operative mechanism causing this strong anomeric effect. The influence of protic solvents (especially trifluoroacetic acid) and the conformational behavior of **5** imply an attractive interaction between the phosphoryl oxygen and the axial hydrogens at C(4,6). In addition, ^{13}C NMR data insinuate that an electron-transfer mechanism may also be responsible for the lower energy of the axial isomers.

Experimental Section

General Information. Proton NMR spectra were recorded on Varian EM-360 (60 MHz) or Varian EM-390 (90 MHz) spectrometers. Carbon-13 NMR spectra were recorded on Varian XL-100 (25.12 MHz) or Jeol FX-90Q (22.9 MHz) instruments operated in pulsed Fourier transform mode and locked on solvent deuterium. Samples were prepared as 5–10% solutions in $CDCl_3$ with 2–5% Me_4Si as internal reference in 5- or 10-mm o.d. tubes.

Flasks, stirring bars, and hypodermic needles used for the generation and reactions of alkyllithiums were dried for ca. 12 h at 120 °C and allowed to cool in a desiccator over anhydrous calcium sulfate. Anhydrous solvents were obtained by distillation from benzophenone ketyl.[40] The *n*-butyllithium employed was titrated according to the methods of Kofron and Baclawski[41] or Juaristi et al.[42] Melting and boiling points are uncorrected.

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

2-[1,3]Dithianyldiphenylphosphine Oxide (1). One gram of 1,3-dithiane (8.33 mmol, recently sublimed) was placed in a 25-mL round-bottom flask provided with a rubber septum before the addition of 20 mL of THF under nitrogen. The flask was immersed in a carbon tetrachloride–dry ice bath (ca. −20 °C) and then 6.67 mL of 1.5 M *n*-BuLi in hexane (20% excess) was added. The reaction mixture was stirred at −20 °C for 1.5 h and then treated with 1.84 g (8.33 mmol) of chlorodiphenylphosphine in 15 mL of THF and 1 g of TMEDA (8.5 mmol). The reaction mixture was stirred at −20 °C for 1.5 h and at room temperature during an additional 3 h and then quenched with saturated ammonium chloride. Extraction with chloroform and the usual workup procedure yielded a yellowish solid, which was recrystallized from benzene to afford 1.07 g (40%) of **1** as white crystals: mp 242–243 °C; ^1H NMR (90 MHz, $CDCl_3$) δ 2.05 (m, 2 H), 2.5 (d of t, J_{gem} = 14.4 Hz, J_{gauche} = 4.5 Hz, 2 H), 3.7 (m, 2 H), 4.0 (d, $^2J_{P-C-H}$ = 6.0 Hz, 1 H), 7.3–8.0 (m, 10 H); ^{31}P NMR (36.23 MHz, $CDCl_3$) δ 34.06; ^{13}C NMR data in Table IV.

Anal. Calcd for $C_{16}H_{17}OPS_2$: C, 59.98; H, 5.35; P, 9.67; S, 20.01. Found: C, 60.16; H, 5.30; P, 9.56; S, 20.18.

***r*-2-(Diphenylphosphinoyl)-*c*-4,*c*-6-dimethyl-1,3-dithiane (2).** See the Experimental Section in ref 23. ^{31}P NMR (36.23 MHz, $CDCl_3$) δ 28.90.

Anal. Calcd for $C_{18}H_{21}OPS_2$: C, 62.04; H, 6.07. Found: C, 61.97; H, 6.14.

***r*-2-(Diphenylphosphinoyl)-*t*-4,*t*-6-dimethyl-1,3-dithiane (3).** **2** (130 mg, 0.37 mmol) was placed in a 25-mL round-bottom flask provided with a rubber septum, and 7 mL of THF was added under nitrogen. The flask was immersed in a carbon tetrachloride–dry ice bath (ca. −20 °C) and then 0.3 mL of 1.3 M *n*-BuLi in hexane (5% excess) was added. The reaction mixture was stirred at −20 °C for 1.5 h and then quenched with saturated ammonium chloride. Extraction with chloroform and the usual workup procedure yielded 103 mg (79.2%) of **3** as white crystals: mp 270–272 °C; ^1H NMR (90 MHz, $CDCl_3$) δ 1.10 (d, $^3J_{CH_3-C-H}$ = 6.6 Hz, 6 H), ca. 1.3 (d of t, 1 H), 2.06 (d of t, J_{gem} = 14.1 Hz, J_{gauche} = 2.5 Hz, 1 H), 3.85 (m, 2 H), 4.11 (d, $^2J_{P-C-H}$ = 4.2 Hz, 1 H), 7.35–7.95 (m, 10 H); ^{31}P NMR (36.23 MHz, $CDCl_3$) δ 34.77; ^{13}C NMR data in Table IV; IR 1181 (vs) cm^{-1}; MS, *m/e* 348 (M^+), 201 (M^+ − 147), 147 (M^+ − 201).

