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On the extent of chair distortion in "tetra-axial" derivatives of 2,3,4-tri-*O*-benzoyl-*β*-D-xylopyranose

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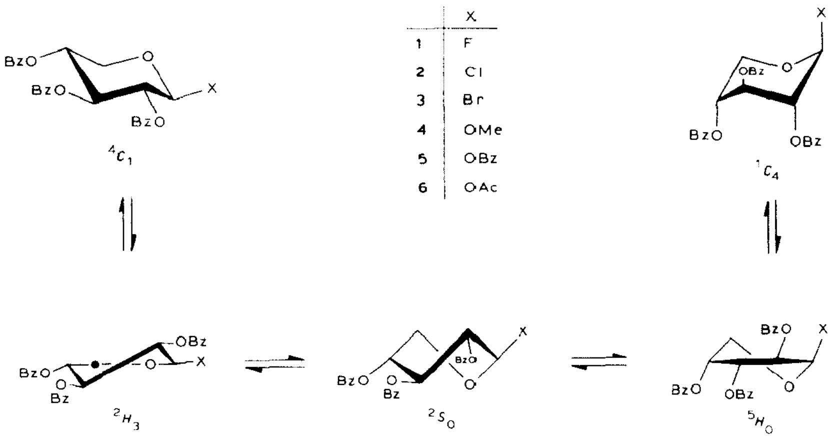
ABSTRACT

An X-ray analysis of 2,3,4-tri-*O*-benzoyl-2-chloro-2-deoxy-*β*-D-xylopyranosyl chloride (**7**) revealed a $^1C_4$ chair conformation slightly distorted toward the ^5H_O half-chair form. The four substituents deviate from idealized axial orientations by only 3–14°, hence, the conformation approximates to a "tetra-axial" arrangement. 1,2,3,4-Tetra-*O*-benzoyl-*β*-D-xylopyranose (**5**) also crystallizes in a $^1C_4 \rightarrow {}^5H_O$ form, 2,3,4-tri-*O*-benzoyl-*β*-D-xylopyranosyl fluoride (**1**) is more markedly deformed, and 2,3,4-tri-*O*-benzoyl-*β*-D-xylopyranosyl bromide (**3**) deviates from a $^1C_4$ form so much as to not to be designated "tetra-axial". In chloroform solution, **7** appears to retain the $^1C_4$ conformation adopted in the crystal, whereas, for **1**, **3**, and **5**, $^4C_1 \rightleftharpoons {}^1C_4$ equilibria are established.

INTRODUCTION

In derivatives of *β*-D-xylopyranose, the anomeric effect of a halogen substituent or benzoyloxy group at C-1 overrides the steric repulsions imposed by *syn*-1,3-diaxial interactions of substituents [1–12]. For 2,3,4-tri-*O*-benzoyl-*β*-D-xylopyranosyl fluoride (**1**), chloride (**2**), and bromide (**3**), the proportions of the "tetra-axial" $^1C_4$ forms have been assessed to be $>90\%$ for solutions in acetone[2,3,7], whereas the 1-*O*-benzoyl[5] (**5**) and 1-*O*-acetyl[6] (**6**) derivatives adopt essentially equal proportions of $^1C_4$ and $^4C_1$ conformers, and the methyl glycoside **4** has a 3:1 preference for the $^4C_1$ form[4]. Whether the non-$^4C_1$-portions of **1**–**6** adopt $^1C_4$ geometries with all substituents axial, or whether there is significant distortion in the ring, remains an open question. From the plethora of data on pyranoid ring interconversions that involve the $^4C_1$ and $^1C_4$ forms [13,14], it is clear that *β*-D-*xylo* derivatives follow the $^4C_1 \rightleftharpoons {}^2H_3 \rightleftharpoons {}^2S_O \rightleftharpoons {}^5H_O \rightleftharpoons {}^1C_4$ track; accordingly, it is unlikely that a perfect $^1C_4$ conformation is adopted, but rather the ^5H_O form, or one between $^1C_4$ and ^5H_O (Scheme 1).

