A Theoretical Study of Intramolecular Hydrogen Bonding in Ortho-Substituted Phenols and Thiophenols

Stephen W. Dietrich,[1a] **Eugene C. Jorgensen,**[1a] **Peter A. Kollman,***[1a] **and Steve Rothenberg**[1b]

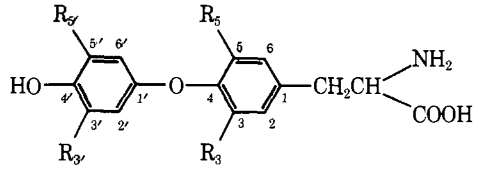
Contribution from the Department of Pharmaceutical Chemistry, University of California, San Francisco, California 94143, and Information Systems Design, Santa Clara, California 95208. *Received February 13, 1976*

Abstract: CNDO/2 and ab initio molecular orbital methods are used to study the intramolecular hydrogen bonding and substituent interactions of ortho-substituted phenols and thiophenols. The two methods are compared in their abilities to predict experimental minimum energy conformational and hydrogen bonding energies as well as far- and near-infrared OH absorption spectra for these compounds. The "anomalous" order of intramolecular hydrogen bonding strengths in the *o*-halophenols (Cl $\gtrsim$ F > Br > I) is further examined by calculations on a number of model systems. The ab initio calculations provide insight into the reasons for the "anomalous" order as well as for the unusual blue shift of the OH hydrogen-bonded IR stretching frequency for *o*-trifluoromethylphenol.

Although molecular orbital calculations have been carried out on a wide variety of hydrogen bonded systems,[2] relatively few studies have involved molecules with an internal hydrogen bond. The intramolecular hydrogen bonds of the enol forms of malonaldehyde and acetylacetone have been examined by a number of MO methods.[3-8] Murthy et al.[3] used EHT and CNDO/2 MO methods to study intramolecular hydrogen bonds and their effects on cis–trans isomerism in *o*-fluorophenol, *o*-nitrophenol, and salicylaldehyde. The influence of intramolecular hydrogen bond formation on the conformation of 1,3-propanediol has been examined by Johansson et al.[9] using ab initio MO calculations. Such studies have generally given reasonable estimates of the energy of intramolecular hydrogen bond formation, although most have dealt with systems which form unusually strong intramolecular hydrogen bonds due to internal geometry constraints.[4-8] It is somewhat surprising, however, that more MO studies of intramolecular hydrogen bonding have not been undertaken in view of the fact that a wide variety of biologically active compounds possess as necessary for activity functional groups capable of forming intramolecular hydrogen bonds.

Some of the first examples of intramolecular hydrogen bonding to be studied experimentally were a number of ortho-substituted phenols.[10,11] Interest in these molecules was stimulated by the observation of two IR O–H stretching bands. From relative IR O–H stretching intensities, the amounts of "cis" hydrogen bonded and "trans" nonhydrogen bonded conformations and hence the energy of the intramolecular hydrogen bond could be estimated. In this manner, for example, Pauling[10] first estimated the intramolecular hydrogen bond energy of *o*-chlorophenol in CCl_4 to be about 1.4 kcal/mol. Since then, the intramolecular hydrogen bonding of a number of ortho-substituted phenols[10-22] and unsymmetrical 2,6-dihalophenols[15,23] has been similarly examined in various solvents and in the gas phase. O–H torsional frequencies of the cis and trans conformations of a number of ortho-substituted phenols have been used to calculate the enthalpy differences between the two conformations.[12,24] The intramolecular hydrogen bonding of *o*-trifluoromethylphenol has been examined by Doddrell et al.[25] using EHT and CF_3 ^{19}F and OH ^1H chemical shift studies. Schaefer[26] has proposed linear relationships of intramolecular hydrogen bond energies with OH ^1H chemical shifts as well as with O–H torsional frequencies. Allan and Reeves[27,28] have also used OH ^1H chemical shifts for the study of intramolecular hydrogen bonds in ortho-substituted phenols.