Anal. Calcd for $C_{18}H_{21}OPS_2$: C, 62.04; H, 6.07. Found: C, 61.93; H, 6.13.

5-Methyl-1,3-dithiane. A solution of 1.7 g (13.9 mmol) of 2-methyl-1,3-propanedithiol (prepared as indicated in Scheme V) and 1.06 g (13.9 mmol) of dimethoxymethane in 3 mL of chloroform was added dropwise to a boiling solution of 3.81 g (26.8 mmol) of boron trifluoride etherate in 8.5 mL of chloroform. The reaction mixture was refluxed during 2 h and then washed with water, aqueous 20% potassium carbonate, and water again. The usual workup procedure afforded the desired product as a clear liquid, which was distilled in a Kugelrohr apparatus, bp 35–43 °C (0.3 mm), yield 0.7 g (38%): ^1H NMR (90 MHz, $CDCl_3$) δ 1.06 (d, $^3J_{CH_3-C-H}$ = 6.6 Hz, 3 H), 2.05 (m, 1 H), 2.60 (m, 4 H), 3.47 (*A*B, J_{gem} = 13.9 Hz, J_W = 1.5 Hz, 1 H), 3.88 (A*B*, J_{gem} = 13.9 Hz, 1 H).

***trans*-2-(Diphenylphosphinoyl)-5-methyl-1,3-dithiane (4).** The procedure described for the preparation of **1** (vide supra) was carried out with 192 mg (1.44 mmol) of 5-methyl-1,3-dithiane to afford 55 mg (13%) of **4** as white needles: mp 260–262 °C; ^1H NMR (90 MHz, CF_3CO_2H) δ 1.07 (d, $^3J_{CH_3-C-H}$ = 6.6 Hz, 3 H), 1.93 (m, 1 H), 2.75 (m, 4 H), 5.22 (d, $^2J_{P-C-H}$ = 12.9 Hz, 1 H), 7.46–8.18 (m, 10 H).

Method of Equilibration of Diastereomers (2 ⇌ 3). The equilibrium was approached from both sides; sodium ethoxide was the catalyst. The progress of the equilibration was conveniently monitored by ^1H NMR spectroscopy. For this purpose, 25–30 mg of the dithiane was placed in a 20-mL ampule and dissolved in 10 mL of ethanolic sodium ethoxide. The ampule was sealed and submerged in a constant temperature bath until equilibrium was reached. Quenching was effected by pouring the equilibrating solution into aqueous HCl. The dithianes were then extracted with chloroform, dried, evaporated, and transferred into 5-mm NMR tubes for analysis.

2-[1,3,5]Trithianyldiphenylphosphine Oxide (5). 1,3,5-Trithiane[34] (600 mg, 4.34 mmol, freshly recrystallized) was placed in a 100-mL round-bottom flask provided with a rubber septum before the addition of 65 mL of diglyme under nitrogen. The flask was immersed in a carbon tetrachloride–dry ice bath (ca. −20 °C), and then 5.8 mL of 1.5 M *n*-BuLi in hexane (8.68 mmol, 100% excess) was added. The reaction mixture was stirred at −20 °C for 1.5 h and then transferred to another flask containing 0.70 mL (0.86 g, 3.9 mmol) of chlorodiphenylphosphine and 0.65 mL (0.5 g, 4.3 mmol) of *N,N,N',N'*-tetramethylethylenediamine dissolved in 35 mL of diglyme. The reaction mixture was stirred at −20 °C for 3 h and at room temperature during an additional 1 h and then quenched with saturated ammonium chloride. Extraction with ethyl acetate and the usual workup procedure yielded a solid, which was crystallized from acetone as a mixture of the starting trithiane and the desired product. Final purification was achieved by flash chromatography[43] of this material [ethyl acetate–hexane (1:3)]. **5** was recrystallized from acetone to afford 59.8 mg (4.1%) of white crystals: mp 263–264 °C; ^1H NMR (90 MHz, CD_3SOCD_3) δ 3.87 (A_2B_2, J_{gem} = 14.4 Hz, 2 H), 5.23 (A_2B_2, J_{gem} = 14.4 Hz, 2 H), 5.52 (d, $^2J_{P-C-H}$ = 6.9 Hz, 1 H),

(37) Modro, T. A. *Can J. Chem.* **1977**, *55*, 3681–3685.