X-Ray data on **1**–**5** clearly showed ^2S_O skew conformations for the chloride **2**[11] and the methyl glycoside **4**[12], whereas the fluoride **1**[9], the bromide **3**[8], and the 1-benzoate **5**[10] crystallize in conformations that approach, but do not reach, the ideal $^1C_4$ geometry, as indicated by ring torsional angles as low as 37° for **1** and **3**, and deviations of the ring substituents from a 1,2-diaxial arrangement (180°) by up to 42°. Consequently, the designation "tetra-axial" for the conformations of **1**, **3**, and **5**, although repeatedly stressed[8–10], is a misleading oversimplification.



Scheme 1. Interchange of the $^4C_1$ and $^1C_4$ conformations of the 2,3,4-tri-*O*-benzoyl-*β*-D-xylopyranose derivatives.

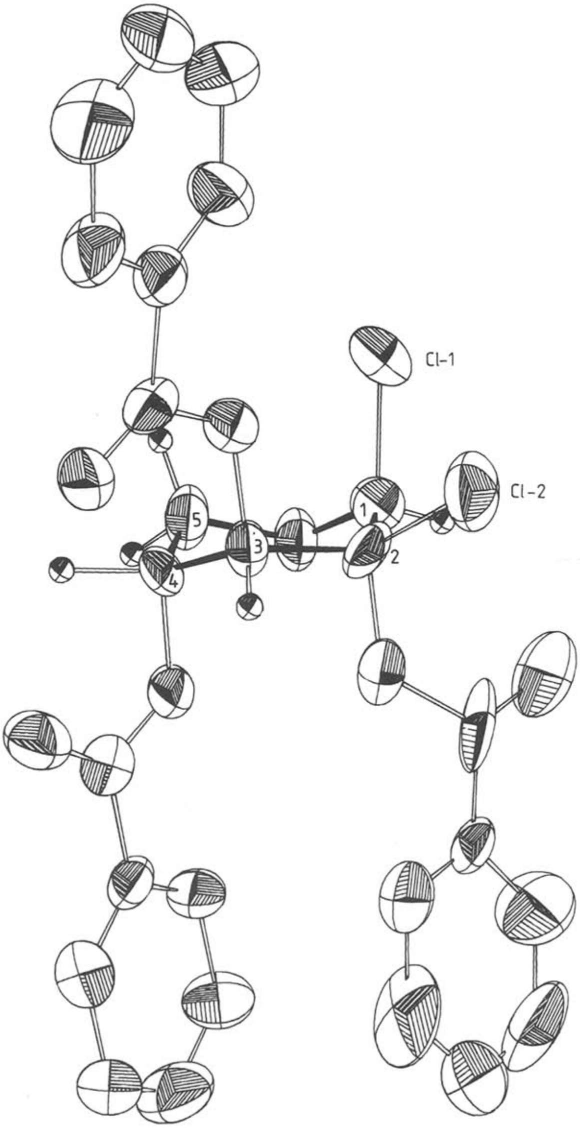
The 2-chloro analogue of **2**, namely, 2,3,4-tri-*O*-benzoyl-2-chloro-2-deoxy-*β*-D-xylopyranosyl chloride (**7**), was selected for study since the 2-chlorine substituent should stabilize the $^1C_4$ conformation in solution as well as in the crystal. ^{1}H-N.m.r. (300 MHz) and X-ray structural analyses of **7** (ref. 15) are now reported[16].

RESULTS OF DISCUSSION

The X-ray structural analysis of **7** (Fig. 1) revealed the two chlorine substituents to be *cis* and, at first sight, BzO-2,3,4 and Cl-1 to be roughly perpendicular to the plane of the pyranoid ring.

Of the six torsional angles in the pyranose ring, two deviate substantially from mean values, *i.e.*, 38.3° for C-1–C-2–C-3–C-4 and −39.1° for C-2–C-3–C-4–C-5 (*cf.* Table I). Accordingly, the ideal $^1C_4$ geometry is somewhat dented at C-3 and C-2, which results in flattening towards the ^5H_O half-chair form. Hence, the conformation of the pyranoid ring is best described as a $^1C_4$ chair slightly distorted towards the ^5H_O half-chair, *i.e.*, $^1C_4 \rightarrow {}^5H_O$.

