SYNTHESIS, NMR AND X-RAY CRYSTALLOGRAPHIC ANALYSIS OF 5-DEOXY-5-C-DIPHENYLARSINO-1,2-O-ISOPROPYLIDENE-3-O-p-TOSYL-α-D-XYLOFURANOSE

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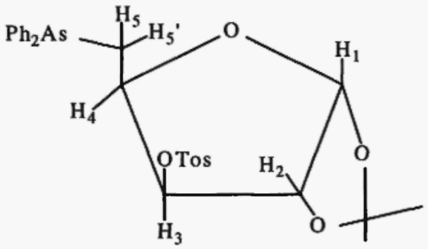
Abstract

The carbohydrate (1) has been synthesized and its crystal and molecular structure has been determined by X-ray crystallography; ^{1}H NMR and ^{13}C NMR data are also presented. Compound (1) was obtained from reaction of Ph_2AsLi with 1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tosyl-α-D-xylofuranose. The X-ray data were used to solve the structure by the Patterson method and refinement converged at a conventional *R* value of 3.67%. The geometry about the arsenic atom is pyramidal with the C-As-C valency angles between 95.1(2)° and 101.8(2)° and the C-As bond length in the range from 1.955(5) to 1.977(4) Å. The shortest As - - - O separation is 3.012(3) Å [to O(1)] ; this is less than the sum of the van der Waal's radii (= 3.40 Å). The furanose ring adopts a C(4) envelope conformation in the solid state, but a $^3T_2$ conformation is apparently preferred in solution.

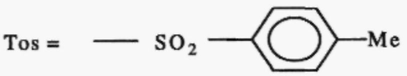
Introduction

Carbohydrates form a vital and well-studied group of organic compounds. However, the use of carbohydrates as C-bonding ligands in organometallic compounds has yet to attract much systematic attention. As a group of functionally-substituted organic moieties, carbohydrates can impart useful properties and features to organometallic compounds, including chirality and enhanced water solubility.

Our previous reported work on metallated carbohydrates has concentrated on tin compounds;[1,2] however, we have also reported the synthesis and structure of the diphenylarsino-monosaccharide derivative, methyl 4,6-*O*-benzylidene-3-deoxy-3-diphenylarsino-α-D-altropyranoside.[3] We now report the synthesis and structure of 5-deoxy-5-*C*-diphenylarsino-1,2-*O*-isopropylidene-3-*O*-*p*-tosyl-α-D-xylofuranose (1).



(1)



Experimental

1,2:3,5-Di-isopropylidene-α-D-xylofuranose was prepared, by a published procedure, from D-xylose and acetone in the presence of $CuSO_4$ and concentrated sulphuric acid[4]. 1,2-*O*-isopropylidene-α-D-xylofuranose was obtained from 1,2:3,5-di-*O*-isopropylidene-α-xylofuranose on treatment with sulphuric acid in methanol; it had m.p. 63-64°C (lit. value[4,5] 64-65°C). 1,2-*O*-Isopropylidene-3,5-di-*O*-*p*-tosyl-α-D-xylofuranose was obtained by a published procedure from 1,2-*O*-isopropylidene-α-D-xylofuranose and p-toluenesulphonyl chloride in pyridine[6]; it was recrystallised from methanol, m.p. 91-93°C, (lit. value[6] 91-92°C).

5-Deoxy-5-C-diphenylarsino-1,2-O-isopropylidene-3-O-p-tosyl-α-D-xylofuranose (1).

To a stirred solution of Ph_2AsLi, obtained from the reaction of Ph_3As (20 mmol) and excess lithium in anhydrous THF (100 ml) at ambient temperature under a nitrogen atmosphere was added a solution of 1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tosyl-α-D-xylofuranose (5g,10 mmol) in anhydrous THF (50 ml). After leaving overnight, water (100 ml) was added to the reaction mixture and the THF was removed under reduced pressure. The aqueous mixture was extracted with ethyl acetate (3x75ml) and the organic extracts washed with water, dried over anhydrous magnesium sulphate and evaporated to give a yellow oily residue. Hexane was added and the solution cooled to give crystals of the desired product. This was recrystallised from ethyl acetate / hexane. Yield 2.9 g (52%) ; m.p. 135-137°C. Analysis found : C, 58.4 ; H, 5.3%. $C_{27}H_{29}AsO_6S$ requires C, 58.3 ; H, 5.2%.

