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ARTICLE *in* THE JOURNAL OF ORGANIC CHEMISTRY · NOVEMBER 1987

Impact Factor: 4.72 · DOI: 10.1021/jo00232a023

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Conformational Preference of the Diphenylthiophosphinoyl Group [$(C_6H_5)_2P(S)$] in Cyclohexane and in the 1,3-Dithian-2-yl Ring†[1]

Eusebio Juaristi,*[2a] Norma A. López-Núñez,[2a] Bertha A. Valenzuela,[2a] Lucía Valle,[2a] Rubén A. Toscano,[2b] and Manuel Soriano-García[2b]

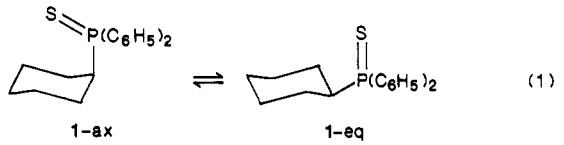
Departamento de Química, Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, 07000-México, D.F., México, and Instituto de Química, Universidad Nacional Autónoma de México, Ciudad Universitaria, 04510-México, D.F., México

Received April 23, 1987

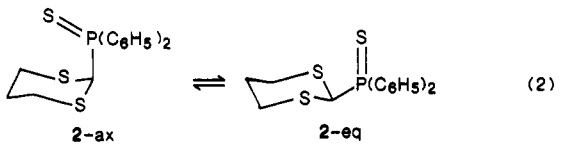
The conformational energy (*A* value) of the diphenylthiophosphinoyl group in cyclohexane was determined from the incorporation of ^{13}C NMR data of mobile *cis*-4-(diphenylthiophosphinoyl)-1-phenylcyclohexane (**4**) and conformationally fixed *cis*- (**5**) and *trans*-4-(diphenylthiophosphinoyl)-1-*tert*-butylcyclohexane (**6**) into Eliel's equation [$K = (\delta_{eq} - \delta_{mobile})/(\delta_{mobile} - \delta_{ax})$]. The strong equatorial preference observed, $\Delta G^0[P(S)Ph_2] = 3.61$ kcal/mol, lies in the little studied region between phenyl ($\Delta G^0 = 2.87$ kcal/mol) and *tert*-butyl ($\Delta G^0 = 4.9$ kcal/mol). Proton NMR spectroscopy and X-ray crystallographic studies demonstrate that the cyclohexane ring in the axially substituted derivative (**5**) remains in a chair conformation, both in the solid state and in solution. The conformational preference of the diphenylthiophosphinoyl group in the 1,3-dithian-2-yl ring was also determined by NMR analysis and by chemical equilibration of diastereomeric models. The slight predominance of axial 2-(diphenylthiophosphinoyl)-1,3-dithiane (**2-ax**) over **2-eq** reflects nonetheless the influence of a strong S–C–P anomeric interaction, worth several kilocalories/mole, and comparable with that observed in 2-(diphenylphosphinoyl)-1,3-dithiane (**7**). The implications of this result on the nature of the anomeric effect operating in the system are discussed.

Introduction

Continuing our analysis of the conformational behavior of phosphorus substituents in cyclohexyl[3] and in 1,3-dithian-2-yl heterocycles,[1,4] we report herein the conformational energy of the diphenylthiophosphinoyl group in both systems (eq 1 and 2), as determined from NMR studies, as well as chemical equilibration of diastereomeric models in the case of the dithianes.



(1)



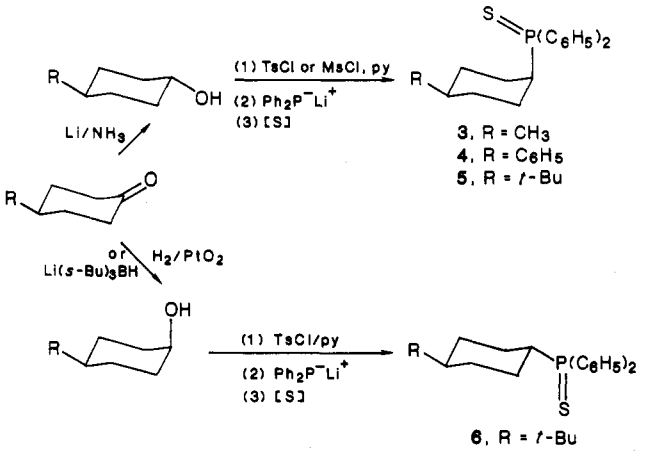
(2)

Results and Discussion

A. Conformational Preference of the Diphenylthiophosphinoyl Group in Cyclohexane. Mobile **3** and **4** and conformationally fixed **5** and **6** compounds were prepared as outlined in Scheme I. (*cis*-4-Phenylcyclohexyl)diphenylphosphine sulfide (**4**) could be prepared from the mesylate, but not from the tosylate precursor, a result in agreement with recent observations of Jackson et al.[5]

Table I contains the chemical shifts for the carbon atoms in **1** and **3–6** at 27 °C in $CDCl_3$. The assignments were based on anticipated shifts due to the inductive and field effects of the phosphinoyl moiety.[3,6] Salient features are the upfield shieldings observed at C(1) and C(3,5) in the axial isomer **5** vis-a-vis equatorial **6**, which amount to ca. δ 6 and ca. δ 4, respectively. The upfield shift at C(3,5) results from the well-known γ-gauche shielding effect,[7] and it is noted that this effect is slightly larger for the $Ph_2P(S)$ group than for the $Ph_2P(O)$ group.[8] On the other hand, the one-bond ^{13}C–^{31}P coupling is independent of the orientation (axial or equatorial) of the diphenylthiophosphinoyl group; a constant J value of 55–56 Hz is observed in **1** and **3–6**.

