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Communications

Conformational Preference of the 2-Diphenylphosphinoyl Group in 1,3-Dioxane. Is There an O–C–P(O) Anomeric Effect?†

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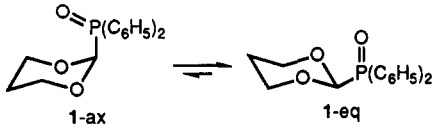
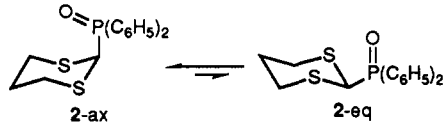
Summary: The use of counterpoise substituents permitted the quantitative determination of the large equatorial preference of the 2-diphenylphosphinoyl group in 1,3-dioxane, $\Delta G°_{307K}[P(O)Ph_2] = -3.23$ kcal/mol. This result contrasts strongly with the significant axial preference of the same group in the 1,3-dithiane ring (+1.0 kcal/mol). Nevertheless, evaluation of the different steric requirements in these heterocycles reveals that the magnitude of the O–C–P(O) and S–C–P(O) anomeric effects in the sulfur and oxygen heterocycles is quite similar, close to 3 kcal/mol.

Sir: Recently, the lack of manifestation of an anomeric effect in 2-diphenylphosphinoyl-1,3-dioxane (**1**) was reported,[1,2] i.e., the equatorial conformer predominates (eq 1).



(1)

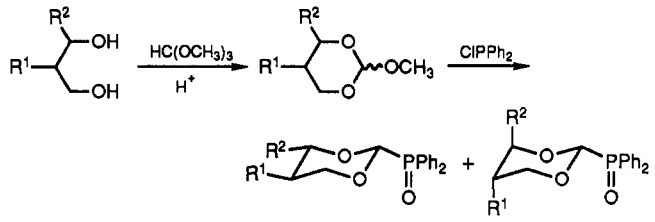
This result could be surprising at first sight in view of the strong axial preference of the 2-diphenylphosphinoyl group of 1,3-dithiane, $\Delta G°[P(O)Ph_2] = +1.0$ kcal/mol[3-5] (eq 2), and because anomeric effects involving second-row elements have been predicted to be much less important than those with first-row elements.[6,7]



(2)

†S–C–P Anomeric Interactions. 7.

Scheme I



R^1 = *t*-Bu, R^2 = H: *trans*-**3** + *cis*-**3** (4:1)

R^1 = H, R^2 = CH_3: *cis*-**4** + *trans*-**4** (5:1)

Nevertheless, because of the shorter C–O bonds (ca. 1.43 Å) relative to the C–S bonds (ca. 1.82 Å), the steric repulsion of the axial diphenylphosphinoyl group (*A* value = 2.74 kcal/mol)[8] could dominate over the O–C–P(O)

(1) Mikolajczyk, M. *Pure Appl. Chem.* **1987**, *59*, 983–988. Mokolajczyk, M.; Graczyk, P.; Wieczorek, M. W.; Bujacz, G.; Struchkov, Y. T.; Antipin, M. Y. *J. Org. Chem.* **1988**, *53*, 3609–3612.

(2) (a) Juaristi, E.; Aguilar, M. A.; Flores-Vela, A.; Valle, L. *Abstracts of Papers*; Third Chemical Congress of North America, Toronto, Canada; American Chemical Society: Washington, DC, 1988; ORGN-406. (b) Juaristi, E.; Flores-Vela, A.; Labastida, V.; Ordóñez, M. *J. Phys. Org. Chem.* **1989**, *2*, 349–358.

(3) Juaristi, E.; Valle, L.; Mora-Uzeta, C.; Valenzuela, B. A.; Joseph-Nathan, P.; Fredrich, M. F. *J. Org. Chem.* **1982**, *47*, 5038–5039.

(4) Juaristi, E.; Valle, L.; Valenzuela, B. A.; Aguilar, M. A. *J. Am. Chem. Soc.* **1986**, *108*, 2000–2005.

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

(6) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6393–6394.

(7) See, However: Juaristi, E.; González, E. A.; Pinto, B. M.; Johnston, J. B.; Nagelkerke, R. *J. Am. Chem. Soc.* **1989**, *111*, 6745–6749.

