g). All showed an IR absorption at 2100 cm^{-1} (azido group).

Acknowledgment. We thank Dr. D. A. Wilson of University College, Cardiff, for the ^{13}C and 360-MHz ^{1}H NMR spectra, and USIC of Madurai Kamaraj University for ^{1}H NMR and IR spectra. One of us (S.A.) thanks the UGC for the award of a Junior Research Fellowship.

Registry No. 2-Azido-1-iodo-1-phenylcyclohexane, 101471-03-8; 2-azido-1-iodo-(4-methylphenyl)cyclohexane, 101471-04-9; 2-azido-1-iodo-(3,4-dimethylphenyl)cyclohexane, 101471-05-0; 2-azido-1-iodo-1-(4-methoxyphenyl)cyclohexane, 101471-06-1; 2-azido-1-iodo-1-(4-*tert*-butylphenyl)cyclohexane, 101471-07-2; 3-azido-2-phenylcyclohexene, 101471-08-3; 3-azido-2-(4-methylphenyl)cyclohexene, 101471-09-4; 3-azido-2-(3,4-dimethylphenyl)cyclohexene, 101471-10-7; 3-azido-2-(4-methoxyphenyl)cyclohexene, 101471-11-8; 3-azido-2-(4-*tert*-butylphenyl)cyclohexene, 101471-12-9; 1-phenylcyclohexene, 771-98-2; 1-(4-methylphenyl)-cyclohexene, 1821-23-4; 1-(3,4-dimethylphenyl)cyclohexene, 101471-13-0; 1-(4-methoxyphenyl)cyclohexene, 20758-60-5; 1-(4-*tert*-butylphenyl)cyclohexene, 60652-09-7; 1-azido-2-iodo-1-phenylcyclohexane, 25022-21-3; 1-azido-2-iodo-1-(4-methylphenyl)cyclohexane, 101471-14-1; 1-azido-2-iodo-1-(3,4-dimethylphenyl)cyclohexane, 101471-15-2; 1-azido-2-iodo-1-(4-methoxyphenylcyclohexane, 101471-16-3; 1-azido-2-iodo-1-(4-*tert*-butylphenyl)cyclohexane, 101471-17-4; iodine azide, 14696-82-3.

Crystal Structures of Isomeric (2,6-Dioxacyclohexyl)phenols: Models for Preassociation Complexes in Acid-Catalyzed Solvolysis of Acetals[1]

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Received July 22, 1985

The crystal structures of 2-, 3-, and 4-(2,6-dioxacyclohexyl)phenol are reported. The crystals of the 2-isomer are monoclinic, space group $P2_1/c$, with four molecules in the unit cell with dimensions $a = 7.520$ (2) Å, $b = 15.593$ (3) Å, $c = 8.550$ (2) Å, and $\beta = 113.13$ (2)°. The crystals of the 3-isomer are orthorhombic, space group $P2_12_12_1$, with four molecules in the unit cell with dimensions $a = 5.617$ (3) Å, $b = 12.127$ (3) Å, $c = 13.394$ (4) Å. The crystals of the 4-isomer are monoclinic, space group $P2_1/c$, with eight molecules in the unit cell with dimensions $a = 18.558$ (2) Å, $b = 5.991$ (1) Å, $c = 18.910$ (1) Å, and $\beta = 118.19$ (1)°. For the 2-isomer $R = 0.033$ for 1041 observed reflections, for the 3-isomer $R = 0.050$ for 740 reflections, and for the 4-isomer $R = 0.040$ for 1676 reflections. The analyses establish that there is intermolecular O–H···O hydrogen bonding in the 2-isomer (O1–H···O2 2.761 Å), the 3-isomer (O1–H···O2 2.730 Å), and the 4-isomer (O1–H···O2′ 2.720 Å and O1′–H···O2 2.770 Å). There is no intramolecular hydrogen bonding in the 2-isomer. Differences in the lengths of the two C–O bonds in the acetal group are sensitive to hydrogen bonding, with the longer C–O bond always containing the hydrogen-bonded oxygen. As such, the structures are models of preassociation complexes that are proposed for acid-catalyzed acetal solvolysis. Hydrogen bonding does lead to a lengthening of the C–O bond, and the orientation of this hydrogen bond appears to control the amount of lengthening. In the 2- and 4-isomers, the lengthened bond is clinal to the aromatic ring. This is consistent with the idea that maximum overlap, hence stabilization, would occur with an electron donor group. Finally, the failure to observe intramolecular catalysis[15] when the phenolic group is adjacent to the acetal because of the conflict between optimal orientation for hydrogen bonding and for stabilization of the incipient oxocarbenium ion is easily visualized in the crystal structure.