Scheme I



Spectroscopic comparison of **1** and **3** with conformationally fixed **5** and **6** by means of Eliel's equation[9] [$K = (\delta_{eq} - \delta_{mobile})/(\delta_{mobile} - \delta_{ax})$] indicated the equilibria **1**-ax $\rightleftharpoons$ **1**-eq and **3**-ax $\rightleftharpoons$ **3**-eq to be too highly biased, with a large (>95%) predominance of the equatorial conformer. Because the methyl substituent in **3** was intended as a counterpoise,[10] its lack of influence suggests a minimum

† Dedicated to Professor Ernest L. Eliel on the occasion of his 65th birthday.

(1) S–C–P Anomeric Interactions. 5. Part 4: Juaristi, E.; Valle, L.; Valenzuela, B. A.; Aguilar, M. A. *J. Am. Chem. Soc.* **1986**, *108*, 2000–2005.
(2) (a) Instituto Politécnico Nacional. (b) Universidad Nacional Autónoma de México.
(3) Juaristi, E.; López-Núñez, N. A.; Glass, R. S.; Petsom, A.; Hutchins, R. O.; Stercho, J. P. *J. Org. Chem.* **1986**, *51*, 1357–1360.
(4) (a) Juaristi, E.; Valle, L.; Mora-Uzeta, C.; Valenzuela, B. A.; Joseph-Nathan, P.; Fredrich, M. F. *J. Org. Chem.* **1982**, *47*, 5038–5039. (b) Juaristi, E.; Valenzuela, B. A.; Valle, L.; McPhail, A. T. *Ibid.* **1984**, *49*, 3026–3027.
(5) Jackson, W. R.; Thomson, R. J.; Mackay, M. F. *Aust. J. Chem.* **1985**, *38*, 111–118.
(6) Buchanan, G. W.; Bowen, J. H. *Can. J. Chem.* **1977**, *55*, 604–611.
(7) Cf.: Stothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic: New York, 1972. Wilson, N. K.; Stothers, J. B. *Top. Stereochem.* **1974**, *8*, 1–158.
(8) $\Delta\delta$[C(3,5)] = 3.69 for the cis/trans pair (4-*tert*-butylcyclohexyl)-diphenylphosphine oxide.[3] $\Delta\delta$[C(3,5)] = 4.28 for the **5**/**6** pair.
(9) Eliel, E. L. *Chem. Ind. (London)* **1959**, 568.
(10) Eliel, E. L.; Della, E. W.; Williams, T. H. *Tetrahedron Lett.* **1963**, 831–835. See also: Eliel, E. L.; Kandasamy, D. *J. Org. Chem.* **1976**, *41*, 3899–3904.

0022-3263/87/1952-5185$01.50/0

Table I. ^{13}C NMR Chemical Shifts (δ) for 1 and 3–6 at 22.49 MHz[a]

compd	C(1)	C(2,6)	C(3,5)	C(4)	C(ipso)	C(ortho)	C(meta)	C(para)	other
1	37.98	25.14	26.11	25.57	131.51	131.35	128.39	131.16	
3	38.09	19.45	31.39	26.65	131.62	131.40	128.45	131.21	*b*
4	36.27	22.60	29.81	38.83	132.33	131.46	128.43	131.06	*c*
5	32.32	24.38	22.65	45.29	132.65	131.27	128.31	131.05	*d*
6	37.79	25.52	26.92	47.08	131.62	131.27	128.37	131.05	*e*

[a] 27 °C in $CDCl_3$. [b] CH_3, 17.28. [c] Phenyl substituent: C(ipso), 145.36; C(ortho), 127.42; C(meta), 128.26; C(para), 125.64. [d] $(CH_3)_3C$, 27.47; $(CH_3)_3C$, 32.67. [e] $(CH_3)_3C$, 27.30; $(CH_3)_3C$, 32.18.

Table II. Temperature Effect on the ^{13}C NMR (22.49 MHz) Chemical Shifts (δ) for the Aliphatic Carbons in 5 at 27 °C and in CD_2Cl_2

T, °C	C(1)	C(2,6)	C(3,5)	C(4)	$(CH_3)_3C$	$(CH_3)_3C$
27	32.69	24.65	23.02	45.62	27.63	32.88
0	32.48	24.70	22.97	45.67	27.63	32.94
−27	32.53	24.76	23.02	45.72	27.63	32.94
−65	32.10	24.87	22.83	45.83	27.58	32.88
−90	31.70	25.08	22.75	46.05	27.52	32.94
$\Delta\delta$(+27 to −90)	−0.99	+0.43	−0.27	+0.43	−0.11	~0

Table III. Lanthanide-Induced Shifts (LIS) (δ) on the ^{13}C NMR (22.49-MHz) Spectrum of 5 after the Addition of Eu(fod)$_3$ in CD_2Cl_2 and at 27 °C

Eu(fod)$_3$, equiv	C(1)	C(2,6)	C(3,5)	C(4)	$(CH_3)_3C$	$(CH_3)_3C$
0	32.89	24.70	23.13	45.67	27.68	32.99
0.1	33.02	24.87	23.24	45.89	27.74	33.10
0.3	33.11	25.03	23.33	45.94	27.79	33.10
0.6	33.29	25.19	23.49	46.10	27.85	33.26
$\Delta\delta$	0.40	0.49	0.36	0.43	0.17	0.27

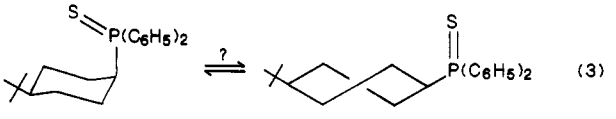
conformational energy (*A* value) of 3.5 kcal/mol for the diphenylthiophosphinoyl group: $-\Delta G^0(CH_3)$ = 1.74 kcal/mol[11] plus >1.76 kcal/mol from the >95:5 **3**-eq/**3**-ax ratio at 27 °C.

