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Conformational Analysis. 118. Application of the Molecular-Mechanics Method to Alcohols and Ethers[1,2]

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Abstract: Force-field calculations previously described for hydrocarbons and other compounds have been extended to include oxa compounds—alcohols and ethers. It was found necessary to explicitly include lone pairs in the calculations. The structures and energies of oxa compounds can be calculated fairly well, although the agreement with experiment is not as good as with hydrocarbons.

The force-field or molecular-mechanics method has been extensively applied to hydrocarbons during the last few years, and it is now clear that for most such compounds it is possible to calculate the structures and energies (and sometimes other properties such as vibrational spectra, and thermodynamic functions) with an accuracy that is usually competitive with the best that can be done experimentally.[3]

While the calculations have been highly successful for hydrocarbons and a number of classes of compounds that do not differ very much from hydrocarbons, such as silanes, carbonyl compounds, alkenes, and a few other classes,[3] very little has so far been reported on compounds containing ether (or alcohol) oxygen. Some preliminary studies[4] showed that most simple oxa compounds could be handled without difficulty, but further work has not been forthcoming. We will report here our calculational studies on this important class of compounds.

As is well known, hydrogen bonding is extremely important with alcohols and similar compounds in condensed phases. Our calculations are strictly for isolated molecules in the gas phase. While these calculations can be used as good approximations for molecules at low concentrations in inert solvents, we have not taken hydrogen bonding into account, and hence extrapolations of the calculations to polar solutions must be made with caution. In addition, for compounds which contain two or more polar groups, there are problems to be expected from the electrostatics of the situation.

The force field for hydrocarbons previously described (our 1973 force field[5]) was used unchanged. To extend the force field to alcohols, one needs to introduce the specific parameters which pertain to bond lengths, bond angles, torsional angles, dipoles, and energetics which involve oxygen. We originally chose dimethyl ether, methyl ethyl ether, methanol, and 1,3-dioxane as the key compounds to fit. Good structural data (microwave) are available for the first three of these compounds. As will be subsequently discussed, 2-methoxypyran was also studied to supply a needed torsional barrier which is missing in the above compounds.

The initial parameterization was carried out and then the parameters deduced from the above compounds were applied to a number of more complex compounds. A serious discrepancy was immediately noted, which involved the 5-alkyl-1,3-dioxanes. Many studies on alkyl-1,3-dioxanes have been recently reported and a large amount of conformational and isomerization equilibrium data are available for these systems. It is known that the 5-methyl compound has the methyl group preferentially equatorial, with the axial conformation being some 0.8 kcal/mol higher in energy. The preliminary force field developed to this point gave approximately 0 kcal/mol for this energy difference.

A force field is developed to fit experimental data and enable one to predict additional related facts. It can be parameterized in any way one desires, as long as it meets those specifications. However, to be most useful, a force field should have one additional qualification. It should present a physical picture which is in accord with ordinary chemical concepts, so that qualitative interpretation of the calculation is readily apparent to the chemist. Of course the lone pairs of electrons on oxygen are chemically very conspicuous in their effects. The molecular-mechanics calculation described above does not explicitly account for these lone pairs. Rather, the oxygen was treated as a spherical atom and the calculations carried out accordingly. Actually, the electron density about the oxygen is not spherical, but, apart from the perturbations due to bonding, is greater in the lone-pair region than elsewhere. We could see no obvious way to fit the methyldioxane data except by explicitly introducing the lone pairs into the molecular-mechanics calculation. This should not be taken to imply that explicit consideration of the lone pairs is required for any molecular-mechanics calculation on oxa compounds, but rather, it appears to be required for the calculation with this particular force field. At least, in spite of a lot of searching, we were not able to find any alternative that would reasonably reproduce the observed result.

As we pointed out earlier,[4] we did not wish to introduce explicit consideration of electron pairs unless it was absolutely required. At that time we were not certain whether such a requirement would be forthcoming. Now it seems that it is. This method of treating the problem is physically reasonable enough, it is consistent with chemical intuition, and it gives a pretty good representation of the experimental facts. Therefore, we feel that it is an acceptable method for handling such compounds. Again, we emphasize that these lone pairs of electrons exist as described only within the present force field and are not necessarily transferable to other situations of interest.