NMR Spectral Data of (1)

NMR spectra were obtained using a Bruker 250MHz instrument.

^{1}H NMR ($CDCl_3$) δ: 1.3 (s, 3H, Me), 1.3 (s, 3H, Me), 1.9 [dd, 1H, J(H_5-$H_{5'}$) 12.4Hz, J(H_4-H_5) 6.4Hz, H_5], 2.30 [dd, 1H, J(H_5-$H_{5'}$) 12.4Hz, J(H_4-$H_{5'}$) 8.4Hz, $H_{5'}$], 2.4 (s, 3H, Me), 4.1 [ddd, 1H, J(H_4-H_5) 6.4Hz, J(H_4-$H_{5'}$) 8.4Hz, J(H_3-H_4) 2.6Hz, H_4], 4.7 [d, 1H, J(H_1-H_2) 3.8Hz, H_2], 4.8 [d, 1H, J(H_3-H_4) 2.6Hz, H_3], 5.9 [d, 1H, J(H_1-H_2) 3.8Hz, H_1], 7.3 [m, 12H] & 7.8 [d, 2H, J(H-H) 7.0Hz] (aryl H).

^{13}C NMR ($CDCl_3$) δ: 21.6 (Me), 25.4 (C5), 26.2 & 26.2 (Me_2 C), 76.7 (C4), 83.2 (C3), 83.4 (C2), 104.1 (C1), 112.0 (Me_2 C), 127.9 (C11), 128.4 & 128.4 C(10), 128.5 (*m*-C of Ph_2As), 129.9 (*p*-C of Ph_2As), 132.7 & 132.9 (*o*-C of Ph_2As), 133.0 (C12), 139.4 & 139.7 (*ipso*-C of Ph_2As), 145.2 (C9).

X-ray Analysis of (1)

A colourless crystal was used in the analysis. Data were collected on a Delft Instruments FAST diffractometer with monochromated Mo-Kα radiation. Corrections were made for Lorentz and polarisation effects only. Crystal data and structure refinement details are listed in Table 1.

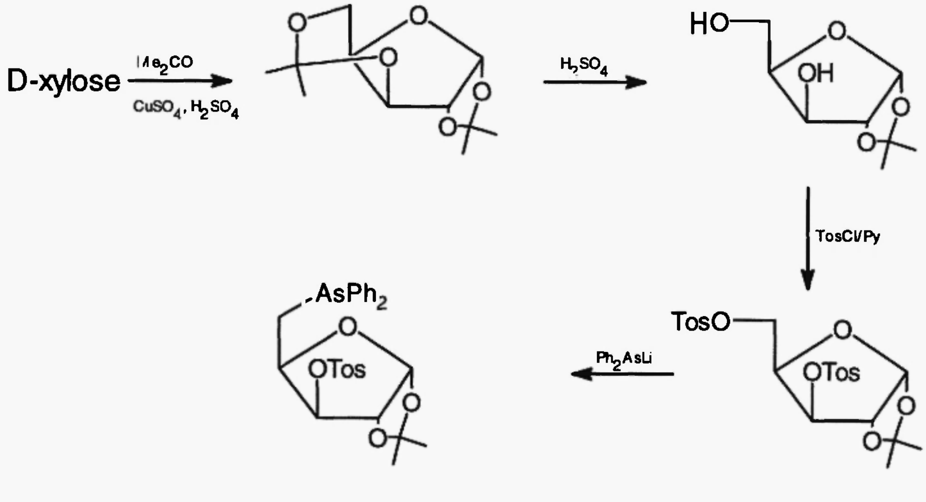
Table 1. Crystal data and structure refinement.