Introduction

Crystallography has risen to prominence in recent years as a major tool for understanding chemical dynamics and reaction mechanisms. The pioneering work of Dunitz and Burgi[2] has inspired many physical organic chemists to search for correlations between molecular structure and reactivity. Indeed, several groups[3–9] have reported correlations for a variety of structures.

Crystallography is attractive for the exploration of stereoelectronic[10,11] and orientation effects in molecules that undergo catalytic reactions. Jones and Kirby,[3e] have shown a linear relationship between bond length and reactivity based on correlations of crystal structural data with hydrolytic rate constants of tetrahydropyranyl acetals. The structural data[3d] reveal that the C–OR bond lengthens and the endocyclic O–C bond shortens with decreases in the pK_a of the conjugate acid of the leaving group. These structural changes are greater with axial rather than equatorial OR groups, suggesting that stereoelectronic factors control the magnitude of these changes. These

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(1) This work was supported by Grant GM 29128 from the National Institutes of Health.

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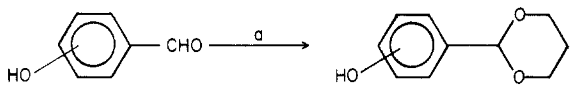
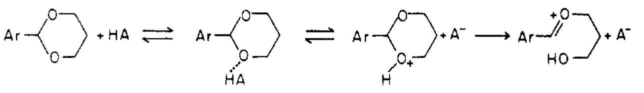
acetals solvolyze by an S_N1 mechanism.



(a) $HOCH_2CH_2CH_2OH$, $HCON(CH_3)_2$, $SO_2(OCH_3)_2$, CH_2Cl_2

This report describes single-crystal X-ray analyses of isomeric 2-, 3-, and 4-(2,6-dioxacyclohexyl)phenols, prepared[12] in one step from the appropriate hydroxybenzaldehyde. These molecules contain a weak acid (phenolic O–H) and an acetal that solvolyzes by the more common acid-catalyzed mechanism.[13] Intermolecular hydrogen bonding occurs in all isomers between the O–H and an acetal O. Hence these crystal structures serve as models for 'preassociation' complexes[14] in acid-catalyzed acetal hydrolysis.

A mechanistic study[15] on acid-catalyzed hydrolysis of (2,6-dioxacyclohexyl)arenes has clearly delineated the reaction steps involved. In most cases, proton transfer occurs in an equilibrium step prior to rate-limiting C–O cleavage. Protonation of the acetal oxygen weakens the C–O bond and facilitates cleavage.



The proposed mechanism[16,17] for proton transfer between oxygen atoms involves the formation of a hydrogen-bonded (preassociation) complex prior to the actual transfer step. While these complexes are difficult to observe spectroscopically or kinetically in solution,[18] the crystalline state affords the opportunity to evaluate stereoelectronic and orientational requirements for their formation. The data on the crystal structures of isomeric 2,6-dioxacyclohexyl phenols reported here show that hydrogen-bonding interactions contribute to lengthening of the C–O bond. In 4-(2,6-dioxacyclohexyl)phenol, stereoelectronic effects appear to control the orientation and interaction of the hydrogen bond.