To treat the electron pair within the framework of our calculations, three quantities are required. The electron pair is assigned van der Waals characteristics, just like an atom, and the size (the van der Waals radius) and the hardness (ϵ) can be chosen so as to fit experimental facts. In addition, one must decide where the lone pair is to be positioned. So we have at least three parameters to fit and only one piece of data (the conformational energy of the methyl group in 5-methyl-1,3-dioxane) with which to fit them. This was resolved by considering also the 5-*tert*-butyl-1,3-dioxane, which gives a second piece of data (the conformational energy of the *tert*-butyl group). Finally, the position of the lone pair was established by the rationale given below.

If it is assumed that the lone pair occupies an orbital which is approximately an sp^3 hybrid, one can integrate along the axis of such n orbital with the appropriate nuclear charge and locate the center of the electron density. This proves to be about 0.5 Å from the nucleus. We therefore decided that for this kind of oxygen (and, looking ahead, also for amine nitrogen) to position the lone pair 0.5 Å from the nucleus. One knows that the angle between the lone pairs on the oxygen must be roughly tetrahedral, so an arbitrary value was picked that would fit with the methyldioxane data. To better fit the asymmetry of the methyl groups in dimethyl ether, the natural angle was opened up to 140°. Since we are using two spheres of electron density to mimic the actual complex charge distribution, the fact that this value is far from tetrahedral is neither worrisome nor of any special physical significance. The lone pairs were arbitrarily chosen to have a van der Waals radius of 1.2 Å and then an ϵ value was picked so as to give what was judged to be adequate agreement between the calculated conformational energies of the methyl- and *tert*-butyldioxane. These numbers are all summarized in Table I.

Table I. Force-Field Parameters

Natural Bond Lengths and Stretching Force Constants

Bond	l_0, Å	k_1, mdyn/Å	Dipole, D[b]
C–O	1.384	5.36	0.73
O–LP	0.500	4.60	0.60
O–H	0.942	4.60	–1.25

van der Waals Parameters

Atom	r, Å	ϵ, kcal/mol
O	1.65	0.002
LP	1.20	0.025
H[c]	1.20	0.040

Natural Bond Angles and Bending Force Constants

Angle[d]	Type[a]	θ_0, deg	k_0, mdyn Å/rad^2
C–C–O	0	109.1	0.56
C–C–O	1	108.1	0.56
C–C–O	2	109.1	0.56
C–O–C		103.16	0.62
C–O–LP		103.26	0.35
LP–O–LP		140.0	0.24
H–C–O	0	102.0	0.43
H–C–O	1	103.0	0.43
H–C–O	2	102.0	0.43
C_{sp^2}–C_{sp^3}–O	1	108.1	0.56
O–C–O		105.0	0.56
C–O–H		106.86	0.35
LP–O–H		101.0	0.24

Stretch–Bend Constants

Angles	$k_{l\theta}$, mdyn/rad
C–O–C	0.12
C–C–O	0.12
O–C–O	0.12
C–O–LP	0
LP–O–LP	0
H–C–O	0.04
C–O–H	0.04
LP–O–H	0

Torsional Effect Parameters

Dihedral angle	Torsional constants, kcal/mol
C–C–C–O	0.53
C–C–O–C	1.21
C–C–O–LP	0
C_{sp^2}–C_{sp^3}–O–C	1.21
C_{sp^2}–C_{sp^3}–O–LP	0
H–C–C–O	0.53
H–C–O–C	1.21
H–C–O–LP	0
O–C_{sp^3}–C_{sp^2}–C_{sp^2}	0
O–C–O–C	1.21
O–C–O–LP (twofold)	0.9
C–C–O–H	0.27
H–C–O–H	0.27

[a] The type refers to the number of hydrogens attached to the central atoms. [b] The atom to the left is the positive end of the dipole unless the sign of the dipole is negative. [c] These parameters apply to a hydrogen attached to oxygen (or nitrogen). Hydrocarbon hydrogens are bigger and harder. [d] The force constants for angles involving oxygen were arrived at beginning with the spectroscopic constants[6] and reducing them by about half as was done with thia compounds,[7] and for that matter with the alkanes, too.[3c] Oxetane was the key compound to fit the heat of formation here, just as thiacyclobutane and cyclobutane were the key compounds in their respective classes.