Empirical formula	$C_{27}H_{29}AsO_6S$
Formula weight	556.48
Temperature	293(2) K
Wavelength	0.71069 Å
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 11.2939(11) Å
	b = 5.4661(7) Å
	c = 22.043(4) Å
	ß = 99.199(11)°
Volume	1343.3(3)$Å^3$
Z	2
Density (calculated)	1.376 Mgm^{-3}
Absorption coefficient	1.381 mm^{-1}
F(000)	576
Crystal size	0.15 x 0.14 x 0.18 mm
θ range for data collection	2.40 to 30.01°
Index ranges	-15<=h<=13,
	-5<=k<=7,
	-29<=l<=30
Reflections collected	9355
Independent reflections	5832 [R(int) = 0.0534]
Refinement method	Full-matrix l.s. on F^2
Number of parameters	319
Goodness-of-fit on F^2	0.507
Final R indices [$I>2\sigma(I)$]	R1 = 0.0367, wR2 = 0.0743
R indices (all data)	R1 = 0.1014, wR2 = 0.0845
Absolute structure parameter	-0.006(11)
Residual diffraction max./ min.	0.355 / -0.152 $eÅ^{-3}$
Final weighting scheme	$w=1/[\sigma^2(Fo^2)+(0.0498P)^2]$
	$\{P=((Fo^2)+2Fc^2)/3\}$

The positions of the arsenic and sulphur atoms were located from a Patterson vector map and confirmed by a direct method procedure using SHELX-86[7]. The positions of the remaining non-hydrogen atoms were located on successive difference Fourier maps using SHELXL-93[8]. The positions of the hydrogen atoms were calculated from geometrical considerations. During refinement the hydrogen atoms were allowed to ride on their attached carbon atoms. Full-matrix least-squares calculations with anisotropic temperature factors for the As, S, O and C atoms and common isotropic temperature factors according to type (methyl, aromatic, etc.) for the H atoms were calculated. The absolute configuration is based on the known stereochemistry of the carbohydrate moiety and the value of absolute structure parameter [-0.006(11)]. Molecular diagrams were obtained by the program SNOOPI[9].

Results and Discussion

5-Deoxy-5-*C*-diphenylarsino-1,2-isopropylidene-3-*O*-*p*-tosyl-α-D-xylofuranose (1) was obtained from D-xylose by the sequence shown in the scheme.



(1)

(2)

Scheme: Tos = *p*-$MeC_6H_4SO_2$.

Of the two *p*-tosyloxy groups in (2), only that in the 5-position reacted with Ph_2AsLi ; even with excess Ph_2AsLi, the 3-tosyloxy group remained unaffected. This is in agreement with previous reports of the low reactivities of 3-*exo*-tosyloxy groups in 1,2-isopropylidene-D-pento- and -hexofuranoses.[10,11]

The major solution conformation of the furanose rings of 1,2-isopropylidene derivatives of α-D-xylofuranose have been deduced from ^1H NMR spectral data to be $^3T_2$,[12] i.e., C(2) and C(3) are displaced below and above, respectively, the plane defined by the other furanose-ring atoms. The values of the coupling constants $J(H_1\text{-}H_2)$, $J(H_2\text{-}H_3)$ and $J(H_3\text{-}H_4)$ of 3.8, 0 and 2.6 Hz respectively, for (1) suggest a similar $^3T_2$ conformation for (1) in solution (Figure 1).

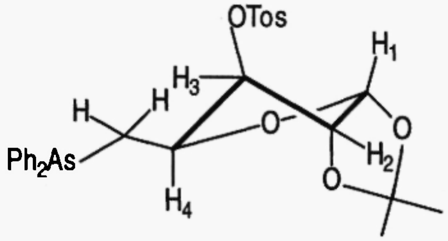


Figure 1. The $^3T_2$ conformation of the furanose ring.

Use of the Karplus equation and its modified version enables estimates of the dihedral angle (|ω|) to be made for hydrogens on adjacent carbons[13] as shown in Table 2.

Table 2. Comparison of torsional angles (ω) and dihedral angles (|ω|) of (1) in solid state and in solution.

	Angles (°)			*Coupling constants*
H(x)-C-C-H(y)	ω^a	$\lvert\omega\rvert^b$	$\lvert\omega\rvert^c$	J(Hx-Hy)
H(1)-C-C-H(2)	0.2	49	46	3.8
H(2)-C-C-H(3)	-95.4	83	80	0.0
H(3)-C-C-H(4)	-43.8	56	54	2.6
H(4)-C-C-H(5)	165.8	162	163	8.4
H(4)-C-C-H(5')	47.6	33	28	6.4

[a] Determined by X-ray crystallography.
[b] Estimated from J(H,H) values in the ^{1}H NMR spectrum using: $J(H,H) = 10.5 \cos^2 \lvert\omega\rvert - 1.2 \cos \lvert\omega\rvert$
[c] Estimated from J(H,H) values in the ^{1}H NMR spectrum using: $J(H,H) = J_0 \cos^2 \lvert\omega\rvert - 0.28$
where $J_0 = 8.5$ for $0° \leq \lvert\omega\rvert < 90°$ and $J_0 = 9.5$ for $90° < \lvert\omega\rvert < 180°$

Crystal Structure of (1)

The atomic arrangement in the molecule is shown in Fig.2 and a diagram of crystal packing is shown in Fig.3.