An equilibrium constant closer to unity was observed for **4**, which incorporates a phenyl [$-\Delta G^0(C_6H_5)$ = 2.87 kcal/mol[12]] as the counterpoise group; this permitted a more precise calculation of ΔG^0. With **4**, the chemical shifts for C(1) offered the best signal spread and were convenient for incorporation into Eliel's equation:[13] K = (37.79 − 36.57)/(36.57 − 32.32) = 0.287, giving a $\Delta G^0(4_{eq} \rightleftharpoons 4_{ax})$ value of 0.74 kcal/mol, and therefore $-\Delta G^0[Ph_2P(S)]$ = 3.61 kcal/mol at 27 °C.[15]

Direct observation of the two conformers **4**-eq and **4**-ax was possible at low temperature (−102 °C, THF-d_8) by ^{31}P NMR spectroscopy (^1H or ^{13}C NMR spectra at this temperature were not useful). The equilibrium constant K(**4**-ax ⇌ **4**-eq) = 2.17 was readily obtained by measurement of the signal intensities at δ 44.76 (**4**-ax) and δ 48.105 (**4**-eq). In this way, $-\Delta G^0_{-102°C}$(**4**-ax ⇌ **4**-eq) = 0.26 kcal/mol; assuming additivity, this implies $\Delta G^0[P(S)(C_6H_5)_2]$ = 3.13 kcal/mol.[12] From the conformational free energy differences at room temperature (27 °C) and at −102 °C, a ΔS^0 = +3.7 Gibbs and $-\Delta H^0$ = 2.50 kcal/mol are obtained. The large entropy term, as well as the observation of Dreiding models, suggests that the axial diphenylthiophosphinoyl group is conformationally constrained to rotamers with the P–S bond above the cyclohexane ring, whereas an equatorial diphenylthiophosphinoyl substituent is apparently free to fully rotate around the C–P bond.[3]

The conformational energy (*A* value) for the diphenylthiophosphinoyl group of 3.61 kcal/mol is remarkably large and falls in the scarcely populated region between phenyl ($-\Delta G^0$ = 2.87 kcal/mol)[12,16] and *tert*-butyl ($-\Delta G^0$ = 4.9 kcal/mol).[17,18] By comparison, the smaller conformational energy of the diphenylphosphinoyl in cyclohexane, $-\Delta G^0[Ph_2P(O)]$ = 2.74 kcal/mol,[3] reflects the different steric demand of the P=O vs P=S groups, since rotamers with the phenyl rings above the cyclohexane must be too high in energy (see ref 3 and below).

Because it has been shown that a cyclohexane with an axial *tert*-butyl group forces an equilibrium between the chair and flexible (boat, twist) conformations,[19] it became of interest to ascertain whether the syn-diaxial interactions present in axial **5** are relieved by adoption of twist forms (eq 3). Considering that these flexible forms have higher



(3)

entropy than does the chair form, it could be expected that an equilibrium such as the one depicted in eq 3 would shift to the left side (chair form) at lower temperature because of lesser influence of the $T\Delta S^0$ term on ΔG^0. Table II presents the ^{13}C chemical shifts for the aliphatic carbons in **5** as a function of temperature (+27 to −90 °C range). The relatively small effect of temperature on the chemical shifts recorded (Table II) argues for a negligible contribution of nonchair forms in the conformational behavior of **5**. This conclusion is supported by a proton NMR experiment in which the Eu(fod)$_3$ shift reagent was added

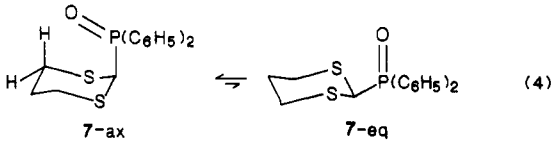
(11) Booth, H.; Everett, J. R. *J. Chem. Soc., Chem. Commun.* **1976**, 278–279.
(12) Eliel, E. L.; Manoharan, M. *J. Org. Chem.* **1981**, *46*, 1959–1962.
(13) The chemical shift for C(1) in the mobile isomer has been slightly corrected (δ +0.3) because of the upshielding effect of similar magnitude observed at C(4) in phenylcyclohexane relative to cyclohexane.[14]
(14) Juaristi, E. Ph.D. Dissertation, University of North Carolina at Chapel Hill, 1977; pp 230–231.
(15) Application of ^{31}P NMR data on **1** and **3**–**6** to Eliel's equation was not feasible due to the very small range of chemical shifts observed in the axial (δ 48.81) and equatorial (δ 49.52) models **5** and **6**.
(16) Garbisch, E. W., Jr.; Patterson, D. B. *J. Am. Chem. Soc.* **1963**, *85*, 3228–3231. These authors suggested a value of 3.0 kcal/mol.
(17) Manoharan, M.; Eliel, E. L. *Tetrahedron Lett.* **1984**, *25*, 3267–3268.
(18) van der Graaf, B.; Baas, J. M. A.; Wepster, B. M. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 268–273. These authors estimated a value of 4.7 kcal/mol by molecular mechanics.
(19) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Interscience: New York, 1965; pp 39, 470.

to a chloroformic ($CDCl_3$) solution of **5** (Table III). A remarkable observation is the significant lanthanide-induced shift (LIS) at C(4); this result would not be reasonable for a predominant twist conformation but agrees with a chair conformer, the diphenylthiophosphinoyl group being axial.