The properties chosen for the lone pair are such that one must also modify the properties of the rest of the oxygen atom in order to retain a total assemblage (oxygen atom plus lone pairs), which shows reasonable van der Waals characteristics when approached by other closed-shell species. This was ac-

Table II. Comparison of the Calculated and Observed Structures of Oxygen Compounds Used to Define the Parameter Set[e]

	Calcd	Obsd	
Dimethyl Ether[a, 13]			
C–O	1.419	1.416 ± 0.006	
C–O–C	111.76	111.72 ± 0.35	
O–C–H_s	106.67	107.17 ± 0.65	
O–C–H_a	110.06	110.83 ± 0.33	
Dipole moment[b]	1.30	1.30	
Energy barrier	2.72	2.72	
Methyl Ethyl Ether[a, 14]			
C–O(Me)	1.414	1.415	
C–O(Et)	1.419	1.425	
C–C–O	108.64	108.88	
C–O–C	112.54	112.58	
1,3-Dioxane[15]			
O–C–(O–C)	1.410	1.41[15a]	1.393 ± 0.025[15b]
O–C–(C–C)	1.410	1.41	1.439 ± 0.039
C–C	1.528	1.50	1.528 ± 0.013
C–C–C	108.23	108	107.7 ± 1.1
C–O–C	110.00	111	110.9 ± 1.5
C–C–O	109.88	109.5	109.2 ± 0.8
O–C–O	110.65	111	115.0 ± 2.8
CO–CO	65.1	63	58.9
CO–CC	59.1	59	56.0
OC–CC	53.0	55	57.4
Dipole moment[c]	1.95	2.13[d]	
Methanol[a, 16]			
O–H	0.944	0.945 ± 0.003	
C–O	1.410	1.431 ± 0.003	
C–O–H	108.44	108.53 ± 0.48	
Barrier	1.08	1.07	
Dipole moment[b]	1.63	1.71	

[a] The bond lengths given for C–C and C–O bonds are 0.006 Å longer than the actual experimental values, which were determined by the microwave method (see Text). [b] Dielectric constant = 1. [c] Dielectric constant = 2.2. [d] In benzene. [e] Bond lengths (Å), bond angles (degrees), dipole moments (debye units), and energy barriers (kcal/mole).

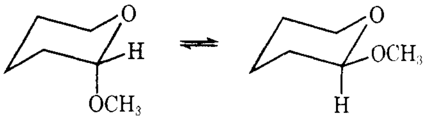
complished by greatly reducing the value of ϵ for the remainder of the oxygen atom. Plots of the energy of the system when a closed shell approaches the assemblage in this construction are rather similar to what was observed when the same closed shell approached the oxygen atom with the "whole atom" parameters deduced earlier. The differences are in the strongly directional effects, which now occur close in to the oxygen. The size and positioning of the lone pairs seem to be in reasonable accord with a similar model independently arrived at from SCF calculations.[8] Finally, so that the lone pairs could be handled by the program without additional effort, they were assigned bending and stretching constants, just as are ordinarily assigned to atoms.

With polar compounds such as the oxa derivatives under discussion, one would like to be able to calculate the dipole moments, and if there is more than one polar group in the molecule, one needs to somehow calculate the electrostatic interactions involved. We have devoted some effort to a study of this general problem, although the work is not yet complete. However, as an interim procedure, we decided in general to simply assign bond moments to bonds involving polar groups other than hydrocarbons. Thus, a C_{sp^3}–H and a C_{sp^3}–C_{sp^3} bond are assigned zero moments, but all other bonds (unless between identical atoms) are in principle assigned a dipole moment. In addition, because of the treatment used in the present work for the oxygen atom, we have also decided to assign moments to the lone pairs. Just how to partition these moments is not completely clear, so we have proceeded in a somewhat arbitrary manner. The moment of a lone pair was given the arbitrary value 0.6 D, with the nucleus positive and the pair negative. (Empirical bond moments of organic molecules are always arbitrary in part, because the number of parameters to be assigned always exceeds the number of indepennt observables.) Then, to fit the observed dipole moments of dimethyl ether[9] and methanol,[9] the C–O was assigned a bond moment of 0.73 D with the carbon positive and the O–H bond was assigned a moment of 1.25 D with the hydrogen positive. To calculate the dipole moment of any given molecule, the bond momens are simply added vectorally in the usual way. To calculate the electrostatic interaction between the dipoles, they were placed at the midpoints of the bonds concerned and the electrostatic interaction was evaluated[3c] with the aid of a procedure originally due to Jeans, following in numerical detail after the procedure by Lehn and Ourisson.[10] Interactions between dipoles which have an atom in common are neglected. This procedure works moderately well for calculating molecular dipole moments. It is not exact, because it neglects induced moments. These can in fact be handled quite well,[3c,11] although the whole scheme then becomes much more elaborate and discussion of this point will be deferred to a later paper. This calculational scheme gives electrostatic energies which are on the whole satisfactory, but there are known cases where it fails and such failures have been attributed to induction.[12] There are serious problems with both this interpretation and the numerical calculation, which again we cannot take up here. We will simply state at this point that the electrostatic calculation as done here is moderately satisfactory in most cases, but failures are known.