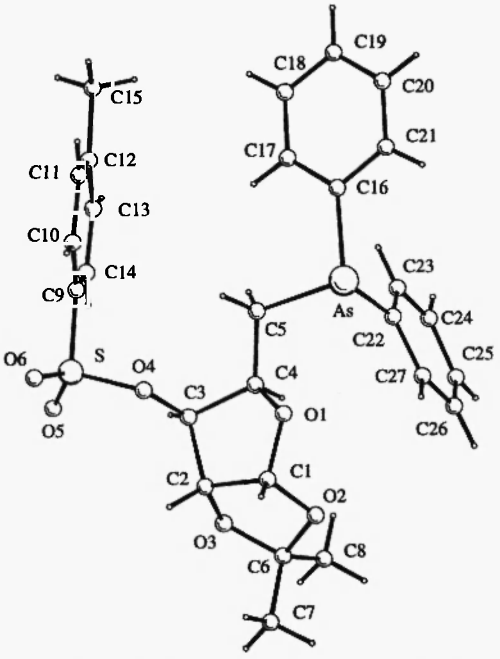


Figure 2. The atomic arrangement in (1)

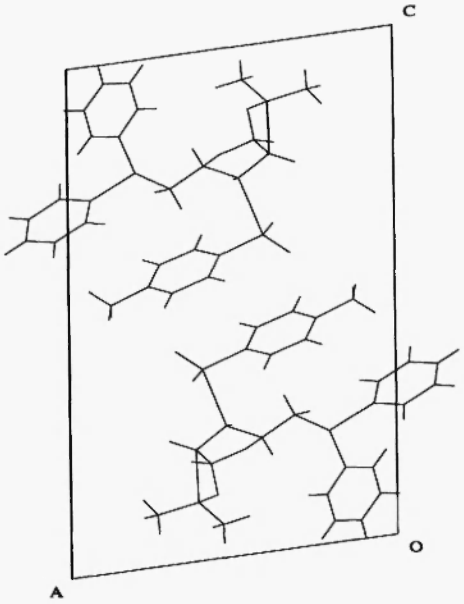


Figure 3. A crystal packing diagram for (1)

Non-hydrogen atom co-ordinates are listed in Table 3 and selected bond lengths and valency angles are given in Table 4.

Table 3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3). U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
As	2066(1)	10192(1)	2216(1)	73(1)
S	5946(1)	4970(3)	3766(1)	82(1)
O(1)	4650(3)	9341(4)	2089(1)	67(1)
O(2)	5531(3)	8222(5)	1256(2)	87(1)
O(3)	6153(3)	4683(5)	1718(2)	74(1)
O(4)	5604(3)	6701(5)	3197(1)	69(1)
O(5)	6259(4)	2631(7)	3557(2)	123(2)
O(6)	6776(3)	6327(8)	4189(2)	122(2)
C(1)	5718(4)	8733(8)	1884(3)	70(1)
C(2)	6175(4)	6352(7)	2193(2)	63(1)
C(3)	5224(3)	5684(8)	2591(2)	56(1)
C(4)	4147(3)	7081(6)	2269(2)	54(1)
C(5)	3131(4)	7600(7)	2621(2)	65(1)
C(6)	6116(5)	5963(9)	1164(3)	84(2)
C(7)	7362(6)	6470(12)	1027(3)	151(3)
C(8)	5355(6)	4564(11)	665(3)	129(2)
C(9)	4600(4)	4716(8)	4055(2)	63(1)
C(10)	4277(6)	6418(9)	4446(3)	86(2)
C(11)	3150(8)	6138(15)	4659(3)	114(3)
C(12)	2436(7)	4236(20)	4472(4)	128(3)
C(13)	2774(9)	2636(15)	4079(4)	134(3)
C(14)	3846(7)	2810(10)	3875(3)	107(2)
C(15)	1278(7)	3999(17)	4737(3)	211(5)
C(16)	681(4)	9707(9)	2638(2)	74(2)
C(17)	542(5)	7928(12)	3052(3)	111(2)
C(18)	-411(6)	7855(13)	3360(3)	119(2)
C(19)	-1295(5)	9538(14)	3250(3)	105(2)
C(20)	-1194(6)	11196(12)	2837(4)	139(3)
C(21)	-241(6)	11308(9)	2526(4)	127(3)
C(22)	1582(4)	8369(8)	1453(2)	70(1)
C(23)	743(5)	6519(9)	1379(3)	80(2)
C(24)	523(4)	5248(15)	845(3)	100(1)
C(25)	1118(6)	5619(17)	377(3)	111(2)
C(26)	1929(7)	7454(18)	430(3)	132(3)
C(27)	2161(5)	8797(11)	967(3)	101(2)