(8) Juaristi, E.; López-Núñez, N. A.; Glass, R. S.; Petsom, A.; Hutchins, R. O.; Stercho, J. P. *J. Org. Chem.* **1986**, *51*, 1357–1360.

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Table I. Ambient Temperature ^{13}C NMR Signal Assignments in Compounds 1–5 (ppm from Me_4Si ($CDCl_3$))[a]

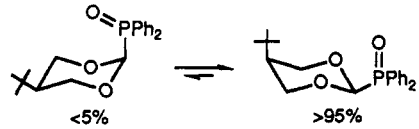
compd	C(2)	C(4)	C(5)	C(6)	C_{ipso}	C_{ortho}	C_{meta}	C_{para}	other
1[b]	101.35	67.85	25.64	67.85	129.47	131.80	127.82	131.72	–
	(118)	(9)		(9)	(101)	(8.5)	(12)		
2[c]	37.15	26.97	24.91	26.97	132.17	131.07	128.30	131.69	–
	(70)				(100)	(9)	(12)	(2.5)	
cis-3	100.14	67.88	43.02	67.88	129.14	131.95	127.97	131.91	*d*
	(115)	(9)		(9)	(99)	(10)	(12)		
trans-3	100.86	69.96	43.33	69.96	129.20	131.87	127.92	131.87	*e*
	(118)	(11)		(11)	(100)	(10)	(12)		
cis-4	101.37	74.76	33.33	68.11	129.74	132.25	128.16	132.01	*f*
	(119)	(10)		(11)	(100)	(9)	(12)	(2)	
trans-4	95.35	68.76	31.03	63.30	130.37	131.95	128.37	132.01	*g*
	(109)	(7)		(7)	(96)	(9)	(12)		
cis-5	107.25	72.45	33.01	66.64	–	–	–	–	*h*
trans-5	99.58	67.29	29.15	61.87	–	–	–	–	*i*

[a] C/P coupling constants in parentheses. [b] Taken from ref 2. [c] Taken from ref 3. [d] $(CH_3)_3C$, 28.42; $(CH_3)_3C$, 31.67. [e] $(CH_3)_3C$, 26.94; $(CH_3)_3C$, 30.24. [f] CH_3, 21.67. [g] CH_3, 18.29. [h] $(CH_3)_3C$, 24.56; $(CH_3)_3C$, 34.78; CH_3-C(4), 21.53. [i] $(CH_3)_3)C$, 24.50; $(CH_3)_3C$, 34.44; CH_3-C(4), 16.41.

anomeric effect in 1. A quantitative evaluation of the conformational preference of the phosphorus substituent was therefore necessary in order to establish the contribution of an anomeric effect, in any.

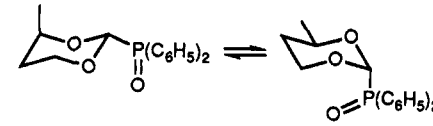
Results

cis- and *trans*-2-(diphenylphosphinoyl)-5-*tert*-butyl-1,3-dioxanes (*cis*- and *trans*-3) were prepared as shown in Scheme I. ^{13}C and ^{31}P NMR data for *cis*- and *trans*-3 (Table I) indicate that the *tert*-butyl group is completely (≳95%) equatorial in *trans*-3, but completely axial in the *cis* isomer (eq 3).[9] Because the conformational energy of the 5-*t*-Bu in 1,3-dioxane is 1.4 kcal/mol,[10] and because $\Delta G° > 1.7$ kcal/mol) in eq 3, a minimum $\Delta G°[P(O)Ph_2] \gtrsim 3.1$ kcal/mol, favoring 1-eq, is determined.



<5% >95% (3)

Better results were achieved in the 4-methyl series, where the methyl group acts as a more demanding counterpoise (2.87 kcal/mol).[10] The synthesis of *cis*- and *trans*-2-(diphenylphosphinoyl)-4-methyl-1,3-dioxane (*cis*- and *trans*-4) was carried out as shown in Scheme I. Most useful is the ^{13}C NMR chemical shift for the methyl group: 21.67 and 18.29 ppm in the cis and trans isomers, respectively. By comparison, $\delta(CH_3) = 16.41$ ppm in the pure axial methyl model *trans*-2-*tert*-butyl-4-methyl-1,3-dioxane (*trans*-5, Table I).[11] Application of Eliel's equation[12] [$K = (\delta_{eq} - \delta_{mobile})/\delta_{mobile} - \delta_{ax}) = (21.67 - 18.29)/(18.29 - 16.41) = 1.80$] provided $\Delta G°_{307K} = +0.36$ kcal/mol (eq 4), and therefore $\Delta G°_{307K}[P(O)Ph_2] = -3.23$ kcal/mol in the absence of the 4-methyl group (eq 1).