Inspection of the ring torsional angles for **1**, **3**, and **5** (*cf.* Table I), which have been assessed[8-10] to adopt the "tetra-axial" $^1C_4$ chair forms, reveal $^1C_4 \rightarrow {}^5H_O$ ring conformations even more clearly. In the two forms of the fluoride **1**, the C-1–C-2–C-3–C-4 dihedral angles are lower (37.1 and 35.8°, respectively) than in **7**, indicating an even greater flattening of the ring around C-3. The 1-bromide **3** responds to the sizeable Br-1/BzO-3 repulsion with substantial flattening of the ring at C-2, as indicated by values of −37.2° for the dihedral angles O-5–C-1–C-2–C-3 and 38.2° for C-1–C-2–C-3–C-4. Accordingly, the pyranoid ring in **3** is even more substantially distorted towards the ^5H_O form than in **7**. For the tetrabenzoate **5**, both forms found in the crystal show ring dihedral angles close to those found for **7** (*cf.* Table I). Thus, none of the known



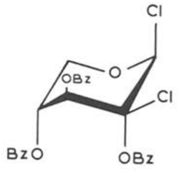


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Fig. 1. ORTEP drawing of 2,3,4-tri-*O*-benzoyl-2-chloro-2-deoxy-β-D-xylopyranosyl chloride (**7**) showing thermal ellipsoids and partial atomic numbering. Hydrogen atoms of benzene rings have been omitted.

β-D-xylopyranose derivatives adopt a ${}^1C_4$ conformation, but rather they crystallize in ${}^1C_4 \rightarrow {}^5H_O$ forms. The extent of deformation of ${}^1C_4$ towards ${}^5H_0$ is comparatively small in the tetra-benzoate **5** and the dichloride **7**, but is substantial in the 1-halides **1** and **3**.

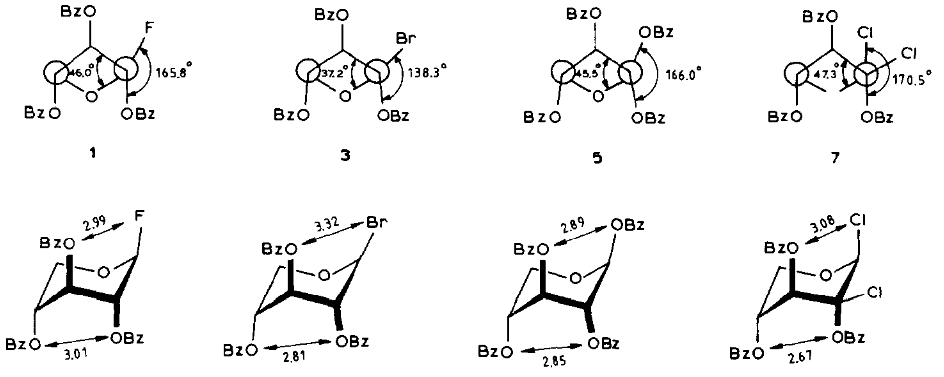
The ${}^1C_4 \rightarrow {}^5H_O$ conformations for **1**, **3**, **5**, and **7** are reflected also in the orientation of the benzoyloxy and halogen substituents and their 1,3-interatomic distances. In **7**, BzO-3,4 are nearly antiparallel (177°, see Table I), as are BzO-2 and Cl-1 (170.5°, *cf.*