We are currently[29-31] engaged in research examining the activities and modes of action of the thyroid hormones and analogues (**1**). It has been shown that the phenolic 4′-OH group is essential for maximal in vivo[32] and in vitro thyromimetic activity.[31,37,38] The role of this phenolic OH has been logically ascribed to involvement in hydrogen bond formation with some appropriate receptor functional group. Little attention has been paid, however, to ortho-substituent interactions with the phenolic OH group, especially with respect to their effect on both intramolecular and intermolecular hydrogen bond formation. Because of the paucity of theoretical MO studies of intramolecular hydrogen bonding and because of our interest in the thyroxine system, we have undertaken the first extensive theoretical examination of the intramolecular interactions of ortho substituents with the phenolic OH group of various phenols (as model systems) using CNDO/2 and ab initio MO calculations. We also examined the intramolecular hydrogen bonding of several ortho-substituted thiophenols in order to compare their hydrogen bonding with that of the phenols.



1, R_3, R_5 = halogen, CH_3
$R_{3'}$, $R_{5'}$ = halogen, alkyl, aryl, OH, NO_2, H

The questions to which we address ourselves in this study are: (1) Can we explain the "anomalous" order[13,15,24,27] of intramolecular hydrogen bonding strengths in the *o*-halophenols (Cl $\gtrsim$ F > Br > I)? (2) Can our theoretical model explain the minimum energy conformational and hydrogen bonding energies of other ortho-substituted phenols? (3) Specifically, for *o*-CF_3-phenol, why is the larger hydrogen-bonded peak in the IR shifted to higher frequencies from the free O–H stretching frequency[16] (to our knowledge, the only known hydrogen bond where such an effect occurs)? (4) Can we rationalize the observed far- and near-infrared absorption spectra using our calculations? (5) Can we predict the intramolecular hydrogen bond energies and properties of ortho-substituted phenols and thiophenols not yet determined experimentally?

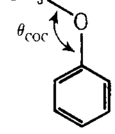
Computational Details

The CNDO/2 molecular orbital method[39-41] was used in some of these calculations. Except for the halogens the standard atomic parameters were used. Except where noted the halogen parameters employed were those previously used by Kollman et al.,[29] and only s and p but no d orbitals were used for F, Cl, Br and I. Unless specifically noted, standard geometrical parameters (selected as suitable average values from available experimental data) were used.[42,43] In particular, if available, bond lengths were taken directly from ref 42, and if not, they were selected from ref 43. For comparison with the CNDO/2 results and experimental data, ab initio molecular orbital calculations using the Gaussian 70 quantum chemistry program[44] with an STO-3G basis set[45] were carried out in selected cases.

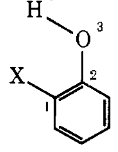
We found[46] that the ability of *o*-iodophenols to form intramolecular hydrogen bonds is best predicted when the iodine Slater exponent, ρ_{I}, is given a value of 1.20 instead of the value of 1.09 originally used by Kollman et al.[29] In order to examine the effects of varying ρ_{I}, we conducted a series of CNDO/2 calculations on the physical properties of CH_3I, C_2H_5I, and C_6H_5I model systems.[46] From these studies it appears that a ρ_{I} value of 1.2 reduces the "effective" coulomb repulsion between I and neighboring atoms enough to bring such properties as rotational barriers and hydrogen bonds, which involve I- - -H nonbonded interactions, into reasonable agreement with experiment.

A CNDO/2 search for a minimum energy θ_{COH}[47] in phenol led to a prediction of 110°, consistent with the neutron diffraction studies of Frey et al.,[48] who found C–O–H angles of 111.1 and 113.0° for the phenolic hydroxyls of L-tyrosine and L-tyrosine·HCl, respectively. It is also consistent with the concept of lone pair–lone pair repulsions on the oxygen reducing the magnitude of θ_{COH} from the pure sp^2 value of 120° for a hydroxyl conjugated with an aromatic ring (just as lone pair–lone pair repulsions on oxygen reduce θ_{HOH} of water to 104.52[49] from the pure sp^3 value of 109.47°). Frey et al.[48] also found C–O bond lengths of 1.369 and 1.378 Å and O–H bond lengths of 0.982 and 0.989 Å for the phenolic hydroxyls of L-tyrosine and L-tyrosine·HCl, respectively. These values are close to the values of 1.36 and 0.96 Å[42] we used for the phenolic C–O and O–H bond lengths, respectively. Further justification for our use of $\theta_{\mathrm{COH}} = 110°$ for phenols in all subsequent calculations in this paper was provided when it was found that the CNDO/2 energies of all the *o*-halophenols (cis and trans conformers), of all the unsymmetrical 2,6-dihalophenols ("cis" and "trans" conformers), and of *o*-cresol (cis and trans conformers; all CH_3 rotamers) are all significantly lowered when the phenolic θ_{COH} is decreased from 120 to 110°.[46]