Additional validation of this conception comes from the stereostructure of **5** as obtained by single-crystal X-ray diffraction. A perspective view of the molecular structure is shown in Figure 1 (supplementary material). Tables IV–VII (supplementary material) present the appropriate Cartesian coordinates, bond distances, bond angles, and torsional angles. The cyclohexane ring exists in a chair conformation, with the thiophosphinoyl substituent at C(1) being axial. The phenyl rings on phosphorus are outside the ring, suggesting that the steric congestion that would be present if a phenyl group was inside the ring is more severe than the steric repulsion between the P=S sulfur and the syn-diaxial hydrogens at C(3,5).

This repulsion is nonetheless manifested as some bending of the C(1)—P and P=S bonds away from the ring [C(2)–C(1)–P = 113.7°, C(6)–C(1)–P = 114.5°, and C(1)–P–S = 116.9°] and by unusually large torsional angles in the C(3)–C(2)–C(1)–P and C(5)–C(6)–C(1)–P segments of 85.2° and 84.2°.

B. Conformational Preference of the Diphenylthiophosphinoyl Group in the 1,3-Dithian-2-yl Ring. 2-(Diphenylthiophosphinoyl)-1,3-dithiane (**2**) was prepared from 1,3-dithiane, *n*-butyllithium, and chlorodiphenylphosphine under nitrogen atmosphere; the phosphine intermediate was then treated with 1 equiv of elemental sulfur. Assignment of the proton NMR spectrum of **2** indicated a large (ca. δ 0.8) 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[20] is ca. 0.09.] This observation is important because finding $\Delta\delta_{ax/eq}$(H(4,6)) = 1.2 in 2-(diphenylphosphinoyl)-1,3-dithiane (**7**) led to the discovery of the strong S–C–P anomeric effect;[4a] at room temperature **7**-ax predominates in the 85:15 equilibrium depicted in eq 4, the axial phosphinoyl group deshielding the syn-diaxial hydrogens at C(4,6).



(4)

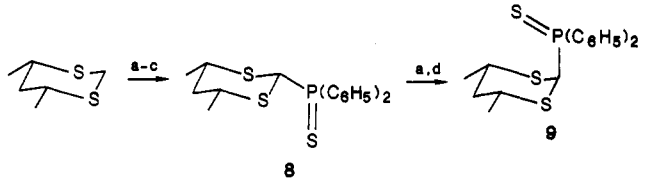
The smaller $\Delta\delta_{ax/eq}$(H(4,6)) found in **2** suggested a diminished predominance of **2**-ax over **2**-eq (eq 2) *or* a weaker deshielding influence by the P=S group relative to the P=O group.

In order to quantitate the **2**-ax ⇌ **2**-eq equilibrium, the conformationally fixed derivatives **8** and **9** were prepared from *cis*-4,6-dimethyl-1,3-dithiane[20] by making use of the highly stereoselective reaction of 2-lithio-1,3-dithianes with electrophiles (Scheme II).[21] The proton NMR spectra of **8** and **9** were compared with that of **2** (all three in $CDCl_3$). As expected,[1,4a] the coupling constants of H(2) to phosphorus in **2**, **8**, and **9** differ considerably: J = 9.0, 13.5, and 6.0 Hz, respectively. A first determination of the equilibrium constant in eq 2 was made by incorporation of the values of $^2J_{H(2)/P}$ in **2**, **8**, and **9** into $K = (J_8 - J_2)/(J_2 - J_9)$ = (13.5 − 9.0)/(9.0 − 6.0) = 1.5, which gives ΔG^0 = 0.24 kcal/mol for the equilibrium presented in eq 2; thus, **2**-ax predominates although to a lesser extent that **7**-ax does in the equilibrium shown in eq 4.

Chemical equilibration of conformationally fixed **8** and **9** confirmed this result; basic catalysis (ethanolic sodium ethoxide, Scheme III) successfully effected the desired **8** ⇌ **9** equilibration, and integration of the H(2) signals 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 VIII summarizes the experimental equilibrium constants for equilibria initiated from both sides; an average value of 0.05 ± 0.03 kcal/mol for the conformational free energy difference was calculated. This result was then averaged with that obtained by the weighted average coupling constant method (vide supra), and therefore a ΔG^0-[$(C_6H_5)_2P(S)$] = 0.15 ± 0.1 kcal/mol is obtained at room temperature.[22]

When the magnitude of the anomeric effect present in **2** is estimated as the difference of the free energy difference for the **2**-ax ⇌ **2**-eq equilibrium and the conformational energy for the same substituent in cyclohexane,[24,25] a

Scheme II[a]



[a] Reagents: (a) *n*-BuLi, THF/TMEDA; (b) $ClP(C_6H_5)_2$; (c) powdered sulfur; (d) NH_4Cl, H_2O.