Experimental Section

Materials. The title compounds were prepared as described previously.[12] Single crystals of each were obtained by recrystallization from an appropriate solvent: 2-, hexane/benzene; 3-, benzene; 4-, dichloromethane/ether.

X-ray Analyses. Intensity data for all three compounds were collected on an Enraf-Nonius CAD4 diffractometer equipped with Mo Kα radiation (λ = 0.71073 Å) and a graphite monochromator. Variable scan rates were employed in the ω–2θ scans in order to achieve approximately equal precision for all observable data. For monoclinic crystals, one quadrant of data was collected; for the orthorhombic crystal, one octant. Data reduction included corrections for background, Lorentz, and polarization effects; no absorption corrections were necessary. Equivalent data, if any, were averaged, and "observed" reflections, having $F_0^2 > 3\sigma(F_0^2)$, were used in the refinements.

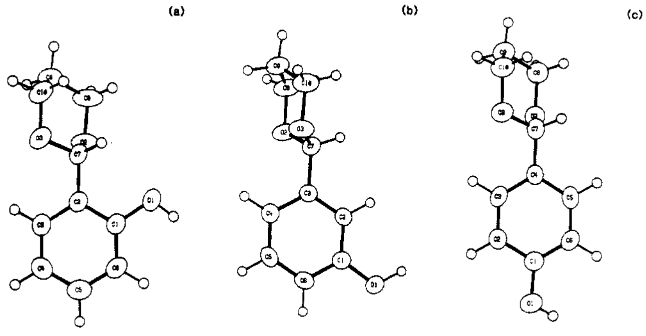


Figure 1. ORTEP drawings of isomeric (2,6-dioxacyclohexyl)phenols showing atom labeling: (a) 2-, (b) 3-, (c) 4-.

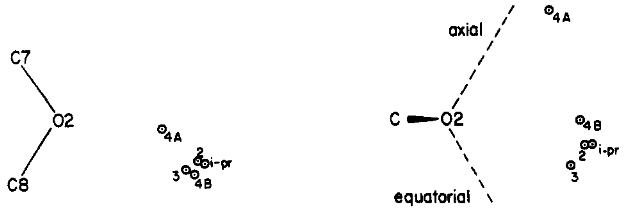


Figure 2. Scatterplots[20] (viewed in two perpendicular directions) illustrating the positions of hydrogen donor atoms O (in H–O) involved in hydrogen bonding to the acetal oxygen, O2. The broken lines illustrate the directions of the idealized sp^3 lone-pair orbitals. Angles are given in Table III. (5-Isopropyl-5-hydroxy-2,6-dioxacyclohexyl)benzene, ref 21.

Table I. Crystal Data Collection Summary for 2-, 3-, and 4-(2,6-Dioxacyclohexyl)phenol

	2-	3-	4-
formula	$C_{10}H_{12}O_3$	$C_{10}H_{12}O_3$	$C_{10}H_{12}O_3$
Mr	180.2	180.2	180.2
crystal system	monoclinic	orthorhombic	monoclinic
space group	$P2_1/c$	$P2_12_12_1$	$P2_1/c$
cell dimensions			
a, Å	7.520 (2)	5.617 (3)	18.558 (2)
b, Å	15.593 (3)	12.127 (3)	5.991 (1)
c, Å	8.550 (2)	13.394 (4)	18.910 (1)
β, deg	113.13 (2)		118.19 (1)
V, Å³	992.0 (8)	912.4 (10)	1853.1 (9)
Z	4	4	8
density calcd, g cm⁻³	1.207	1.319	1.292
crystal dimensions, mm	0.24 × 0.28 × 0.46	0.30 × 0.34 × 0.52	0.18 × 0.26 × 0.48
μ(cm⁻¹)	0.89	0.90	0.89
θ limits, deg	1–25	1–27	1–25
unique data	1616	1182	3250
observed data	1041	740	1676
variables	167	118	332
extinction	3.1 (3) × 10⁻⁶		4.0 (6) × 10⁻⁷
R	0.033	0.050	0.040
R_w	0.046	0.055	0.047
residual density, eA⁻³	0.17	0.19	0.19

Crystal data and angular limits for each structure are given in Table I.