(38) See, for example: McEwen, W. E.; Smalley, A. W.; Sullivan, C. E. *Phosphorus* **1972**, *1*, 259–263. McEwen, W. E.; Fountaine, J. E.; Schulz, D. N.; Shiau, W.-I. *J. Org. Chem.* **1976**, *41*, 1684–1690. McEwen, W. E.; Smith, J. H.; Woo, E. J. *J. Am Chem. Soc.* **1978**, *100*, 7312–7317. McEwen, W. E.; Janes, A. B.; Knapzyk, J. W.; Kyllingstad, V. L.; Shiau, W.-I.; Shore, S.; Smith, J. H. *Ibid.* **1978**, *100*, 7304–7311. McEwen, W. E.; Cooney, J. V. *J. Org. Chem.* **1983**, *48*, 983–987.

(39) We are grateful to Professor McEwen, University of Massachusetts, for this suggestion.

(40) Brown, H. C. "Organic Synthesis via Boranes"; Wiley: New York, 1975; p 256.

(41) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.

(42) Juaristi, E.; Martinez-Richa, A.; Garcia-Rivera, A.; Cruz-Sánchez, J. S. *Ibid.* **1983**, *48*, 2603–2606.

(43) Still, W. C.; Kahn, M.; Mitra, A. *Ibid.* **1978**, *43*, 2923–2925.

7.4–8.1 (m, 10 H); MS, *m/e* 338 (M^+), 201 ($M^+ - 137$), 91 ($M^+ - 247$), 77 ($M^+ - 261$), 45 ($M^+ - 293$).

Anal. Calcd for $C_{15}H_{15}OPS_3$: C, 53.23; H, 4.46. Found: C, 53.16; H, 4.55.

***cis*-2-(Diphenylphosphinoyl)-4-methyl-1,3,5-trithiane (6).** 2-Methyl-1,3,5-trithiane[44,45] (152 mg, 1 mmol, freshly sublimed) was placed in a 50-mL round-bottom flask provided with a rubber septum before the addition of 30 mL of THF under nitrogen. The flask was immersed in an acetone–dry ice bath at −50 °C and then 0.8 mL of 1.25 M *n*-BuLi in hexane (1 mmol) was added. The reaction mixture was stirred at −50 °C for 1.5 h and then transferred to another flask containing 0.18 mL (0.22 g, 1 mmol) of chlorodiphenylphosphine and 0.15 mL (0.12 g 1 mmol) of *N,N,N',N'*-tetramethylethylenediamine dissolved in 15 mL of THF. The reaction mixture was stirred at −20 °C for 6 h and at room temperature during an additional 6 h and then quenched with saturated ammonium chloride. Extraction with ethyl acetate and the usual workup procedure yielded a solid which was recrystallized from chloroform–ether (95:5) to afford 78.4 mg (22.5%) of **6** as white crystals: mp 234–236 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.51 (d, $^3J_{CH_3-C-H}$ = 6.6 Hz, 3 H), 4.05 (d of d, J_{gem} = 14.4 Hz, $^4J_{H/P}$ = 4.5 Hz, 1 H), 4.38 (q, $^3J_{CH_3-C-H}$ = 6.6 Hz, 1 H), 4.45 (d, J_{gem} = 14.4 Hz, 1 H), 5.33 (d, $^2J_{P-C-H}$ = 15.0 Hz, 1 H), 7.4–8.1 (m, 10 H); MS, *m/e* 352 (M^+), 247 ($M^+ - 105$), 201 ($M^+ - 151$), 151 ($M^+ - 201$), 77 ($M^+ - 275$).

Anal. Calcd for $C_{16}H_{17}OPS_3$: C, 54.52; H, 4.86. Found: C, 54.30; H, 4.86.

***trans*-2-(Diphenylphosphinoyl)-4-methyl-1,3,5-trithiane (7).** **6** (20 mg, 0.056 mmol) was placed in a 10-mL round-bottom flask provided with a rubber septum and 5 mL of THF was added under nitrogen. The flask was immersed in a carbon tetrachloride–dry ice bath (ca. −20 °C) and then 0.05 mL of 1.25 M *n*-BuLi in hexane (0.062 mmol, 10% excess) was added. The reaction mixture was stirred at −20 °C for 1.5 h and then quenched with saturated ammonium chloride. Extraction with ethyl acetate and the usual workup procedure yielded 16 mg (80%) of **7** as white crystals: mp 228–230 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.41 (d, $^3J_{CH_3-C-H}$ = 7.2 Hz, 3 H), 3.61 (*A*B, J_{gem} = 15.0 Hz, 1 H), 4.33 (d, $^2J_{P-C-H}$ = 6.0 Hz, 1 H), 5.56 (q, $^3J_{CH_3-C-H}$ = 7.2 Hz, 1 H), 5.62 (A*B*, J_{gem} = 15.0 Hz, 1 H), 7.4–8.0 (m, 10 H).

Anal. Calcd for $C_{16}H_{17}OPS_3$: C, 54.52; H, 4.86. Found: C, 54.25; H, 4.66.