Scheme III

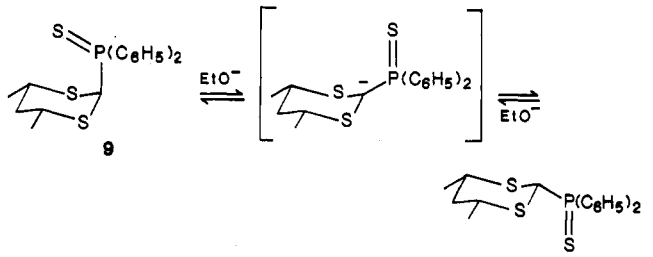


Table VIII. Chemical Equilibration of Anancomeric 8 and 9 with Ethanolic Sodium Ethoxide at 25 °C[a]

entry	starting diastereomer	9:8 ratio at equilibrium	K	$\Delta G°$, kcal/mol
1	**8**	50.9:49.1	1.04	0.02
2	**9**	53.4:46.6	1.14	0.08
3	**9**	51.4:48.6	1.05	0.04

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

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

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

(22) This value is somewhat smaller than the $\Delta G^0_{25°C}$[$(C_6H_5)_2P(S)$] = 0.50 kcal/mol recently obtained by Mikolajczyk, Graczyk, and Balczewski from the equilibration of *cis*- and *trans*-2-(diphenylthiophosphinoyl)-5-*tert*-butyl-1,3-dithianes.[23] In these compounds, the *tert*-butyl group at C(5) is intended to serve as a biasing substituent; however, it is known[20] that the preference of alkyl substituents at position 5 in 1,3-dithianes for the equatorial orientation is much less than in cyclohexane [thus, $-\Delta G^0$(*tert*-butyl) = 1.85 and 4.9[17] kcal/mol, respectively], and as a consequence the effectiveness of these compounds as conformationally fixed models can be questioned.

(23) Mikolajczyk, M.; Graczyk, P.; Balczewski, P. *Tetrahedron Lett.* **1987**, *28*, 573–576.

(24) See: Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: Berlin, 1983; pp 7–11.

(25) Of course, there is a well-recognized difficulty with evaluation of anomeric type effects in this fashion:[26] in the system at hand, the steric requirement of the diphenyl(thio)phosphinoyl group in the 1,3-dithian-2-yl ring might be smaller (because of the long C–S bonds) than the steric requirement in a cyclohexane.

Table IX. Room-Temperature ^{13}C NMR Signal Assignments in Compounds 2, 8, and 9 (δ from Me_4Si, $CDCl_3$)[a]

compd	C(2)	C(4,6)	C(5)	C(ipso)	C(ortho)	C(meta)	C(para)	other
2	42.38 (52)	28.42 (3.7)	24.57	131.14 (81)	131.75 (10)	128.18 (12)	131.62	
8	51.23 (52)	41.33 (8)	42.91	b	132.18 (9)	128.25 (12)	131.73	Me, 21.37
9	40.37 (54)	34.57	42.85 (2)	132.64 (82)	131.41 (9)	128.15 (11)	131.22	Me, 21.72

[a] C/P coupling constants in parentheses. [b] Obscured by base-line noise.

calculated value of 0.15 + 3.61 = 3.76 kcal/mol is obtained. This value is similar to that found in 7[1] and could indicate that the nature of the S–C–P anomeric effect is the same with P=O and P=S. That is, despite the bigger size and lower electronegativity of sulfur vis-a-vis oxygen the factor(s) responsible for the predominance of the axial substituent in 2 (or 8 ⇌ 9) and 7 seem(s) to be equally effective.

In this respect, while attractive interactions between the phosphoryl oxygen and the axial hydrogens at C(4,6) may be (at least partially) responsible for the stability of the axial isomers,[1,27] it is remarkable that the analysis of the ^{13}C NMR spectra of 2, 8, and 9 (Table IX) suggests some form of electron transfer to the axial thiophosphinoyl group. Indeed, as was the case with 7 and its anancomeric models,[1] the chemical shifts for the ortho and para carbons in the axial isomers 2 and 9 appear at significantly higher fields than those in equatorial 8. By contrast, the signal for the meta carbons in 2, 8, and 9 is essentially constant.[28] It has been suggested[1] that the ostensible increased electron density at phosphorus in the axial isomers may be the result of through-space 3p–3d electron donation from sulfur to phosphorus. We are presently experimenting with other systems related to 2 and 7 whose conformational behavior might shed additional light on this point, and hopefully theoretical chemistry will be helpful in this respect too.

Experimental Section

General Information. Proton NMR spectra were recorded on Varian EM-360 (60-MHz) or Varian EM-390 (90-MHz) spectrometers. ^{13}C and ^{31}P NMR spectra were recorded on a JEOL FX-90Q (22.49- and 36.23-MHz, respectively) instrument operated in pulsed Fourier transform mode and locked on solvent deuterium. ^{31}P NMR data are reported in δ from external phosphoric acid. Mass data were obtained on a Hewlett-Packard 5985-A spectrometer.

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.[29] The *n*-butyllithium employed was titrated according to the method of Juaristi et al.[30]

Melting points, determined with a Mel-Temp or an Electrothermal apparatus, are uncorrected.