All structures were solved using direct methods program MULTAN78,[19] completed by Fourier techniques, and refined by full-matrix least squares based upon *F* with weights $w = \sigma^{-2}(F_0)$. Carbon and oxygen atoms were refined anisotropically. Hydrogen atoms were located from difference maps, and were refined iso-

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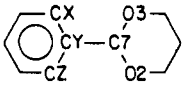
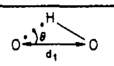
Table II. Noteworthy Structural Parameters for (2,6-Dioxacyclohexyl)arenes



	2-OH	3-OH	4-OH, A	4-OH, B	H, 5-OH, ipr[a]	4-Br, 5-hex[b]	4-Br, 3,5-diMe[c]	$4-CF_3$, 3,5-diMe[d]	4-Cl[e]
				Distances, Å					
02–C7	1.412 (2)	1.411 (4)	1.431 (3)	1.410 (3)	1.430 (4)	1.38 (1)	1.418 (4)	1.412 (3)	1.404 (8)
03–C7	1.395 (2)	1.397 (3)	1.398 (3)	1.390 (3)	1.399 (4)	1.38 (1)	1.404 (4)	1.408 (3)	1.402 (8)
C4–C7	1.495 (2)	1.499 (4)	1.493 (3)	1.506 (3)	1.493 (4)	1.56 (1)	1.511 (5)	1.532 (3)	1.495 (9)
				Angles, deg					
02–C7–03	110.0 (2)	111.6 (3)	110.2 (3)	110.8 (2)	109.8 (2)	111.9 (9)	111.7 (3)	112.5 (2)	110.4 (5)
02–C7–CY	108.2 (2)	108.3 (3)	109.1 (2)	108.5 (2)	108.6 (2)	107.5 (7)	106.7 (3)	112.4 (2)	109.4 (5)
03–C7–CY	110.2 (2)	109.0 (2)	109.8 (2)	109.8 (3)	109.7 (2)	108.2 (9)	109.3 (3)	112.9 (2)	109.4 (5)
				Torsion Angles, deg					
CX–CY–C7–02	86.3	–57.8	90.0	90.2	–72.4	76.8	87.4	–157.3	–155.7
CZ–CY–C7–02	93.7	121.2	–91.1	–89.0	109.4	–101.5	–89.0	28.9	25.5
CX–CY–C7–03	–153.4	63.8	–30.9	–31.0	167.5	–162.0	–33.5	–28.7	–34.7
CZ–CY–C7–03	26.7	–117.2	148.1	149.8	–10.7	19.7	150.1	157.5	146.6

[a] (5-Isopropyl-5-hydroxy-2,6-dioxacyclohexyl)benzene, ref 21. [b] 4-Bromo-1-(5-hexyl-2,6-dioxacyclohexyl)benzene, ref 22. [c] 4-Bromo-1-(3,5-dimethyl-2,6-dioxacyclohexyl)benzene, ref 23. [d] 4-Trifluoromethyl-1-(3,5-dimethyl-2,6-dioxacyclohexyl)benzene, ref 23. [e] 4-Chloro-1-(2,6-dioxacyclohexyl)benzene, ref 24.

Table III. Parameters for Hydrogen Bonding in 2-, 3-, and 4-(2,6-Dioxacyclohexyl)phenols



isomer	d_1, Å	O···H–O, deg	θ, deg	angle I,[a] deg	angle II,[b] deg
2-	2.761 (2)	160 (2)	6 (2)	15.8	e11.0
3-	2.730 (3)	146	12	20.2	e20.9
4-, form A, donor	2.720 (2)	165 (2)	5 (2)	4.5	a45.0
4-, form B, donor	2.770 (2)	167 (2)	9 (2)	21.3	e1.1

[a] Angle projection of O···O vector on C8–O2–C7 plane makes with bisector of C8–O2–C7; see Figure 2 (left). [b] Angle O···O vector makes with its projection on the C8-O2-C7 plane; e, equatorial; a, axial; see Figure 2 (right).