(4)

Discussion

The anomeric effect is usually defined as the *tendency* of an electronegative substituent to assume the axial rather than the equatorial orientation at anomeric carbons.[13] Manifestation of an anomeric effect in 1 would require that the magnitude of such effect overcomes the stringent steric hindrance experienced by axial 2-substituents. For example, the equatorial preference of a methyl group in cyclohexane amounts to 1.74 kcal/mol,[14] whereas it increases (by a factor of 2.2) to 3.9 kcal/mol in 2-methyl-1,3-dioxane.[10] Thus, the expected size of the diphenylphosphinoyl group in 1 is ca. 2.2 × 2.74 kcal/mol[8] = 6.0 kcal/mol.[15] The difference between this value and the one experimentally obtained, ca. 3.2 kcal/mol, affords an anomeric effect worth ca. 2.8 kcal/mol!

It is of interest to compare this value with that estimated in 2: it has been shown[16] that the $\Delta G°$(2-*tert*-butyl) in 1,3-dithianes is about 60% of $\Delta G°$(*tert*-butyl) in cyclohexane. Thus, the expected size of the diphenylphosphinoyl group in 2 is 60% of 2.74 kcal/mol,[8] which affords an anomeric effect equal to 1.0 + (0.60 × 2.74) = 2.64 kcal/mol.[15]

By the same token, a 2-methyl group in 1,3-oxathiane shows an equatorial preference of 3.25 kcal/mol,[17] larger by a factor of 1.87 than its *A* value. The expected equatorial preference of the 2-diphenylphosphinoyl group in 1,3-oxathiane is therefore 1.87 × 2.74 = 5.12 kcal/mol. The

(9) For comparison: $\delta(C(CH_3)_3) = 27.68$ ppm in *trans*-2-methyl-5-*tert*-butyl-1,3-dioxane; $\delta(C(CH_3)_3) = 29.71$ ppm in *cis*-2-methyl-5-*tert*-butyl-1,3-dioxane: Jones, A. J.; Eliel, E. L.; Grant, D. M.; Knoeber, M. C.; Bailey, W. F. *J. Am. Chem. Soc.* **1971**, *93*, 4772–4777. Perhaps even more significant, the ^{31}P NMR chemical shifts (36.23 MHz, $CDCl_3$) for *cis*- and *trans*-3 are identical, $\delta = 23.98$ ppm, showing the exclusively equatorial orientation of the diphenylphosphinoyl group in both isomers. (A 6–7 ppm downfield shift is observed for the axial phosphorus in the dithiane and oxathiane analogues).[2b]

(10) Eliel, E. L.; Knoeber, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 3444–3458.

(11) A mixture of *cis*- and *trans*-2-*tert*-butyl-4-methyl-1,3-dioxanes (*cis*- and *trans*-5) was prepared by condensation of (±)-1,3-butanediol and pivalaldehyde. See also Jones, et al. paper in ref 9 for the ^{13}C NMR spectrum of (neat) *cis*-5.

(12) Eliel, E. L. *Chem. Ind. (London)* **1959**, 568. This, of course, assumes that the only effect on the chemical shift of the 4-methyl group is conformational, which may not be true. Nevertheless, because of the one-sidedness of the equilibrium, a small error in *K* (which is near unity) will make relatively little difference to the $\Delta G°$ in the *absence* of the methyl group (−3.23 kcal/mol).

(13) Lemieux, R. U.; Chu, N. J. *Abstracts of Papers*; 133rd National Meeting of the American Chemical Society, San Francisco; American Chemical Society: Washington, DC, 1958; N-31.

(14) Booth, H.; Everett, J. R. *J. Chem. Soc., Chem. Commun.* **1976**, 278–279.