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

Cyclohexyldiphenylphosphine Sulfide (1). Magnesium (0.67 g, 0.028 mol), a crystal of iodine, and 20 mL of diethyl ether were placed in a 100-mL round-bottom flask provided with a condenser, addition funnel, and a stirring bar. The cyclohexyl chloride (3 g, 25.1 mmol) dissolved in 10 mL of dry diethyl ether was added at such a rate as to maintain gentle reflux. A solution of chlorodiphenylphosphine (4.5 mL, 25.1 mmol) in 10 mL of tetrahydrofuran (THF) was then added dropwise, and the reaction mixture was stirred for 2.5 h at gentle reflux. The resulting whitish solution was then treated with 1.35 g (0.042 mol) of sulfur, and stirring was continued for an additional 2 h at gentle reflux. Quenching of the reaction was effected with saturated aqueous ammonium chloride. Extraction with methylene chloride and the usual workup procedure afforded the crude product, which was purified by recrystallization from hexane/methylene chloride (2:1) to afford 3.09 g (41% yield) of the pure product: mp 165–166.5 °C; ^1H NMR (90 MHz, CCl_4) δ 1.0–1.95 (m, 10 H, C(2–6)H), 2.45 (m, 1 H, C(1)H), 7.42 (m, 6 H, C(meta,para)H), 7.90 (m, 4 H, C(ortho)H); ^{13}C NMR in Table I; ^{31}P NMR δ 49.82; MS, *m/e* 300 (M^+). Anal. Calcd for $C_{18}H_{21}PS$: C, 71.97; H, 7.05. Found: C, 71.84; H, 6.81.

(1,3-Dithian-2-yl)diphenylphosphine Sulfide (2). 1,3-Dithiane (1 g, 8.33 mmol, freshly 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 2.206 g (10.0 mmol) of chlorodiphenylphosphine in 15 mL of THF and TMEDA (0.968 g, 8.33 mmol). The reaction mixture was stirred at −20 °C for 1.5 h and then transferred via cannula to another flask containing powdered sulfur (0.533 g, 8.33 mmol). Stirring was continued at −20 °C for 4 h and at room temperature during an additional 1 h, and then the reaction was quenched with saturated ammonium chloride. Extraction with chloroform and the usual workup procedure yielded a yellowish solid (1.32 g, 46.9% yield), which was crystallized from methanol to afford 1.2 g (42.8%) of 2 as white crystals: mp 177–178 °C; ^1H NMR (90 MHz, $CDCl_3$) δ 2.02 (m, 2 H), 2.68 (dt, J_{gem} = 13.8 Hz, J_{gauche} = 5.4 Hz, 2 H), 3.50 (m, 2 H), 4.73 nd, $^2J_{PCH}$ = 9 Hz, 1 H), 7.55 (m, 6 H), 8.02 (m, 4 H); ^{31}P NMR (36.23 MHz, $CDCl_3$, H_3PO_4 external reference) δ 48.81; ^{13}C NMR (22.49 MHz, $CDCl_3$) δ 24.65 (s, $CH_2(CH_2S)_2$, 28.41 (d, $^3J_{CP}$ = 4 Hz, 2 CH_2S), 42.50 (d, $^1J_{CP}$ = 52 Hz, SCHS), 128.34 (d, $^3J_{PC}$ = 12 Hz, meta C), 131.54 (d, $^1J_{CP}$ = 80 Hz, ipso C), ca. 131.70 (d, $^4J_{CP}$ = 2 H, para C), ca. 131.97 (d, $^2J_{CP}$ = 10 Hz, ortho C). Anal. Calcd for $C_{16}H_{17}PS_3$: C, 57.11; H, 5.09. Found: C, 57.03; H, 5.12.

(*cis*-4-Methylcyclohexyl)diphenylphosphine Sulfide (3). Lithium metal (0.5 g, 0.072 mol) and 50 mL of dry THF were placed in a 500-mL round-bottom flask provided with condenser, addition funnel, and a magnetic bar, and the mixture was heated to reflux before the dropwise addition of 3.86 g (3.14 mL, 17.5 mmol) of chlorodiphenylphosphine in 100 mL of dry THF. The orange-red mixture was refluxed for 1 h, and then the excess lithium was removed by transferring the solution via cannula, under positive pressure of nitrogen, to another flask capped with a rubber septum and submerged in a water–ice bath. *trans*-4-Methylcyclohexyl-*p*-toluenesulfonate (2.01 g, 7.5 mmol; prepared from *trans*-4-methylcyclohexanol[31] according to the usual procedure[32]) in 100 mL of dry THF was then added, and when the addition was completed, the cooling bath was removed, and the reaction mixture refluxed for 1 h. Treatment with sulfur (0.55 g, 17.2 mol; 2 h stirring), quenching with saturated aqueous ammonium chloride, extraction with ethyl acetate, and the usual workup procedure yielded the crude product, which was purified by flash chromatography[33] [ethyl acetate/hexane (70:30)] followed by recrystallization from hexane/methylene chloride (2:1) to afford 446 mg (19% yield) of the pure product: mp 162–164 °C; ^1H NMR