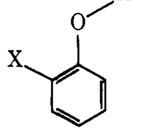
Because we were also interested in examining the intramolecular hydrogen bonding of *o*-methoxyphenol, we conducted a CNDO/2 search for a minimum energy θ_{COC} for anisole (**2**;



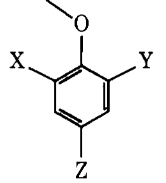
2



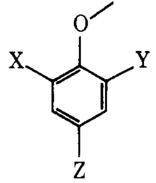
3



4



5



6

CH_3 protons staggered). The resulting prediction of $\theta_{\mathrm{COC}} = 113°$ was used in subsequent calculations on *o*-methoxyphenol.

Table I. Experimental[a] and Theoretical Values for Intramolecular Hydrogen Bond Strengths of the *o*-Halophenols (**3** and **4**)

X	$E(6\rightarrow 7)$, kcal/mol	Method of study[b]	Solvent	Ref
F	0.2	A		3
	1.1	B		3
	1.44	C	Cyclohexane	24
	1.63	C	Vapor	24
	1.37	B		*d*
	1.68	D		*d*
Cl	1.62	C	Cyclohexane	24
	1.63	C	Vapor	24
	1.44	E	CCl_4	15
	2.38	E	CCl_4	13
	2.36	F	CS_2	27
	2.30	B		*d*
	1.77	D		*d*
Br	1.57	C	Cyclohexane	24
	1.53	C	Vapor	24
	1.21	E	CCl_4	15
	2.15	E	CCl_4	13
	2.14	F	CS_2	27
	1.68	B		*d*
I	1.45	C	Cyclohexane	24
	1.32	C	Vapor	24
	1.08	E	CCl_4	15
	1.54	E	CCl_4	13
	1.65	F	CS_2	27
	0.75[c]	B		*d*

[a] ΔE values estimated, if necessary, from the experimental data. [b] A = EHT MO calculations; B = CNDO/2 calculations; C = IR OH torsional frequencies; D = ab initio MO calculations; E = IR OH stretching frequencies; F = NMR: ^1H chemical shifts. [c] $\rho_{\mathrm{I}} = 1.20$; $\Delta E(3\rightarrow 4) = -0.86$ kcal/mol for $\rho_{\mathrm{I}} = 1.09$. [d] This study.

This value is not far from $\theta_{\mathrm{COC}} = 116.9°$ found for the two aromatic methoxy groups of 1-rotenene in the x-ray crystal study of Arora et al.[50]

In order to estimate relative populations of different conformations or geometries of certain molecules, classical Boltzmann distribution partition functions, $T = 298$ K, and constant entropy contributions between the different conformations or geometries were assumed (see ref 51 and 52 for discussion and examples of this type of treatment).

Our assumption that ΔS for the cis → trans conversion for unsymmetrically ortho-substituted phenols and thiophenols is essentially zero is supported by experimental thermodynamic studies on *o*-*tert*-butylphenol,[20] 2-*tert*-butyl-6-methylphenol,[20] *o*-bromophenol,[22] 2,4-dibromo-6-*tert*-butylphenol,[22] and *o*-iodophenol.[53] (See ref 54 for a more complete discussion of this area.)

Results and Discussion

(A) Intramolecular Hydrogen Bond Energies in *o*-Halophenols. The first ortho-substituted phenols we examined were the *o*-halophenols. CNDO/2 and ab initio cis → trans energy differences and data from a number of sources and representative of a variety of experimental and theoretical methods are presented in Table I. A CNDO/2 value of 1.09 for the iodine exponent ρ_{I} does not adequately predict the intramolecular hydrogen bond strength of *o*-iodophenol. Increasing ρ_{I} to 1.20 significantly improves the agreement of the CNDO/2 results with the experimental data. Because of this improvement, we elected to use a value of 1.20 for ρ_{I} in all subsequent calculations. Our CNDO/2 calculations predict that the order of intramolecular hydrogen bond strengths for the *o*-halophenols is Cl > Br > F > I, while the ab initio calculations, although

Table II. Experimental, CNDO/2, and ab Initio Intramolecular Hydrogen Bond Strengths of Unsymmetrical 2,6-Dihalophenols (**5** and **6**)