For dimethyl ether, the geometry (microwave) is known[13] (but, while there are some general rules that permit one to determine on approximate electron diffraction equivalent of a microwave geometry, the corresponding relationships for oxa compounds are not known, but are assumed the same as for hydrocarbons), as is the dipole moment and the torsional barrier. The natural bond lengths, natural bond angles, and torsional constants were chosen so as to give satisfactory agreement with experiment here (Table II). Some conflict with experiment is unavoidable because the observed C–O bond length for methanol[16] is 1.431 Å, while that for the corresponding bond in the ether[13] is only 1.416 Å. Because of the repulsion between the methyl groups in the ether, the bond lengths are calculated in the reverse order. The bond lengths chosen represent a compromise weighted in favor of the ether.

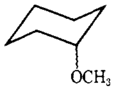
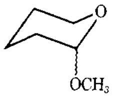
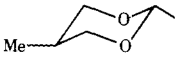
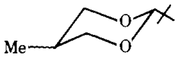
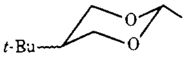
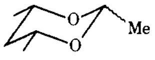
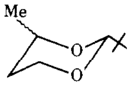
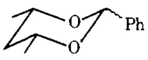
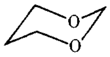
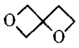
The structure for methyl ethyl ether was fit rather well and allowed a few more parameters to be fixed. For 1,3-dioxane, the available experimental information is on a substituted molecule and of rather low accuracy.[15] However, again this experimental structure was fit, which allows specification of all of the remaining parameters except one.

The final parameter was determined by a consideration of 2-methoxytetrahydropyran. It is known from a temperature-dependent study of the NMR spectrum in tetralin solvent[17]

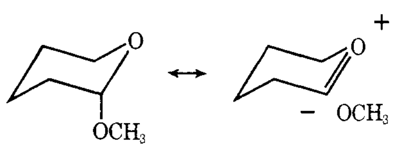


that the equilibrium shown has $\Delta H°$ equal to 1.05 kcal/mol and $\Delta G°$ equal to 0.81 kcal/mol. Other measurements of this equilibrium under various conditions give somewhat different values, depending in particular on the solvent, but they are of this general magnitude. Our initial calculations here were unsatisfactory, giving the wrong sign to the enthalpy change. A consideration of the physical reason for the observed effect of a more stable axial isomer (the so-called *anomeric effect*[18]) led us to the following conclusion. If one imagines a lone-pair orbital (sp^3 hybrid) on the ring oxygen which is axial, it is

Table III. Conformational Energies of Some Ethers

Compd	Favor	Exptl values, kcal/mol ΔG	Exptl values, kcal/mol ΔH	Calcd value, kcal/mol, ΔH	Ref
$CH_3CH_2OCH_2CH_3$	TT	–	1.1	0.84	21
$CH_3OCH_2OCH_3$	GG			3.16	22, 23
	Equatorial	0.45	–	0.33	24
	Axial	–	1.05	1.11	17, 24
	Equatorial	–	0.9	0.67	25
	Equatorial	0.89	0.86 ± 0.09	0.44	26
	Equatorial	1.46		2.33	27
	Equatorial	4.0	4.0	2.44	27, 28
	Equatorial	2.8	–	1.72	29
	Same	0	–	0.0	30
Ph ∥ and Ph ⊥				Favor ⊥	
	Chair	–	6–9	4.2 (benzene)	31
					