TABLE I

Selected torsional angles for **1**–**5** and **7**

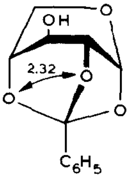
Torsional angles (°)	**1** *(1-fluoride)*		**2** *(1-chloride)*	**3** *(1-bromide)*	**4** *(methyl xyloside)*		**5** *(1-benzoate)*		**7** *(1,2-dichloride)*
Pyranoid ring	*Form A*	*Form B*			*Form A*	*Form B*	*Form A*	*Form B*	
C-1–C-2–C-3–C-4	37.1	35.8	−64.1	38.2	−58.4	−59.0	39.3	40.6	41.0
C-2–C-3–C-4–C-5	−40.9	−39.8	28.9	−50.4	32.1	32.7	−43.8	−46.1	−41.7
C-3–C-4–C-5–O-5	51.0	49.5	33.4	58.9	28.4	27.9	53.4	55.0	55.4
C-4–C-5–O-5–C-1	−60.5	−59.1	−67.3	−59.5	−71.7	−70.5	−60.7	−59.7	−58.5
C-5–O-5–C-1–C-2	57.3	55.8	29.3	48.7	43.5	42.6	56.4	53.2	56.1
O-5–C-1–C-2–C-3	−46.0	−44.3	34.2	−37.2	20.1	20.9	−45.5	−43.3	−50.1
Substituents									
X-1–C-1–C-2–O-2	−165.8	−163.8	−92.6	−138.3	−99.5	−97.9	−166.0	−164.0	−170.4
O-2–C-2–C-3–O-3	162.9	162.4	−62.1	159.5	65.4	65.7	163.9	170.7	−162.7
O-3–C-3–C-4–O-4	−159.7	−165.3	−96.3	−179.2	−95.9	−95.3	−172.8	−167.1	−177.3
Conformation	${}^1C_4 \rightarrow {}^5H_O$		${}^2S_O$	${}^1C_4 \rightarrow {}^5H_O$	${}^2S_O$	${}^2S_O$	${}^1C_4 \rightarrow {}^5H_O$		${}^1C_4 \rightarrow {}^5H_O$
Location of flattening of the chair form	C-3	C-3	–	C-2	–	–	C-3	C-3	C-3

Scheme 2). Only the dihedral angle between BzO-2,3 deviates from an ideal 1,2-diaxial orientation by 14°, which is the result of flattening the ring at C-3, conceivably caused by 1,3-*syn*-diaxial interactions of BzO-3 and Cl-1.



Scheme 2. Torsional angles and interatomic distances for the $^4C_1 \rightarrow {}^5H_0$ conformations of the 2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl derivatives.

The distances between *syn*-1,3-diaxial substituents in **7** are small, that (2.67 Å) for O-2,4 being shorter than the van der Waals contact distance of 2.8 Å (*cf.* 2.81–3.01 Å for **1**, **3**, or **5**; Scheme 2). A search of the Cambridge Data File revealed 2.67 Å to be the smallest *syn*-1,3-diaxial distance observed so far in non-bridged pyranoid or cyclohexanoid compounds; only rigid systems such as the α-D-xylose orthobenzoate **8**[17] or the trioxa-adamantane **9**[18] have smaller values.



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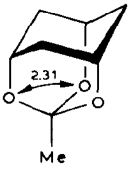

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With respect to the *syn*-1,3-diaxial distances between oxygen and halogen, **1**, **3**, and **7** appear to be the only examples. Whereas in **1**, the F/O-3 distance is comparatively unstrained at 2.99 Å (*cf.* the O/F contact distance of 2.75 Å), the Br/O-3 distance in **3** (3.32 Å) is just less than the combined van der Waals radii of 3.35 Å, and the resulting repulsive interactions force the bromine into a non-axial orientation (Fig. 2). For **7**, the Cl–O-3 distance (3.08 Å, Scheme 2) is smaller than the van der Waals contact distance of 3.20 Å, conceivably due to the dipolar interactions of Cl-1,2. This interaction results in a smaller deviation from the $^1C_4$ conformation than in the other β-D-xylopyranoses (**1**, **3**, and **5**) that have been subjected to an X-ray structural analysis so far.

Thus, benzoylated β-D-xylopyranose derivatives *in the crystalline state* adopt conformations at the ${}^5H_O \rightleftharpoons {}^1C_4$ side of the ${}^4C_1 \rightleftharpoons {}^1C_4$ interconversion track shown in Scheme 1, the extent of distortion ${}^1C_4 \rightarrow {}^5H_O$ being least in the dichloride **7** and tetrabenzoate **5**, more pronounced in the fluoride **1**, and most in the 1-bromide **3**.

In solution, there are changes from the conformations adopted in the crystal and ${}^4C_1 \rightleftharpoons {}^1C_4$ equilibria exist, their positions being dependent on temperature and solvent but without a direct correlation with the polarity of the solvent. This situation is indicated by the coupling constants, obtained for solutions in $CDCl_3$, listed in Table II. On the basis of averaged couplings[3,6], the equilibrium lies at the ${}^1C_4$ side (3:2 ratio of conformers in $CDCl_3$, *cf.* 1:1 in acetone[6]), yet is clearly shifted towards ${}^4C_1$ for **1**–**3** (*cf.* Table II). For **7**, the vicinal coupling constants are small and correlate well with the X-ray-derived torsional angles ($J_{3,4}$ 3.7 Hz and 71° for H-3–C-3–C-4–H-4, $J_{4,5}$ 2.4 and 2.6 Hz versus H-4–H-5 dihedral angles of 54 and −64°). These data, together with the long-range couplings observed for **7**, indicate similar conformations in the solid state and in solution; the equilibrium, if there is any, lies distinctly towards ${}^1C_4$.