***r*-2-(Diphenylphosphinoyl)-*c*-4,*c*-6-dimethyl-1,3,5-trithiane (8).** *cis*-2,4-Dimethyl-1,3,5-trithiane[45] (312 mg, 1.87 mmol, recently sublimed) was placed in a 100-mL round-bottom flask provided with a rubber septum before the addition of 50 mL of THF under nitrogen. The flask was immersed in an acetone–dry ice bath at −60 °C and then 1.5 mL of 1.25 M *n*-BuLi in hexane (1.88 mmol) was added. The reaction mixture was stirred at −60 °C for 1.5 h and then transferred to another flask containing 0.33 mL (0.41 g, 1.87 mmol) of chlorodiphenylphosphine and 0.28 mL (0.22 g, 1.87 mmol) of *N,N,N',N'*-tetramethylethylenediamine dissolved in 30 mL of THF. The reaction mixture was stirred at −20 °C for 6 h and at room temperature during an additional 6 h and then quenched with saturated ammonium chloride. Extraction with ethyl acetate and the usual workup procedure yielded a solid, which was crystallized from methanol to afford 135 mg (20%) of white crystals: mp 245–246.5 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.54 (d, $^3J_{CH_3-C-H}$ = 6.6 Hz, 6 H), 4.15 (q, $^3J_{CH_3-C-H}$ = 6.9 Hz, 2 H), 5.04 (d, $^2J_{P-C-H}$ = 17.1 Hz, 1 H), 7.4–8.1 (m, 10 H); MS, *m/e* 366 (M^+), 306 ($M^+ - 60$), 201 ($M^+ - 165$), 165 ($M^+ - 201$).

Anal. Calcd for $C_{17}H_{19}OPS_3$: C, 55.71; H, 5.22. Found: C, 55.42; H, 5.37.

***r*-2-(Diphenylphosphinoyl)-*t*-4,*t*-6-dimethyl-1,3,5-trithiane (9).** **8** (25 mg, 0.069 mmol) was placed in a 10-mL round-bottom flask provided with a rubber septum, and 5 mL of THF was added under nitrogen. The flask was immersed in a carbon tetrachloride–dry ice bath (ca. −20 °C) and then 0.055 mL of 1.25 M *n*-BuLi in hexane (0.069 mmol) was added. The reaction mixture was stirred at −20 °C for 1 h and then quenched with saturated ammonium chloride. Extraction with ethyl acetate and the usual workup procedure yielded 22 mg (85.9%) of **9** as white crystals: mp 238–239.5 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.43 (d, $^3J_{CH_3-CH}$ = 6.6 Hz, 6 H), 4.47 (d, $^2J_{P-C-H}$ = 6.0 Hz, 1 H), 5.40 (q, $^3J_{CH_3-C-H}$ = 6.6 Hz, 2 H), 7.4–8.0 (m, 10 H).

Anal. Calcd for $C_{17}H_{19}OPS_3$: C, 55.71; H, 5.22. Found: C, 56.01; H, 5.28.

Acknowledgment. We are grateful to Professor E. L. Eliel for several useful discussions, to J. Espiñeira and G. Uribe for recording the FT NMR spectra, to Professor R. O. Hutchins for a generous gift of *cis*-4,6-dimethyl-1,3-dithiane, and to CONACYT (México) for partial financial support.

Registry No. **1**, 83476-36-2; **2**, 83463-92-7; **3**, 83509-98-2; **4**, 100763-22-2; **5**, 100763-23-3; **6**, 100763-24-4; **7**, 100763-25-5; **8**, 100763-26-6; **9**, 100838-26-4; $CDCl_3$, 865-49-6; CD_3CO_2D, 1186-52-3; CF_3CO_2D, 599-00-8; CD_2Cl_2, 1665-00-5; CD_3COCD_3, 666-52-4; CD_3OD, 811-98-3; DMF-d_7, 4472-41-7; CD_3CN, 2206-26-0; Me_2SO-d_6, 2206-27-1; 1,3-dithiane, 505-23-7; chlorodiphenylphosphine, 1079-66-9; 5-methyl-1,3-dithiane, 38761-25-0; 2-methyl-1,3-propanedithiol, 5337-95-1; 2-methyl-1,3-propanediol, 2163-42-0; diethyl 2-methylpropanedioate, 609-08-5; 1,3,5-trithiane, 291-21-4; 2-methyl-1,3,5-trithiane, 24614-75-3; *cis*-2,4-dimethyl-1,3,5-trithiane, 35641-70-4.

(44) Fukunaga, M.; Sugawara, T.; Ōki, M. *Chem. Lett.* **1972**, 55–58.
(45) Seebach, D.; Corey, E. J.; Beck, A. *Chem. Ber.* **1974**, *107*, 367–379.