	Same	0 ± 0.3		0.36	32
Half-chair and envelope					
	Envelope			1.35 (benzene)	32b
		–	0.15	0.82 (vacuum)	32c
	Planar	–		Favor planar	33

parallel to and well positioned for an interaction with the axial C–O bond of the methoxyl group. The equatorial methoxyl cannot similarly interact with either of the lone pairs. This is reminiscent of the situation with axial halo ketones[19] and Bohlmann bands in infrared spectra,[20] although the details are somewhat different. In any event, one can write a resonance structure indicated, and this suggests the presence of a twofold barrier about the O1–C2 bond. In order to fit the observed equilibrium for 2-methoxytetrahydropyran, the magnitude of this barrier was chosen to be 0.9 kcal/mol and the orientation is such that the energy is a minimum when the lone pair–O–C–O angle is 0 or 180° and a maximum at 90°.[20a]



All of the structural parameters were now fit and may be presumed to lead to reasonably good structural calculations for simple ethers and also for alcohols, although some systematic error in the C–O bond is expected for the latter. Many compounds were studied. Since there is virtually no accurate structural information concerning these compounds, these calculations will not be discussed here in detail, but it will simply be mentioned that the results seem quite unexceptional.

We then turned to a number of more unusual kinds of compounds, which should have their structures more or less accurately calculable by the force field described above. Some of the more interesting of these are listed in Table III. A number of these will be discussed here in turn. Beginning with diethyl ether, the calculations favored the trans–trans conformation; the only other apparently reasonable conformation is trans–gauche, which is calculated to be less stable than the trans–trans by 0.84 kcal/mol. An experimental value for this energy difference is 1.1 kcal/mol.[21]

Next we looked at 2,4-dioxapentane, for which the gauche–gauche conformation is favored over the trans–gauche by 3.16 kcal/mol by calculation. Experimentally, only the gauche–gauche form is detected.[22,23]

For methoxycyclohexane, the equatorial conformation is calculated to be more stable than the axial by 0.3 kcal/mol, while the experimental values vary somewhat, 0.4 being the best estimate.[24]

Then we come to a series of 1,3-dioxanes.[25–29] It was not possible to fit the conformational energies of the 5-alkyl groups as well as one would like. However, the difficulty here seems to stem from the hydrocarbon part of the force field and it is not something that we have any control over at this point. The 5-methyldioxanes with alkyl groups at C2 to fix the conformation gave calculated values of 0.4–0.7 kcal/mol for the conformational energies, the equatorial always being more stable. The experimental values are around 0.9 kcal/mol. The usual rationale applied in understanding such situations has been that the absence of axial hydrogens at atoms 1 and 3 results in relatively little repulsion for the axial methyl, and hence the latter has a much lower energy than in cyclohexane.

Table IV. Heat of Formation Parameters (kcal/mol)

	C-O	O-H	$O\text{-}\overset{H}{\underset{H}{C}}\text{-}H$	$O\text{-}\overset{H}{\underset{C}{C}}\text{-}C$	$O\text{-}\overset{C}{\underset{C}{C}}\text{-}C$	O-C-O
General	−16.92	−25.462	2.395	−2.868	−5.142	−5.874
Strainless	−12.413	−27.252	4.346	−5.426	−11.010	−4.695

Table V. Heats of Formation (kcal/mol)[a]

Compd	Tor. en-ergy	Conf. en-ergy	Steric energy	ΔH, calcd	ΔH, exptl	Calcd − exptl	Exptl error
Dimethyl ether	0	0	12.80	−44.17	−43.99	−0.18	0.12
Methyl ethyl ether	0.3	0.28	12.75	−51.63	−51.72	0.09	0.16
Diethyl ether	0.6	0.50	12.69	−59.15	−60.26	1.11	0.19
Methyl propyl ether	0.6	0.36	13.99	−56.89	−56.82	−0.07	0.26
Dipropyl ether	1.2	0.55	15.16	−69.81	−69.85	−0.04	0.40
Methyl isopropyl ether	0.1	0.08	13.26	−59.98	−60.24	0.26	0.23
Tetrahydrofuran	0	0.09	17.92	−44.21	−44.02	−0.19	0.17
Tetrahydropyran	0	0	14.40	−54.70	−53.39	−1.31	0.24
Diisopropyl ether	0.2	0	13.36	−76.30	−76.20	−0.10	0.54
Di-*tert*-butyl ether	0	0	18.05	−87.54	−87.10	−0.44	0.4
Dimethoxymethane	0.6	0	22.96	−83.24	−83.27	0.03	0.14
1,3-Dioxane	0	0	21.40	−83.74	−83.71	−0.04	0.27
Oxetane	0	0	35.67	−19.66	−19.25	0.41	0.15
Methanol	−0.3	0	4.65	−48.40	−48.07	−0.33	0.05
Ethanol	0	0.04	4.54	−56.14	−56.24	0.10	0.07
Isopropyl alcohol	0	0.06	3.89	−65.24	−65.12	−0.12	0.13
tert-Butyl alcohol	0	0	2.48	−74.58	−74.72	0.14	0.21

[a] The values obtained for the parameters are listed in Table VI.