(15) This procedure applies Franck's methodology to calculate the purely steric preference of the diphenylphosphinoyl group: cf. Franck, R. W. *Tetrahedron* **1983**, *39*, 3251–3252. Because of the structural differences between the alkyl and phosphinoyl groups, the resulting values for the anomeric effect are only approximate as a consequence.

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

(17) Pasanen, P.; Pihlaja, K. *Tetrahedron* **1972**, *28*, 2617–2626.

experimental value, 1.42 kcal/mol,[2b] suggests an anomeric effect of ca. 3.7 kcal/mol.[15]

Seen in this light, it appears that the anomeric effects operative in O–C–P(O) and S–C–P(O) segments are of similar magnitude, close to 3 kcal/mol.[18]

(18) The nature of the O–C–P(O) and S–C–P(O) anomeric interactions operative in 1 and 2, respectively, could be different.[3,4,19]

(19) Mikolajczyk, M.; Graczyk, P.; Kabachnik, M. I.; Baranov, A. P. *J. Org. Chem.* **1989**, *54*, 2859–2861.

Acknowledgment. We are indebted to Norma González-Rojano for technical assistance, to Guillermo Uribe for recording the ^{13}C and ^{31}P NMR spectra, and to CONACYT for partial financial support.

Registry No. *cis*-**3**, 122700-51-0; *trans*-**3**, 122700-52-1; (±)-*cis*-**4**, 122700-53-2; (±)-*trans*-**4**, 122700-54-3; (±)-*cis*-**5**, 122700-55-4; (±)-*trans*-**5**, 122700-56-5; (±)-$CH_3CH(OH)CH_2CH_2OH$, 18826-95-4; $HOCH_2CH(Bu\text{-}t)CH_2OH$, 2819-05-8; $ClPPh_2$, 1079-66-9; $HC(OCH_3)_3$, 149-73-5; pivaldehyde, 630-19-3.

Catalytic Palladium-Mediated Tetraene Carbocyclizations[1]

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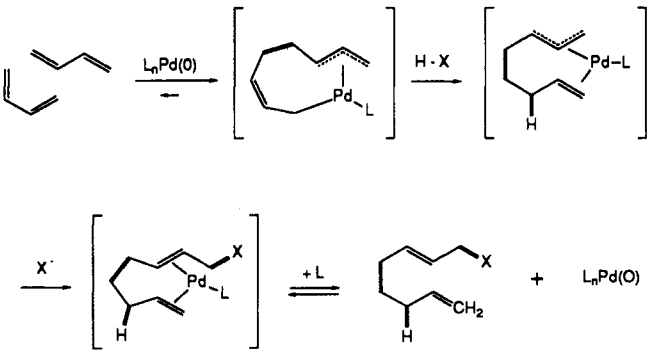
Summary: A new palladium-catalyzed carbocyclization of substrates containing two 1,3-diene moieties leads to the efficient, stereoselective preparation of functionalized cyclopentanes and pyrrolidines. Treatment of tetraenes with 5 mol % of a palladium catalyst and 2–10 equiv of an H–X trapping reagent effects carbocyclization under mild reaction conditions (25–65 °C) in good-to-excellent yields (50–94%) and with good-to-excellent stereoselectivity (5 to >20:1,trans:cis). Of particular note is the exceptional versatility of this methodology; versatility arising from the fact that the tetraene substrate is regioselectively coupled to an H–X (X = C, N, O, S) trapping reagent during the course of the cyclization.

Sir: The palladium-catalyzed linear telomerization of 1,3-butadiene was first reported in 1967 from the groups of Smutny and Hagihara.[2] Since those early reports the methodology has been extended to include the use of other metal catalysts, a few substituted 1,3-dienes, and a wide range of H–X trapping reagents (X = nucleophilic carbon, oxygen, nitrogen, or sulfur). The chemical yield, catalytic efficiency, and isomer selectivity observed in the telomerizations of 1,3-butadiene have typically been quite high. The simple 1,3-butadiene-derived linear dimers have found use as intermediates in synthesis.[3] The field has been independently reviewed by Smutny, Tsuji, Jolly, and Behr.[4] In recent years Jolly has spectroscopically and/or crystallographically characterized intermediates consistent with the proposed catalytic cycle outlined in Scheme I.[5,6]