The sulphur is in a distorted tetrahedral environment, with valency angles in the range 102.9(2)° to 120.6(3)°. As expected, the largest angle of the tetrahedron is found between O(5) and O(6). There are no significant differences in valency angles or bond lengths about the sulphur atom when compared to those of previously studied tosylated carbohydrates, e.g., methyl 2,3-*O*-isopropylidene-5-*O*-*p*-tosyl-β-D-ribofuranoside[14] and 1,2-*O*-isopropylidene-5-(*p*-toluenesulphonyl)-α-D-xylofuranose.[15] The arsenic atom lies in a pyramidal arrangement with the arsenic lying 0.945(3)Å above the plane produced by C(5), C(16) and C(22). The valency angles about the arsenic range between 95.1(2)° and 101.8(2)°. The C(16) - As - C(22) angle being significantly greater then the other two, due to the presence of the bulky phenyl groups. The As-C(aryl) bond lengths [1.955(5) and 1.962(5)Å] compare favourably to those of a previously studied diphenyl arsenic carbohydrate methyl 4,6-benzylidene-3-deoxy-3-diphenylarsino-α-D-altropyranoside[3] [1.965(6) and 1.967(6)Å]. There is no significant difference between the As-C(alkyl) bond lengths for the two compounds [1.977(4)Å and 2.003(6)Å]. The angle of inclination formed between the planes of the two phenyl groups attached to the arsenic has a value of 83°.

The closest oxygen to the arsenic atom is O(1) with an intramolecular distance of 3.012(3)Å. This value is less than the sum of the Van der Waals radii (3.40Å).

Table 4. Selected bond lengths [Å] and angles [°].

As-C(22)	1.955(5)
As-C(16)	1.962(5)
As-C(5)	1.977(4)
C(22)-As-C(16)	101.8(2)
C(22)-As-C(5)	95.1(2)
C(16)-As-C(5)	99.3(2)
C(4)-C(5)-As	111.1(3)
C(21)-C(16)-As	118.3(4)
C(17)-C(16)-As	127.0(4)
C(27)-C(22)-As	119.1(4)
C(23)-C(22)-As	124.6(4)

The bond lengths and valency angles of the furanose and isopropylidene rings compare favourably with those in 6-deoxy-1,2-*O*-isopropylidene-6-(triphenylstannyl)-α-D-glucofuranose[16], the only significant difference being in the C(2)-O(3) bond length. This difference could possibly be due to the influence of the inter- and intramolecular H-bonding exhibited by the tin carbohydrate.

The furanose ring of (I) in the solid state adopts a C(4) envelope conformation (Figure 4). Atom C(4) is 0.581(6)Å from the plane defined by the remaining ring atoms and the rms deviation from the plane of the fitted atoms is 0.003Å and ΔC_S = 2.6°. Thus the conformation of this ring in the solid state is different from that in solution (see Table 2). The isopropylidene ring adopts a C(6) envelope conformation with C(6) displaced 0.386(7)Å from the plane formed by the remaining ring atoms (rms deviation = 0.013Å and ΔC_S = 3.8°). The following Cremer Pople puckering constants were calculated using the program Pucker[17]. The furanose ring has Q=0.382, q2=0.381 and ϕ=323.1° and the isopropylidene ring has Q=0.248, q2=0.248 and ϕ=221.6°.