			ΔE(**5**→**6**), kcal/mol		
X	Y	Z	CNDO/2[a]	Ab Initio[a]	Exptl[b]
Cl	F	H	0.89	0.04	0.18[d]
Cl	F	Cl			0.25[e]
Br	F	H	0.27		0.10[d]
Br	F	Br			0.08[d]
Cl	Br	H	0.61		0.19[e]
Cl	Br	Cl			0.28[e]
F	I	H	0.68[c]		0.36[d]
F	I	I			0.33[d] 0.40[e]
Cl	I	H	1.52[c]		0.55[d]
Cl	I	Cl			0.56[d]
Br	I	H	0.90[c]		0.70[e]
Br	I	Br			0.47[e]

[a] This study. [b] Method of study = E, footnote *b*, Table I; solvent = CCl_4. [c] $\rho_1 = 1.20$. [d] Reference 15. [e] Reference 23.

lacking the Br and I compounds, suggest the order Cl $\gtrsim$ F > Br > I. The various experimental data give the order to be either Cl > Br > F > I or Cl > F > Br > I, depending on both the experimental method of study and the solvent used. Our calculations should relate most directly to the gas phase where the order appears to be Cl $\gtrsim$ F > Br > I.[24]

In either case, the magnitudes of the calculated internal hydrogen bond strengths are both reasonable and in moderately good agreement with the experimental data. Considering the relative electronegativities, one might expect the order of intramolecular hydrogen bond strengths to be F > Cl > Br > I. Yet both the theoretical calculations and the experimental data are in agreement with the fact that *o*-fluorophenol forms a weaker internal hydrogen bond than expected. This finding will be discussed in more detail below.

In order to further investigate this "anomalous" trend in the intramolecular hydrogen bond strengths of the *o*-halophenols, we next examined the intramolecular hydrogen bonding of the unsymmetrical 2,6-dihalophenols. The CNDO/2 and ab initio results are summarized in Table II. Experimental data on some unsymmetrical 2,6-dihalophenols are also presented for comparison. The CNDO/2 calculations predict the intramolecular hydrogen bond strength order of the halogens of the unsymmetrical 2,6-dihalophenols as Cl > Br > F > I. Again, although lacking the Br- and I-containing compounds, the ab initio calculations suggest the order to be Cl $\gtrsim$ F > Br > I. The CNDO/2 calculations generally slightly overestimate the differences between the relative hydrogen bond strengths. Once again, however, both the experimental data and the theoretical calculations predict an anomalously weak intramolecular hydrogen bond for F when located ortho to a phenolic OH group.

This "anomalous" ordering of the intramolecular hydrogen bond strengths of the *o*-halophenols has been attributed to differences in: (1) interactions of halogens with solvent;[15,17,18,20,55,56] (2) tendencies to dimerize;[24] (3) deviations from optimal hydrogen bonding geometries;[13,18,23,24,28,55] (4) intrinsic hydrogen bonding capabilities of the halogens;[24] (5) inductive and mesomeric capabilities of the halogens;[13,23] and (6) repulsive halogen–oxygen and halogen–hydrogen "interorbital" interactions.[13] Since both the experiments and ab initio calculations find the "anomalous" order (Cl $\gtrsim$ F > Br > I) to hold for gas phase intramolecular hydrogen bonding, we feel explanations 1 and 2 cannot be used to explain the anomalous order.