Table VI. Additional Heats of Formation (kcal/mol)[a]

Compd	Tor. en-ergy	Conf. en-ergy	Steric energy	ΔH, calcd	ΔH, exptl	Calcd − exptl	Exptl error
n-Propyl alcohol (TG)	0.3	0.21	5.85	−61.26	−61.17	−0.09	0.30
1-Butanol (TTG)	0.6	0.56	7.16	−66.19	−65.79	−0.40	0.14
2-Butanol	0.3	0.27	5.49	−70.01	−69.98	−0.03	0.23
Di-*n*-butyl ether (TTTTTT)	1.8	1.2	17.76	−79.73	−79.82	0.09	0.27
Methyl *tert*-butyl ether	0	0	13.22	−68.06	−69.7	1.6	1.3
Cyclohexanol (ω = 180°)	0	0.21	8.98	−69.94	−68.38	−1.56	0.42
1,3-Dioxolan	0	0.14	23.38	−74.74	−71.1	−3.64	0.2
2-Methoxytetra-hydropyran	0	0.27	23.37	−96.91	−95.5	−1.41	0.5
4-Methyl-1,3-dioxane	0	0	20.77	−92.84	−90.46	−2.38	0.35
cis-2,4-Dimethyl-1,3-dioxane	0	0	19.21	−104.00	−102.26	−1.74	0.50
5,5-Dimethyl-1,3-dioxane	0	0	21.96	−99.19	−100.67	1.48	0.42

[a] These compounds were not used in deriving the parameters in Table V.

When the *tert*-butyl group is placed at the 5-position, the equatorial conformation is more stable than the axial experimentally[27] by 1.5 kcal/mol, and this is calculated to be 2.3 kcal/mol, somewhat high.

The methyl at the 2-position in 2,4,6-trimethyl-1,3-dioxane is experimentally stable in the equatorial position and very much less stable when axial (4.0 kcal/mol[27,28]). This energy difference may be compared with the corresponding energy difference in methylcyclohexane (1.7 kcal/mol). This sizable increase compared to the cyclohexane case has been interpreted in terms of the short C-O bond length combined with the rather small C-O-C bond angle, which leads to a considerably increased repulsion between the methyl and the syn-axial hydrogens. We calculated the value to be much larger than in cyclohexane (2.4 kcal/mol), but smaller than observed. Similarly, the conformational energy of a methyl at C4 is observed to be large (2.8 kcal/mol) and calculated to be sizable (1.72 kcal/mol) and smaller than the axial methyl at C2, but the absolute value is again too small.

Finally, the phenyl group at C2 is calculated to have a zero rotational barrier, and this is what has been determined experimentally.[30] The calculation indicates that this is primarily from a balancing of two effects. When the phenyl ring is parallel to the symmetry plane of the molecule, an ortho hydrogen has a severe repulsion with the axial hydrogen at C2. When the phenyl is perpendicular, there are moderately severe repulsions between the ortho hydrogens on the benzene ring and the equatorial lone pairs on the oxygens. The two interactions just balance out.

The chair-boat-twist conformations of 1,3-dioxane were examined. It is calculated that the classical boat forms are unstable, the unsymmetrical twist-boat form being an energy minimum, 4.2 kcal/mol higher in energy than the chair (for D = 2.2). Experimental values exist only for substituted dioxanes and are of the order 6–9 kcal/mol.[31]

Finally, some smaller rings were examined. Tetrahydrofuran is calculated to be more stable in the half-chair than in the envelope conformation by 0.4 kcal/mol, while the experimental is 0 ± 0.3 kcal/mol.[32] Dioxolane is calculated to be more stable in the envelope conformation by 0.82 kcal/mol under vacuum, increasing to 1.35 kcal/mol at D = 2.2. The calculated dipole moments are 0.75 and 1.58 D for the half-chair and envelope forms, respectively, compared with measured values of 1.47 D in benzene.[9] Experimentally the molecule is an almost free pseudo-rotor in the gas phase (barrier 0.15 kcal/mol[32c]), and it is claimed that in solution the envelope form is stable.[32b] Oxetane is calculated to be planar, which is observed experimentally.[33]

We conclude that our calculational model is reasonably good for structure, although less so than for hydrocarbons. While part of the problem is thought to be due to the relative paucity and inaccuracy of data for oxa compounds as compared with hydrocarbons, we are left with the distinct impression that the model simply is not as good at portraying the physical situation with these compounds as it is with hydrocarbons. Doubtlessly it can be improved, however, and clearly it will be adequate for many purposes.