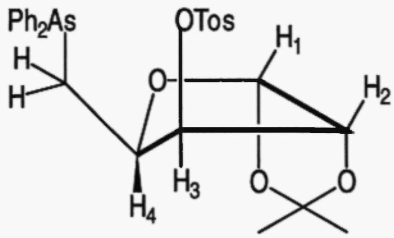


Figure 4. The envelope conformation of the furanose ring.

The H(1) - C(1) - C(2) - H(2) torsion angle has a value of 0.23° producing a cis arrangement of hydrogen atoms at the junction of the two rings. The fold at the C(1)-C(2) bond has an angle of 117.6(4)° and the O(4) - C(3) - C(4) - C(5) torsion angle has a value of -46.8(4)°, which allows an intramolecular contact of 2.918(5)Å between O(4) and C(5). This value is less than the sum of the Van der Waals radii (3.25Å). A similar arrangement was also reported in 1,2-*O*-isopropylidene-5-(*p*-toluenesulphonyl)-α-D-xylofuranose[15].

Acknowledgements

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References

1. S.M.S.V. Doidge-Harrison, I.W. Nowell, P.J. Cox, R.A. Howie, O.J. Taylor and J.L. Wardell, *J. Organomet. Chem.*, **401**, (1991),273.
2. O.J. Taylor and J.L. Wardell, *Recl. Trav. Chim. Pays-Bas*, **107**, (1988), 267; C.M. McDonough, O.J. Taylor and J.L. Wardell, *Appl. Organomet. Chem.*, **3**, (1989), 417; O.J. Taylor and J.L. Wardell, *J. Chem. Res. (S)*, 98, 1989; O.J. Taylor, J.L. Wardell and M.Mazhar, *Main Group-Metal Chem.*, **12**, (1989), 107; P.J. Cox,S.M.S.V. Doidge-Harrison, R.A. Howie, I.W. Nowell, O.J. Taylor and J.L. Wardell, *J. Chem. Soc. Perkin Trans. 1*, 2017, (1989).
3. M.A. Brown, J.L. Wardell, P.J. Cox and O.A. Melvin, *J. Organomet. Chem.*, in press.
4. P.A. Levene and A.L. Raymond, *J. Biol. Chem.*, (1933), 317.
5. O. Svanberg and K. Svoberg, *Ber.*, **56**, (1923), 863.
6. P. Karrer and A. Boettcher, H*elv. Chem. Acta*, **36**, (1953), 837.
7. G.M. Sheldrick, *Acta Crystallogr., Sect. A*, **46**, 1990, 467.
8. G.M. Sheldrick, *J. Appl. Crystallogr.*, in preparation.
9. K. Davies. (1983) SNOOPI. A program for producing molecular diagrams from X- ray data (part of the chemgraf package).
10. N.A. Hughes and P.R.H. Speakman, *Carbohydrate Res.*, 1, 1966, 341.
11. J.A. Mills, *Adv. Carbohydrate Chem.*, **10**, (1955),1; A.C. Cope and T.Y. Shen, *J. Am. Chem. Soc.*, **78**, (1956), 3177.
12. R.J. Abraham, L.D. Hall, L. Hough and K.A. Mclauchlan, *J. Chem. Soc.*, (1962), 3699; R.C. Young, P.W. Kent and R.A. Dwek, *Tetrahedron*, **26**, (1970), 3983; L. Neeser, J.M.J. Tronchet and E.J. Charollais, *Can. J. Chem.*, **61**, (1983), 1387.
13. C. Altona and M. Sundaralingam, *J. Am. Chem. Soc.*, **95**, (1973), 2333.
14. A.J. Blake, P.J. Cox, O.A. Melvin and J.L. Wardell, *J. Chem. Research (S)*, 1994,291.
15. P.J. Cox, O.A. Melvin and J.L. Wardell, in preparation.
16. P.J. Cox, R.A Howie, O.A. Melvin and J.L. Wardell, *J Organomet. Chem.*, 1994, in press.
17. R.O. Gould and P. Taylor. (1994) PUCKER. A program for calculating Cremer Pople ring puckering parameters, University of Edinburgh, Scotland.

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