The next possible explanation we examined was geometric. The optimal strength for an intermolecular O–H- -X hydrogen bond should occur when $\theta_{HOX} = 0$.[2,57] Hence, the magnitude of the deviation of θ_{HOX} from 0° should be reflected in a corresponding deviation in the H- -X hydrogen bond strength. Although there is a full 10° variation in θ_{HOX} in the *o*-halophenols,[46] the difference in θ_{HOX} between X = F (50.54°) and X = Cl (44.26°) is only 6.28°, too small a change to account by itself for the weaker than expected H- -F hydrogen bond. Based on the angles alone, *o*-iodophenol ($\theta_{HOX} = 39.11°$) should form the strongest hydrogen bond. Besides the hydrogen bond angle, the intramolecular geometry constraints might cause some repulsions which do not follow the same order as electronegativity. By comparing $R(\text{X- -H})_{\text{calcd}}$ and the sums of van der Waals radii for H + X,[46] one can see that the degree of overlap of the van der Waals radii of H and X is in the order F < Cl < Br < I. In particular, while there is significant overlap for Cl, Br, and I, for F the overlap is considerably less. This suggests that the weaker than expected intramolecular hydrogen bond of F in *o*-fluorophenol may be partially due to the unfavorably (as compared to the halogens of the other *o*-halophenols) large H- -F internuclear distance. This is qualitatively supported by the fact that the CNDO/2 calculated energy dependence on θ_{COH} is apparently essentially independent of the ortho substituent for the trans conformers of the ortho-monosubstituted phenols, but not for the cis conformers.[46] As θ_{COH} is decreased from 120 to 110° for the cis conformers of the *o*-halophenols, R(H- -X) decreases and the overlap of the H and X van der Waals radii should increase. For *o*-fluorophenol, the minimal overlap of the H and F van der Waals radii at $\theta_{COH} = 120°$ is not significantly changed at $\theta_{COH} = 110°$. For *o*-chlorophenol, the overlap of the H and Cl van der Waals radii is significant (and perhaps nearly optimal) and hence $\Delta E(\theta_{COH} = 110° \rightarrow \theta_{COH} = 120°)$ is much larger than for *o*-fluorophenol. Thus, decreasing θ_{COH} from 120 to 110° causes a small increase in hydrogen bonding for *o*-fluorophenol and a larger increase for *o*-chlorophenol, in addition to the inherent stabilization seen in phenol. This causes the $\Delta E(\theta_{COH} = 110° \rightarrow \theta_{COH} = 120°)$ ordering to be Cl > F > H for X. While the overlap of the van der Waals radii also increases significantly for X = Br and I, apparently the overlap is greater than the optimal value and H- -X repulsive interactions also increase significantly as θ_{COH} is decreased, to the point where $\Delta E(\theta_{COH} = 110° \rightarrow \theta_{COH} = 120°)$ is only slightly greater for *o*-iodophenol than for phenol itself. These trends for the *cis*-*o*-halophenols are mirrored by parallel trends for the unsymmetrical 2,6-dihalophenols.[46]

Geometrical constraints clearly do not provide a complete and satisfactory explanation for the order of the intramolecular hydrogen bond strengths. To determine what the "intrinsic" hydrogen bond acceptor capabilities of aromatically substituted halogens are, we carried out a series of CNDO/2 and ab initio model calculations on the *intermolecular* hydrogen bond strengths of the four different H_2O/halobenzene dimers. This was done so that we might examine the deviations of the hydrogen bond strengths and the halogen- -H and halogen- -O internuclear distances of the *o*-halophenols from the "ideal" equilibrium values of these model systems. The model system's geometry (**7**, Y = H) was defined as follows. The halogen, oxygen, and proton involved in the hydrogen bond are colinear since this geometry should give maximal hydrogen bond strength.[2,57] The O–H bond involved in the hydrogen bond lies in the plane of the halobenzene in order to best approximate the cis geometry of the respective *o*-halophenol. The second O–H bond of H_2O lies in a plane perpendicular to the halobenzene ring plane in order to minimize any interactions of this second H_2O proton with the halobenzene. With $\theta_{COX} = 180°$, a geometry search for the minimum energy R(X- -O) was conducted for each halobenzene (see **7**). Then, at this

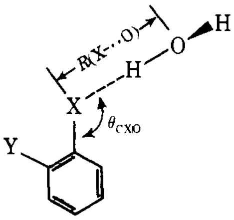
Table III. CNDO/2 and ab Initio Hydrogen Bond Energies and Geometrical Parameters for H_2O/Halobenzene Dimers (**7**)[a]

X	Y	ΔE_{calcd},[b,c] kcal/mol	θ_{CXO}, deg	$R(X\text{- -}O)_{calcd}$,[c,d] Å	$R(X\text{- -}H)_{calcd}$,[e] Å	
F	H	3.82	180	2.56	1.60	CNDO/2
		3.92	120[g]	2.56	1.60	
Cl	H	5.50	180[g]	2.97	2.01	
Br	H	3.73	180[g]	3.20	2.24	
I	H	1.94	180[g]	3.47	2.51	
F	H	1.52	180	2.91	1.95	Ab initio
		2.09	120[g]	2.91	1.95	
Cl	H	0.66	180	3.93	2.97	
		0.91	120[g]	3.93	2.97	
F	OH[f]	2.21	120[h]	2.91[h]	1.95[h]	
Cl	OH[f]	0.97	120[h]	3.93[h]	2.97[h]	