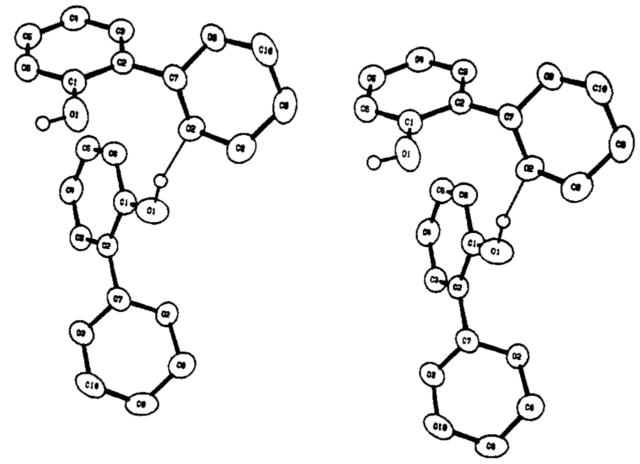


Figure 3. Stereoscopic view illustrating intermolecular hydrogen bonding in 2-(2,6-dioxacyclohexyl)phenol.

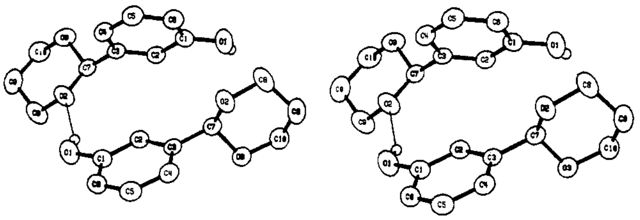


Figure 4. Stereoscopic view illustrating intermolecular hydrogen bonding in 3-(2,6-dioxacyclohexyl)phenol.

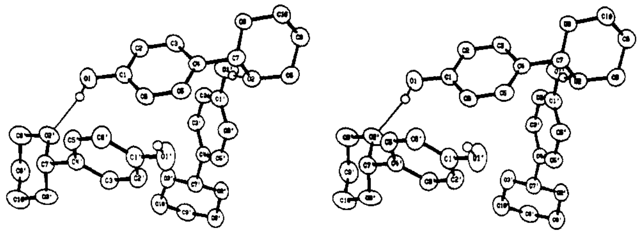


Figure 5. Stereoscopic view illustrating intermolecular hydrogen bonding in 4-(2,6-dioxacyclohexyl)phenol. Form A, unprimed labels; form B, primed labels.

tropically for the 2- and 4-isomers, but fixed with isotropic $B = 6.0$ Å^2 for the 3-isomer. Secondary extinction coefficients were refined for the two isomers.

R factors as well as residual densities in final difference maps are given in Table I.

Results

Perspective drawings are shown in Figure 1 while noteworthy bond distances, bond angles, and torsion angles are given in Table II. The 2,6-dioxyacyclohexyl ring in all the structures is in the chair conformation with the aryl group equatorial. Intermolecular hydrogen bonds between the phenolic hydroxyl and an acetal oxygen are present in all the structures as well. Positions of the donor and acceptor oxygens in these hydrogen bonds are shown in two scatterplots[20] (Figure 2). Other parameters associated with these hydrogen bonds are given in Table III.

2-(2,6-Dioxacyclohexyl)phenol. No intramolecular hydrogen bonding occurs, but there is intermolecular hydrogen bonding between the phenolic hydroxyl and the acetal oxygen that is orthogonal to the aromatic ring. As viewed in the stereoscopic drawing (Figure 3), the hydrogen atom lies close to both the plane defined by C7–O2–C8 as well as the plane that bisects C7–O2–C8.