(26) Eliel, E. L.; Giza, C. A. *J. Org. Chem.* **1968**, *33*, 3754–3758.
(27) Mikolajczyk, M.; Balczewski, P.; Wroblewski, K.; Karolak-Wojciechowska, J.; Miller, A.; Wieczorek, M. W.; Antipin, M. Y.; Struchkov, Y. T. *Tetrahedron* **1984**, *40*, 4885–4892.
(28) Also, no variation in the ^{13}C NMR chemical shifts for the aromatic carbons in the cyclohexane analogues 1, 5, and 6 is observed (Table I).
(29) Brown, H. C. *Organic Synthesis via Boranes*; Wiley: New York, 1975; p 256.
(30) Juaristi, E.; Martínez-Richa, A.; García-Rivera, A.; Cruz-Sánchez, J. S. *J. Org. Chem.* **1983**, *48*, 2603–2606.
(31) Obtained by Birch reduction of the corresponding ketone: Huffman, J. W.; Charles, J. T. *J. Am. Chem. Soc.* **1968**, *90*, 6486–6492.
(32) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. I, pp 1179–1181.
(33) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(90 MHz, CCl_4), δ 0.98 (d, 3 H, CH_3), 1.0–2.1 (m, 9 H, C(2–6)H), 2.4 (m, 1 H, C(1)H), 7.42 (m, 6 H, C(meta,para)H), 7.92 (m, 4 H, C(ortho)H); ^{13}C NMR in Table I; ^{31}P NMR δ 49.72; MS, m/e 314 (M^+).

(*cis*-4-Phenylcyclohexyl)diphenylphosphine sulfide (4) was similarly prepared from *trans*-4-phenylcyclohexyl methanesulfonate (0.7 g, 2.75 mmol; prepared from *trans*-4-phenylcyclohexanol[31] according to the usual procedure[32]). The crude product was purified by crystallization from methanol to afford 506 mg (49.1% yield) of the desired product: mp 167–168 °C; ^1H NMR (90 MHz, $CDCl_3$) δ 1.3–3.0 (m, 10 H, C(1–6)H), 7.25 (m, 5 H, $C_6H_5C(1)$), 7.46 (m, 6 H, C(meta,para)H), 7.93 (m, 4 H, C(ortho)H); ^{13}C NMR in Table I; ^{31}P NMR δ 48.92; MS, m/e 376 (M^+). Anal. Calcd for $C_{24}H_{25}PS$: C, 76.56; H, 6.69. Found: C, 76.48; H, 6.65.

(*cis*-4-*tert*-Butylcyclohexyl)diphenylphosphine sulfide (5) was similarly prepared from *trans*-4-*tert*-butylcyclohexyl *p*-toluenesulfonate (2.33 g, 7.5 mmol; prepared from *trans*-4-*tert*-butylcyclohexanol[31] according to the usual procedure[32]). The desired product was purified by flash chromatography[33] [ethyl acetate/hexane (70:30)] and recrystallization from hexane/methylene chloride (2:1) to furnish 354 mg (13.2% yield) of pure **5**: mp 134–135 °C; ^1H NMR (90 MHz, CCl_4) δ 0.83 (s, 9 H, *t*-Bu), 1.2–2.2 (m, 9 H, C(2–6)H), 2.8 (m, 1 H, C(1)H), 7.45 (m, 6 H, C(meta,para)H), 7.95 (m, 4 H, C(ortho)H); ^{13}C NMR in Table I; ^{31}P NMR δ 48.81; MS, m/e 356 (M^+). Anal. Calcd for $C_{22}H_{29}PS$: C, 74.12; H, 8.20. Found: C, 74.32; H, 8.16.

(*trans*-4-*tert*-Butylcyclohexyl)diphenylphosphine sulfide (6) was similarly prepared from *cis*-4-*tert*-butylcyclohexyl *p*-toluenesulfonate (1.5 g, 4.2 mmol; prepared from *cis*-4-*tert*-butylcyclohexanol[34] according to the usual procedure[32]). The crude product was purified by recrystallization from hexane/methylene chloride (2:1) to afford 518 mg (30.3% yield) of pure **6**: mp 177–178 °C; ^1H NMR (90 MHz, $CDCl_3$) δ 0.83 (s, 9 H, *t*-Bu), 0.96–2.1 (m, 9 H, C(2–6)H), 2.5 (m, 1 H, C(1)H), 7.5 (m, 6 H, C(meta,para)H), 7.95 (m, 4 H, C(ortho)H); ^{13}C NMR in Table I; ^{31}P NMR δ 49.52; MS, m/e 356 (M^+). Anal. Calcd for $C_{22}H_{29}PS$: C, 74.12; H, 8.20. Found: C, 73.79; H, 7.96.

***rel*-2-(Diphenylthiophosphinoyl)-*cis*-4,*cis*-6-dimethyl-1,3-dithiane (8).** *cis*-4,6-Dimethyl-1,3-dithiane[21] (200 mg, 1.3 mmol) was placed in a dry round-bottomed flask provided with a magnetic stirring bar and capped with a rubber septum. The flask was flushed with nitrogen prior to the addition of 7 mL of dry THF via a cannula, after which the solution was cooled to −20 °C and *n*-butyllithium (1.0 mL of a 1.37 M hexane solution, 1.365 mmol, 5% excess) was syringed into it dropwise. The resulting solution was stirred for 90 min at −20 °C, following which it was added to a THF solution (ca. 10 mL) of chlorodiphenylphosphine (345 mg, 1.56 mmol, 20% excess) and tetramethylethylenediamine (151 mg, 1.3 mmol) also at −20 °C. The reaction mixture was stirred at this temperature for 90 min and then treated with 43 mg (1.3 mmol) of powdered sulfur. Stirring was continued for 4 h at −20 °C and 2 h at room temperature before quenching with saturated ammonium chloride. Extraction with $CHCl_3$ followed by the usual workup procedure and crystallization from methanol afforded 102 mg (49% yield) of **8** as a white solid: mp 213–215 °C; ^1H NMR (90 MHz, $CDCl_3$) δ 1.23 (d, $^3J_{CH_3CH}$ = 7.5 Hz, 6 H), 1.35 (m, 1 H), 2.06 (d of m, J_{gem} = 14.7 Hz, 1 H), 2.90 (m, 2 H), 5.03 (d, $^2J_{HCP}$ = 13.5 Hz, 1 H), 7.53 (m, 6 H), 8.03 (m, 4 H); ^{13}C NMR in Table IX; ^{31}P NMR δ 45.98. Anal. Calcd for $C_{13}H_{21}PS_3$: C, 59.31; H, 5.80. Found: C, 59.33; H, 5.90.