Scheme I. A Proposed Catalytic Cycle for the Palladium-Catalyzed Telomerization of 1,3-Butadiene and Substituted 1,3-Dienes[5]



To date, the use of telomerization methods as a cyclization strategy for the direct construction of functionalized ring systems has found limited utility.[7] This is perhaps not surprising. Substituted 1,3-dienes typically telomerize with much less facility than 1,3-butadiene, and mixtures of isomeric linear-dimer products are obtained. From our experience with catalytic iron-mediated ene carbocyclizations[8] and from the growing list of other catalytic metal-mediated carbocyclization methods,[9–12] it is apparent

(1) All new compounds isolated were fully characterized spectroscopically and the elemental composition determined by combustion analysis and/or high-resolution mass spectrometry.

(2) (a) Smutny, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 6793. (b) Takahashi, S.; Shibano, T.; Hagihara, N. *Tetrahedron Lett.* **1967**, 2451.

(3) Behr, A. *Industrial Application of Homogeneous Catalysis*; Mortreux, A., Petit, F., Eds.; Reidel: Dordrecht, Netherlands, 1988; pp 141–75.

(4) (a) Behr, A. *Aspects Homogeneous Catal.* **1984**, *5*, 3–73. (b) Jolly, P. W. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 283–295. (c) Tsuji, J. *Adv. Organomet. Chem.* **1979**, *17*, 141–193. (d) Smutny, E. J. *Ann. N. Y. Acad. Sci.* **1973**, *214*, 125.

(5) (a) Jolly, P. W.; Mynott, R.; Raspel, B.; Schick, K.-P. *Organometallics* **1986**, *5*, 473–81. (b) Benn, R.; Jolly, P. W.; Joswig, T.; Mynott, R.; Schick, K.-P. *Z. Naturforsch.* **1986**, *41b*, 680–91. (c) Benn, R.; Jolly, P. W.; Mynott, R.; Raspel, B.; Schenker, G.; Schick, K.-P.; Schroth, G. *Organometallics* **1985**, *4*, 1945–53.

(6) For an alternative mechanistic proposal, see: Behr, A.; Ilsemann, G. v.; Keim, W.; Kruger, C.; Tsay, Y.-H. *Organometallics* **1986**, *5*, 514–8.

(7) To date, the applications of telomerization methods to the construction of functionalized rings usually involve the sequential capture of the butadiene linear dimer by trapping reagents (X = Y) containing double or triple bonds. For representative examples, see: (a) Braunstein, P.; Matt, D.; Nobel, D. *J. Am. Chem. Soc.* **1988**, *110*, 3207–12. (b) Ohno, K.; Tsuji, J. *J. Chem. Soc. Chem. Commun.* **1971**, 247–8. (c) Ohno, K.; Mitsuyasu, T.; Tsuji, J. *Tetrahedron* **1972**, *28*, 3705–20. (d) Benn, R.; Gabor, G.; Jolly, P. W.; Mynott, R.; Raspel, B. *J. Organomet. Chem.* **1985**, *296*, 443–7. (e) Reference 4.

(8) (a) Takacs, J. M.; Anderson, L. G.; Creswell, M. W.; Takacs, B. E. *Tetrahedron Lett.* **1987**, *28*, 5627–30. (b) Takacs, J. M.; Anderson, L. G. *J. Am. Chem. Soc.* **1987**, *109*, 2200–02.

(9) (a) Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988**, *110*, 5904–6. (b) Wender, P. A.; Snapper, M. L. *Tetrahedron Lett.* **1987**, *28*, 2221–4. (c) Wender, P. A.; Ihle, N. C. *J. Am. Chem. Soc.* **1986**, *108*, 4678–9. (d) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 5231–33. (e) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 5268–70.

(10) (a) Trost, B. M.; Luengo, J. I. *J. Am. Chem. Soc.* **1988**, *110*, 8239–41. (b) Trost, B. M.; *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 213–5. (c) Trost, B. M.; Lee, D. C. *J. Org. Chem.* **1989**, *54*, 2271–4. (d) Trost, B. M.; Matsuda, K. *J. Am. Chem. Soc.* **1988**, *110*, 5233–5. (e) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988**, *110*, 7255–8. (e) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 1636–8.

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