3-(2,6-Dioxacyclohexyl)phenol. The conformation about the bond connecting the two rings is such that the C–H bond of the acetal coincides with the plane of the aromatic ring. As shown in Figure 4, the hydrogen atom lies out of the plane defined by C7–O2–C8 but close to the bisecting plane.

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4-(2,6-Dioxacyclohexyl)phenol. Each of the two intermolecular hydrogen bonds in the crystal gives rise to a different form of the molecule. Both hydrogen bonds are between the phenolic hydroxyl and the acetal oxygen that is orthogonal to the aromatic ring. As seen in Figure 5, for one hydrogen bond, the hydrogen atom nearly resides in both the plane defined by C7′–O2′–C8′ and the bisecting plane. In the other hydrogen bond, the hydrogen atom lies off the C7–O2–C8 plane toward the axially hybridized lone-pair orbital. In form A (unprimed atom labels) the hydrogen bond is to the acetal oxygen's axial lone pair, while in form B (primed atom labels) the hydrogen bond resembles those seen in both the 2- and 3-isomers.

Comparison of Hydrogen Bonds. Parameters for the hydrogen bonds (Table II) reveal no particular patterns. The O···O distances are quite similar and are not related to orientation. The O···H–O angles are also quite close except for the 3-isomer. The scatterplots (Figure 2) show only one axially oriented donor, lying along a vector corresponding to an idealized sp^3 lone-pair orbital. The other donors are close to in-plane but on the equatorial side. All the donors lie close to the bisecting plane on the C8 side rather than the more crowded C7 side.

Discussion

C–O Bond Lengths at Acetalic Carbon. The C–O bond lengths at the acetalic carbon for the four phenolic structures reported here as well as five nonphenolic structures reported by others[21–24] are compared in Table II. In several cases, one bond is significantly longer than the other. The differences between the two C–O bonds in the phenolic acetals are 0.019, 0.014, 0.033, and 0.020 Å for 2-, 3-, 4-A, and 4-B isomers, respectively. The hydrogen-bonded oxygen always has the longer C–O bond at the acetalic carbon. In 4-A where the C–O bond difference is the largest, the oxygen, O2, utilizes its axial lone-pair orbital as the hydrogen bond acceptor. In (5-isopropyl-5-hydroxy-2,6-dioxacyclohexyl)benzene,[21] the C–O bond difference is 0.031 Å with the longer bond to the hydrogen bonded oxygen. This hydrogen bond is oriented near the C–O–C plane, e16.2°, and close to the bisecting plane, 10.8°. In 4-bromo-1-(3,5-dimethyl-2,6-dioxacyclohexyl)benzene,[23] there is no hydrogen bonding but the difference is still 0.014 Å, and the longer bond is orthogonal to the aromatic ring. This pattern is also found in the phenolics, except in the 3-isomer, where both bonds are gauche. In the other nonhydrogen-bonding structures, 4-bromo-1-(5-hexyl-2,6-dioxacyclohexyl)benzene,[22] 4-(trifluoromethyl)-1-(3,5-dimethyl-2,6-dioxacyclohexyl)benzene,[23] 4-chloro-1-(2,6-dioxacyclohexyl)benzene,[24] the differences are less than 0.01 Å and none of the bonds is orthogonal. In summary, lengthening of an acetalic C–O bond occurs when it is orthogonal to the aromatic ring or when its oxygen is hydrogen-bonded.

Other structures with a (2,6-dioxacyclohexyl)arene fragment found by a search of the Cambridge Crystal Data Files[25] are sugar derivatives. All twenty of these benzylic acetals involve the oxygens at carbons 4 and 6 of the hexoses. When the difference in the acetalic C-O bond lengths is greater than 0.01 Å, the longer bond is always the one to the oxygen attached to carbon 4, a secondary carbon, instead of carbon 6, a primary.