***rel*-2-(Diphenylthiophosphinoyl)-*trans*-4,*trans*-6-dimethyl-1,3-dithiane (9).** **8** (120 mg, 0.33 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, the usual workup procedure, and recrystallization from methanol afforded 60 mg (50% yield) of **9** as white crystals: mp 185–186 °C, ^1H NMR (90 MHz, $CDCl_3$) δ 1.13 (d, $^3J_{CH_3CH}$ = 7.5 Hz, 6 H), 1.30 (m, 1 H), 2.12 (dt, J_{anti} = 13.5 Hz, J_{gauche} = 2.5 Hz), 4.23 (m, 2 H), 4.60 (d, $^2J_{HCP}$ = 6.0 Hz, 1 H), 7.50 (m, 6 H), 7.96 (m, 4 H); ^{13}C NMR in Table IX; ^{31}P NMR δ 51.34.

Method of Equilibration of Diastereomers 8 ⇌ 9. 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.

Structural X-ray Analysis. A crystal measuring approximately 0.16 × 0.16 × 0.34 mm was used to collect intensity data on a Nicolet R3m four-circle diffractometer within the angular range $3.0 < 2\theta < 45°$, using monochromatic Mo Kα radiation and ω scan mode. Least-squares refinement of the setting angles of 25 reflections with a good distribution throughout reciprocal space provided the unit cell dimensions: triclinic, a = 6.577 (1), b = 10.829 (3), c = 15.024 (5) Å; α = 99.84 (3), β = 98.60 (2), γ = 91.97 (2)°; V = 1040.5 Å^3; F_{000} = 384; μ(Mo Kα) = 2.39 cm^{-1}; Z = 2; d_{calcd} = 1.136 g·cm^{-3}. Systematic absences indicated the triclinic space group $P\bar{1}$. Of the 2718 independent reflections measured and corrected for Lorentz and polarization effects, 794 had intensities less than $3\sigma(F_o)$ and were flagged as unobserved. The remaining 1924 reflections were used to solve and refine the structure.

Positions of all non-hydrogen atoms were located by the direct-methods program available as part of the SHELXTL package.[37] Idealized hydrogen positions were calculated and tied to the associated non-hydrogen positions through a riding model. Final refinement of 24 non-hydrogen atoms using anisotropic thermal parameters and 29 hydrogen atoms using fixed isotropic thermal parameters, U = 0.06 Å^2, gave residual values of R_1 = 0.0524 and R_2 = 0.0595 where $R_1 = \sum||F_o| - |F_c||\sum/||F_o|$ and $R_2 = |\sum_w(|F_o| - |F_c|)^2/\sum_w|F_o|^2|^{1/2}$.

Acknowledgment. We are grateful to Guillermo Uribe for recording the FT NMR spectra, to Humberto Bojórquez and Luis Velasco for recording the mass spectra, and to Laboratorios Pro-Salud, S.A., as well as COSNET (SEP, Mexico), for partial financial support.

Registry No. **1**, 6591-42-0; **2**, 107841-53-2; **3**, 110458-15-6; **4**, 110458-16-7; **5**, 110458-17-8; **6**, 110458-18-9; **8**, 110458-19-0; **9**, 110508-53-7; cyclohexyl chloride, 542-18-7; chlorodiphenylphosphine, 1079-66-9; 1,3-dithiane, 505-23-7; *trans*-4-methylcyclohexyl *p*-toluenesulfonate, 34866-36-9; *trans*-4-phenylcyclohexyl methanesulfonate, 110458-20-3; *trans*-4-*tert*-butylcyclohexyl *p*-toluenesulfonate, 7453-05-6; *cis*-4-*tert*-butylcyclohexyl *p*-toluenesulfonate, 7453-04-5; *cis*-4,6-dimethyl-1,3-dithiane, 22452-23-9.

Supplementary Material Available: Listings of the Cartesian coordinates (Table IV), bond distances (Table V), bond angles (Table VI), torsional angles (Table VII), anisotropic thermal parameters for all non-hydrogen atoms (Table X), isotropic thermal parameters for hydrogen atoms (Table XI), and nonbonded distances (Table XII) and an ORTEP drawing of **5** (10 pages). Ordering information is given on any current masthead page.

(34) Obtained by reduction of 4-*tert*-butylcyclohexanone with hydrogen over platinum oxide[35] or with Li(*s*-Bu)$_3$BH.[36]

(35) Eliel, E. L.; Ro, R. S. *J. Am. Chem. Soc.* **1957**, *79*, 5992–5994.

(36) Krishnamurthy, S.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 3383–3384.

(37) Sheldrick, G. M. *Nicolet SHELXTL Operations Manual*; Nicolet XRD: Cupertino, CA, 1981.