The data in Table II show that the two chlorides **2** and **7** have similar vicinal and long-range couplings, the latter being absent from the more averaged couplings, as for **1** and **5**. Thus, **2** and **7** have similar conformations in solution in chloroform, approaching the ${}^1C_4$ form (Scheme 1), yet **2** crystallizes in the ${}^2S_O$ form and **7** in a ${}^1C_4$ form slightly distorted toward the ${}^5H_O$ form.

TABLE II

Coupling constants ($CDCl_3$) of 2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl derivatives

J *values (Hz)*	**1**[a,2]	**2**[b]	**3**[a,7]	**5**[b]	**7**[b]
$J_{1,2}$	~2.5	0.9	<1	4.4	
$J_{1,3}$		0.9			1.3
$J_{1,5}$			<1		0.7
$J_{2,3}$	~4.5	4.7		5.9	–
$J_{2,4}$		1.8			–
$J_{3,4}$	~3.5	3.0	~1	5.9	3.7
$J_{3,5}$		1.8	~1		1.3
$J_{4,5e}$	2.5	1.8	1.7	4.5	2.4
$J_{4,5a}$	3.5	2.0	2.0	5.6	2.6
$J_{5,5}$	−13.1	−13.3	−13.2	−12.5	−14.4

[a] 100-MHz spectra. [b] 300-MHz spectra.

EXPERIMENTAL

The following compounds were prepared as described.

1,2,3,4-Tetra-*O*-benzoyl-β-D-xylopyranose[19] (**5**) had m.p. 175°. ¹H-N.m.r. data (300 MHz, $CDCl_3$): δ 4.01 and 4.57 (2 dd, each 1 H, H-5,5), 5.40 (ddd, 1 H, H-4), 5.62 (dd, 1 H, H-2), 5.83 (dd, 1 H, H-3), 6.37 (d, 1 H, H-1). See Table II for the *J* values.

2,3,4-Tri-*O*-benzoyl-β-D-xylopyranosyl chloride[3] (**2**) had m.p. 143–144°, $[\alpha]_D^{20}$

TABLE III

X-ray data for 7

Formula	$C_{26}H_{20}Cl_2O_7$
Mol. wt.	515.44
Space group	$P2_12_12_1$
a	29.45 (1) Å
b	13.501 (5) Å
c	6.215 (5) Å
V	2468.9 Å^3
Z	4
Density (calc.)	1.387 g.cm^{-3}
2θ range	8–120°
No. of reflections	
measured	1280
with $\|F\| > 2\sigma_F$	1277
No. of variables	321
U (H atoms)	0.115(15)
R	0.070
Largest peak in final difference Fourier synthesis	0.40 e/Å^3

−109° (*c* 1, chloroform). ^{1}H-N.m.r. data (300 MHz, $CDCl_3$): δ 4.13 and 4.70 (2 dd, each 1 H, H-5,5), 5.26 (ddd, 1 H, H-4), 5.45 (ddd, 1 H, H-2), 5.63 (ddd, 1 H, H-3), 6.21 (dd, 1 H, H-1). See Table II for the *J* values.

2,3,4-Tri-*O*-benzoyl-2-chloro-2-deoxy-β-D-xylopyranosyl chloride[16] (**7**) had m.p. 183–184°, $[\alpha]_D^{20}$ −109.5° (*c* 1, chloroform). ^{1}H-N.m.r. data (300 MHz, $CDCl_3$): δ 4.04 (ddd, 1 H, H-5*e*), 4.73 (dd, 1 H, H-5*a*), 5.37 (dq, 1 H, H-4), 6.57 (dt, 1 H, H-3), 6.81 (d, 1 H, H-1). See Table II for the *J* values.