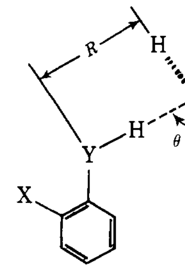
[a] H_2O geometry; see ref 60. [b] ΔE = hydrogen bond strength. [c] ΔE and R(X- -O) were calculated exactly with CNDO/2. With ab initio, R(X- -O) was calculated to be ±0.07 Å; ΔE and R(X- -O) were then estimated by a three-point quadratic fit. [d] $R(X\text{- -}O)_{calcd}$ = minimum energy R(X- -O) were value at $\theta_{CXO} = 180°$. [e] $R(X\text{- -}H)_{calcd} = R(X\text{- -}O)_{calcd} - 0.96$ Å. [f] O–H trans to X. [g] θ_{CXO} = minimum energy θ_{CXO} value for 30° variations in θ_{CXO} from 180 to 90°. [h] Minimum energy geometry for H_2O/C_6H_5X dimer.

minimum energy R(X- -O), a geometry search (30° variations in θ_{CXO} to 90°) for the minimum energy θ_{CXO} was conducted. The results are presented in Table III and help a great deal in explaining the CNDO/2 and ab initio orders for the intramolecular hydrogen bond strengths of the *o*-halophenols. The calculated orders of equilibrium intermolecular hydrogen bond energies for the H_2O/halobenzene dimers are Cl > F > Br > I (CNDO/2) and F > Cl > Br > I (extrapolating for the Br and I points, ab initio). So the ab initio calculated intermolecular hydrogen bond energies apparently are of the same order as the halogen electronegativities, as expected. With CNDO/2, however, the F value is anomalously out of line with the trend expected for the halogen electronegativities. The ab initio ordering appears to be the correct one for these intermolecular hydrogen bonds, since experimentally the ordering for intermolecular hydrogen bond strengths is F > Cl > Br > I for the phenol/cyclohexyl halide dimers[61,62] and for the phenol/*n*-pentyl halide dimers.[63] The CNDO/2 intramolecular hydrogen bond strengths of the *o*-halophenols (Table I) range from 35 to 45% of the intermolecular hydrogen bond strengths of the respective H_2O/halobenzene dimer model systems. These decreases from the theoretically "optimal" intermolecular hydrogen bond strengths appear with CNDO/2 to be due to the geometrical constraints of the *o*-halophenols. On the other hand, the ab initio intramolecular hydrogen bond strength of *o*-fluorophenol is approximately equal to the intermolecular hydrogen bond strength of the respective H_2O/fluorobenzene dimer model system, and the ab initio *intramolecular* hydrogen bond strength of *o*-chlorophenol is actually significantly greater than the *intermolecular* hydrogen bond strength of the respective H_2O/chlorobenzene dimer. It appears reasonable that a significant amount of this greater intramolecular hydrogen bond strength in *o*-chlorophenol might be due to relief of O- -Cl repulsions existing in the trans isomer (**4**, X = Cl) rather than to the intrinsic H- -Cl hydrogen bond strength. The overlap of the halogen and O van der Waals radii is approximately equal for all four of the H_2O/halobenzene dimers (Table III) but increases dramatically as a function of halogen size from very little for *o*-fluorophenol to quite significant for *o*-iodophenol.[46] This, coupled with the ab initio ΔE(cis → trans) for *o*-chlorophenol being much greater than ΔE for the H_2O/chlorobenzene dimer, suggests that the intramolecular hydrogen bond energies of the *o*-halophenols may be in part due to the phenols attempting to relieve halogen- -O repulsion and in part due to specific H- -halogen attractions. O- -halogen repulsive bond orders increase F < Cl < Br < I and H- -halogen attractive bond orders increase I > Br > Cl > F[46]and, thus, it is not surprising that the observed hydrogen bond strengths do not follow the order of electronegativity. The order of intramolecular hydrogen bond strengths parallels the intermolecular order in the CNDO/2 calculations because this method is known to generally underestimate interatomic repulsions. So, the intrinsic H- -halogen attractions play the dominant role in this series.