We now turn to the heats of formation of oxa compounds. Again, all of the hydrocarbon numbers from our 1973 force field are used here unchanged. In addition, it was necessary to evaluate six parameters, as shown in Table IV. This was done by fitting the calculated heats of formation to the experimentally known values[34] for the 17 compounds which are listed in Table V. Note that for most of these the fit is good. The only two significant errors occur in the case of diethyl ether and tetrahydropyran. We believe that the tetrahydropyran error can be traced to a systematic error in the 1973 hydrocarbon force field, as six-membered rings containing other kinds of functional groups (including cyclohexene and cyclohexanone) quite consistently have their heats of formation calculated to be too negative. The problem with diethyl ether is not evident and is possibly due to experimental error. However, overall the results are certainly reasonable.

Then in Table VI are listed additional heats of formation calculated for a number of interesting compounds using the parameters developed above (plus two more as indicated). For the first six compounds, relatively simple ones, the calculations are in reasonable agreement with experiment. Cyclohexanol is too negative, a failing with six-membered rings pointed out above.

The additional compounds listed in Table VI are shown to illustrate the difficulties, not to advocate the usefulness of this scheme for the calculation of such quantities. The very large errors here (1-3 kcal/mol) are discouraging. We are unable to decide at present why these numbers are as poor as they are. The point we wish to make is that for simple compounds (containing one oxygen) the heat of formation calculations look to be nearly as reliable as they are for hydrocarbons, although the number and types of compounds investigated have been much less (because of a lack of experimental data for comparison). However, when there are two oxygens in the molecule, the results are best described as poor. Presumably they can be improved, although whether they can be really made adequate or not is not clear at this time. The reasons for the difficulty here are uncertain, but are likely to involve, at least in part, the electrostatics of the molecules. The reliability of the experimental data is also far from certain. For one thing, the heats of vaporization of the molecules are often estimated and the reliability of such estimates for these kinds of compounds is completely unknown.

References and Notes

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(2) This was supported in part by the grant AM-14042 from the National Institutes of Health, Institute of Arthritic and Metabolic Diseases.

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Kinetic Applications of Electron Paramagnetic Resonance Spectroscopy. 26. Quantum-Mechanical Tunneling in the Isomerization of Sterically Hindered Aryl Radicals[1]

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Abstract: Rate constants for the isomerization of 2,4,6-tri-*tert*-butylphenyl to 3,5-di-*tert*-butylneophyl have been measured from −26 to −160 °C, and for the corresponding isomerization of 2,4,6-tri-*tert*-(perdeuteriobutyl)phenyl from 20 to −150 °C. This pair of reactions has an exceptionally large deuterium kinetic isotope effect at all temperatures. Arrhenius plots for both reactions are nonlinear and over any range of temperature the activation energy and Arrhenius preexponential factor are much larger for deuterium than for hydrogen transfer. The experimental results can be quantitatively accounted for by quantum-mechanical tunneling through a potential barrier. The analogous isomerization of 2,4,6-tri(1′-adamantyl)phenyl, which was studied from −28 to −167 °C, also occurs by quantum-mechanical tunneling. Attempts to detect other aryl radicals by EPR spectroscopy are described.

Phenyl is a destabilized[5] σ radical[6-8] which is highly reactive both in atom abstractions and in additions to unsaturated molecules. It therefore has only a transitory existence under most conditions. For this reason, attempts to detect phenyl and other aryl radicals in solution by physical methods have not met with much success.[9] Prior to the preliminary account of the present work,[10] only two aryls had been detected in solution by EPR spectroscopy.[11] These two radicals [o-$CH_3OC(O)C_6H_4\cdot$ and o-$(CH_3)_2NC(O)C_6H_4\cdot$] were generated by rapid reduction of the appropriate arenediazonium ion with

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