X-Ray analysis of **7**. — Dissolution of **7** in hot ethanol and slow concentration afforded thin needles. A summary of the X-ray data is given in Table III. Data were collected on a STOE two-circle diffractometer (Cu-K_α radiation) equipped with a graphite monochromator. The cell constants were determined from θ values of axis reflections with $8° < \theta < 80°$. The structure was solved by direct methods. Anisotropic refinement of the C and O atoms with fixed positions and a common isotropic temperature factor for the H atoms converged to $R = 0.070$. The positional parameters for the heavy atoms are given in Table IV*. Programs used: SHELX-76[20], ORTEP[21].

ACKNOWLEDGMENTS

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*Supplementary material, including the H-atom parameters, observed and calculated structure factors, bond lengths, and bond angles, has been deposited with, and is available from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/434/*Carbohydr. Res.*, 200 (1990) 91–99.

TABLE IV

Atom positions for the heavy atoms in 2,3,4-tri-*O*-benzoyl-2-chloro-2-deoxy-β-D-xylopyranosyl chloride (**7**)

Atom	x/a	y/b	z/c	U (*eq*)
Cl-1	−0.1627(01)	−0.2296(02)	−0.5297(09)	0.078(02)
Cl-2	−0.1155(01)	−0.2086(03)	−0.0729(09)	0.080(02)
C-1	−0.1299(05)	−0.3307(10)	−0.4072(32)	0.062(10)
C-2	−0.1279(04)	−0.3288(11)	−0.1949(36)	0.067(10)
C-3	−0.1734(04)	−0.3694(08)	−0.0631(28)	0.043(07)
C-4	−0.1901(04)	−0.4623(09)	−0.1841(34)	0.060(09)
C-5	−0.1883(04)	−0.4488(11)	−0.4182(36)	0.065(10)
O-5	−0.1437(03)	−0.4205(06)	−0.5050(20)	0.064(06)
O-2	−0.0965(03)	−0.3971(07)	−0.0806(23)	0.072(06)
C-21	−0.0515(05)	−0.3959(13)	−0.1469(38)	0.079(12)
O-21	−0.0356(04)	−0.3456(10)	−0.2813(29)	0.123(11)
C-22	−0.0264(04)	−0.4678(11)	0.0108(39)	0.068(11)
C-23	−0.0439(06)	−0.5036(13)	0.1884(37)	0.073(12)
C-24	−0.0200(07)	−0.5676(15)	0.3385(51)	0.127(18)
C-25	0.0223(07)	−0.6007(17)	0.2462(66)	0.155(24)
C-26	0.0405(07)	−0.5658(18)	0.0525(56)	0.124(20)
C-27	0.0154(05)	−0.4993(13)	−0.0754(42)	0.094(13)
O-3	−0.2062(03)	−0.2919(06)	−0.1002(17)	0.046(05)
C-31	−0.2399(04)	−0.2904(09)	0.0532(27)	0.040(07)
O-31	−0.2458(03)	−0.3551(07)	0.1835(19)	0.062(06)
C-32	−0.2665(04)	−0.1968(09)	0.0322(33)	0.060(09)
C-33	−0.2961(05)	−0.1768(11)	0.2055(34)	0.078(11)
C-34	−0.3227(06)	−0.0919(12)	0.1994(48)	0.116(15)
C-35	−0.3209(07)	−0.0305(13)	0.0307(57)	0.130(18)
C-36	−0.2907(06)	−0.0481(13)	−0.1330(50)	0.115(16)
C-37	−0.2633(05)	−0.1329(10)	−0.1338(35)	0.074(11)
O-4	−0.1588(03)	−0.5427(06)	−0.1408(21)	0.063(06)
C-41	−0.1662(05)	−0.5995(09)	0.0205(27)	0.041(08)
O-41	−0.1975(03)	−0.5893(07)	0.1584(21)	0.067(07)
C-42	−0.1296(04)	−0.6744(09)	0.0519(30)	0.050(08)
C-43	−0.0979(04)	−0.6881(10)	−0.1073(33)	0.063(10)
C-44	−0.0633(05)	−0.7583(11)	−0.0695(42)	0.087(12)
C-45	−0.0619(06)	−0.8136(12)	0.0978(41)	0.088(13)
C-46	−0.0937(05)	−0.7989(13)	0.2831(40)	0.102(14)
C-47	−0.1280(05)	−0.7287(11)	0.2475(35)	0.077(11)

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