Conformational Relationship between the Two Rings. Torsion angles for the acetalic carbon–phenyl carbon bond are given in Table II. For all 2,6-dioxacyclohexyl phenols except the 3-isomer, one of the C–O bonds is approximately orthogonal to the aromatic ring. This conformational preference is due to hydroxy's resonance donor character which stabilizes the antibonding σ^* orbital of the orthogonal C–O bond. The results necessitate modification of previous statements,[22,23] based on the structural data for the halo derivatives, that intrinsic factors do not affect this conformation. There is no doubt that an orthogonal conformation is required for maximum stabilization of the putative oxocarbenium ion in an acid-catalyzed solvolysis of the acetal. The data suggest that in the ground-state conformation about the bond connecting the two rings, the electron-donating aromatic rings (OH, ortho or para) are aligned to stabilize formation of an oxocarbenium ion.

Intermolecular Hydrogen Bonding. The structural parameters for hydrogen bonds observed in these molecules satisfy the criteria for hydrogen bonding established from surveys of crystallographic X-ray data,[20] neutron diffraction data,[26] and molecular orbital calculations.[27] The data reported here are consistent with findings that hydrogen bonding to a divalent oxygen occurs within in a kidney bean shaped volume element that includes the directions corresponding to the positions of both lone pairs.

Hydrogen bonding affects the difference in the C–O distances of the acetal, i.e., the hydrogen-bonded oxygen in an acetal has the longer C–O bond. This experimental result is consistent with a result from a computational study on a related system. Newton[28] has shown by ab initio calculations that the difference in lengths of the two C–O bonds in hemiacetals is sensitive to hydrogen bonding. Electron density used for hydrogen bonding arises in part from the other bonds to the donor atom, and these would be weakened. In form A of the 4-isomer, where the hydrogen bond is oriented toward a lone-pair position, the difference is the largest, 0.033 Å. A similar difference, 0.031 Å, is seen in (5-isopropyl-5-hydroxy-2,6-dioxacyclohexyl)benzene,[21] but the hydrogen atom lies close to the C–O–C plane.

Because hydrogen bonds are electrostatic interactions, they orient to minimize dipolar forces. Hence, in this case, they align in the plane defined by C–O–C. In a preassociation complex however, the preferred orientation might be along a lone pair. The product of proton transfer would have the proton attached at a lone-pair position. In the optimal orientation for intermolecular proton transfer, the donor's proton would be nearly colinear with the donor and acceptor atom. But if in a preassociation complex, the hydrogen bond is oriented in the plane, then rotation is required prior to or during transfer. In a fairly rigid system, e.g., an enzyme, such rotation would not occur as readily, making proper alignment of the hydrogen bond more critical than in simple bimolecular reactions.

The question of interest is whether or not the orientation, lone-pair versus in-plane, of a hydrogen bond affects the magnitude of the perturbation in C–O bond distance.

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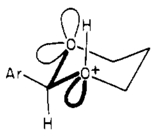
While the available structural data cannot definitively answer this question, the trend identified has important implications for acid-catalyzed solvolysis. In a lone-pair oriented complex, the proton is positioned much as a proton would be after transfer, i.e., a protonated 2,6-dioxacyclohexyl group would have the proton axial or equatorial. Complete protonation lengthens the C–O bond even more, as shown by ab initio calculations[29] of protonated dihydroxymethane. A lone-pair-oriented hydrogen bond should therefore have a larger effect on lengthening a C–O bond than one oriented in the C–O–C plane.[30]

Implications for Acid-Catalyzed Hydrolysis. The finding that hydrogen bonding lengthens C–O in the crystal structures of 2,6-dioxacyclohexylphenols suggests that these structures are models of preassociation complexes in acid catalysis. This finding also supports the hypothesis that bond cleavage is initiated before proton transfer. In the case of 2,6-dioxacyclohexyl acetal solvolysis, protonation would occur axially or equatorially in a separate step preceding bond cleavage.



In accord with stereoelectronic effects, the axial rather than the equatorial lone pair should be protonated. The equatorial lone pair is antiperiplanar to the other acetalic C–O bond. Deslongchamps[31] has pointed out the importance of the stereochemistry of protonation and the preference for maintaining the antiperiplanar relationship between a lone pair and a C–O bond. The data reported here support his conclusions. Wipff's calculations[29] suggest that the largest bond lengthening occurs when each oxygen has a lone pair antiperiplanar to a C–O bond. In 2,6-dioxacyclohexyl groups, this occurs when the axial position is protonated.

The structural results for the 4-isomer suggest a similar situation in hydrogen bonding. In this case, the lone-pair oriented hydrogen bond lengthens the C–O bond more than the in-plane hydrogen bond. Furthermore, the orientation of the lone-pair hydrogen bond is axial.

The orientation question is more important in rigid systems than in bimolecular reactions in solution. In a bimolecular reaction, ease of rotation of both donor and acceptor allows for their ready alignment before or during proton transfer. In rigid systems, catalytic efficacy may be reduced because donor and acceptor cannot achieve an optimal orientation. An illustration of this is the hydrolysis of the 2-isomer.

The lack of intramolecular catalysis[15] in the hydrolysis of the 2-isomer can be explained by examining the crystal structure. Since one of the C–O bonds is orthogonal to the phenyl ring, the other C–O bond forms a torsion angle of 30°. The optimal arrangement for intramolecular hydrogen bonding requires the acceptor oxygen to be nearly coplanar with the phenolic oxygen. This coplanarity requirement severely restricts the overlap of the aryl ring with the forming oxocarbenium ion. Although the C-O bond does not have to be exactly coplanar for hydrogen bonding, the tolerance for the positioning of the acceptor oxygen is quite small. Rotation of only a few degrees moves the acceptor oxygen to a position in which the hydrogen atom is no longer within the oxygen's kidney bean shaped volume element that defines the electron density available for hydrogen bonding. Since the optimal conformation for hydrogen bonding (coplanar) and the optimal conformation for stabilization of the oxocarbenium ion (orthogonal) are so different, the potential for intramolecular catalysis is reduced.

Summary and Conclusions

Crystal structures of hydrogen bonded 2,6-dioxacyclohexyl acetals have been analyzed as models of preassociation complexes for acid-catalyzed acetal hydrolysis. Keeping in mind the standard caveat, the effect of packing forces, of extrapolating crystal structure results to solution results, the analysis is consistent with previous suggestions about the consequence and stereochemistry of the protonation step in the hydrolysis. Although the number of structures analyzed is small, the trends are clear. Hydrogen bonding weakens the C–O bond and the orientation of the hydrogen bond controls the degree of weakening. The observation of an orthogonal conformation of the aromatic ring with respect to the weakened C–O bond supports the idea that maximum overlap, hence stabilization, occurs with an electron donor group. Finally, an examination of the crystal structure of the 2-isomer explains the failure to observe intramolecular catalysis in its hydrolysis because of the difference between the optimal conformations for intramolecular hydrogen bonding and for stabilization of the incipient oxocarbenium ion.

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Registry No. 2-(2,6-Dioxacyclohexyl)phenol, 6052-79-5; 3-(2,6-dioxacyclohexyl)phenol, 24393-13-3; 4-(2,6-dioxacyclohexyl)phenol, 6052-80-8.

Supplementary Material Available: Tables of bond lengths and bond angles, coordinates, and anisotropic thermal parameters (12 pages). Ordering information is given on any current masthead page.

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[30] The best available estimate (ab initio calculations of the water dimer at the 6-31G* level, M. D. Newton, personal communication) on the effects of the direction of the hydrogen bond indicate that the form in which the donor is oriented along the direction of the idealized sp^3 lone pair is more stable than the in-plane orientation by ca. 0.5 kcal·mol^{-1}. The former configuration also shows lengthening of the O–H covalent bond of the acceptor by 0.1 Å.

[31] Reference 10, pp 29–32.