The ab initio intermolecular hydrogen bonding results for the H_2O/halobenzene dimers are not totally definitive because we have used a model hydrogen bond (HOH- -X-C_6H_5) to represent the intramolecular hydrogen bonds and have compared them with the actual *o*-X-C_6H_4OH intramolecular hydrogen bond. We thus calculated and compared the hydrogen bond energies of H_2O/*o*-halophenol dimers (**7**, Y = OH trans to X) with the intermolecular hydrogen bond energies of the corresponding H_2O/halobenzene dimers (**7**, Y = H). In order to enable direct comparison of hydrogen bond energies, the hydrogen bonding geometries of the H_2O/*o*-halophenol dimers were taken to be the minimum energy geometries calculated for the corresponding H_2O/halobenzene dimers. As can be seen from Table III, an *o*-hydroxyl substituent slightly increased the intrinsic hydrogen bonding capabilities of fluorobenzene and chlorobenzene by essentially the same percentages: 5.9 and 6.5%, respectively.



7



8

Reversing the situation, the effect of an *o*-halo substituent on the intrinsic hydrogen bonding capability of phenol was next examined. For C_6H_5OH as a proton donor to H_2O (**8**, X = H; Y = O), a "linear" dimer was assumed with the two monomeric units lying in perpendicular planes and with the two O atoms and the H involved in the hydrogen bond colinear.[2,57] θ (see **8**) was taken as 57° (from the STO3G H_2O dimer value[64]). Only R (the O- -O internuclear distance) was varied in our geometry search. The ab initio minimum energy geometry determined for the H_2O/C_6H_5OH dimer was then assumed (in order to enable direct comparison of hydrogen bond energies) for calculating the intermolecular hydrogen bond energies of the H_2O/*o*-halophenol dimers (**8**, X = F or

Table IV. CNDO/2 and ab Initio Hydrogen Bond Energies (ΔE)[a] and Geometries[b] for H_2O/o-X-C_6H_4YH (Y = O or S) Dimers (**8** and **32**)

Dimer structure	X		Y = S CNDO/2	Y = S Ab initio	Y = O CNDO/2	Y = O Ab initio
32	H	R	2.90	3.35	2.54	2.79
		ΔE	2.31	2.57	6.12	4.31
11	H	R	2.76	3.56	2.56	2.64
		ΔE	10.54	1.12	6.04	8.97
11	F	R				2.64[c]
		ΔE				9.31
11	Cl	R				2.64[c]
		ΔE				10.10

[a] Energies in kcal/mol. [b] R = Y- -O internuclear distance in Å. [c] Minimum energy R value for H_2O/C_6H_5OH dimer **8**.

Cl; Y = O). As seen in Table IV an electron-withdrawing, ortho halogen increases the intermolecular hydrogen bonding energy of phenol as a proton donor. The increases, however, are of the opposite order (F with a 3.8% increase < Cl with a 12.5% increase) as the halogen electronegativities (F > Cl), probably as a result of the ability of F to more easily (than Cl) donate electron density by resonance back into the aromatic ring and hence to the OH group. Mulliken populations show that in both the halobenzenes and the o-halophenols, the fluoro compound donates ~0.04 more π electrons into the ring than the chloro. (The $\sigma + \pi$ charge of fluorine (-0.130) is slightly more negative than that of Cl (-0.117).) The partial positive charge on the proton is also consistent with the relative strength of O–H as a proton donor, being +0.217 (phenol), +0.220 (*trans*-o-fluorophenol), and +0.224 (*trans*-o-chlorophenol). This suggests that Cl in o-chlorophenol may have a greater effect than F in o-fluorophenol in reinforcing the intramolecular hydrogen bond. Estimating the intrinsic hydrogen bond energy for the dimer o-F-C_6H_4OH- - -F-C_6H_5-o-OH by (hydrogen bond energy for o-OH-C_6H_4F- - -H-O-H dimer)·(hydrogen bond energy ratio for o-F-C_6H_4OH- - -OH_2 dimer vs. H-O-H- - -OH_2 dimer) = (2.21 kcal/mol)(9.31 kcal/mol/5.88 kcal/mol[64]), a value of 3.50 kcal/mol is obtained.

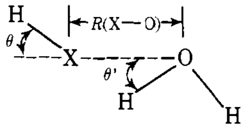
That this is significantly larger than the actual ab initio calculated intramolecular hydrogen bond energy of o-fluorophenol of 1.68 kcal/mol can, as before, be primarily ascribed to deviations in o-fluorophenol from the "optimal" hydrogen bonding geometry. A similar estimation of the intramolecular hydrogen bond energy of o-chlorophenol yields a value of (0.97 kcal/mol)(10.0 kcal/mol/5.88 kcal/mol) = 1.67 kcal/mol, which is still slightly less than the actual ab initio calculated intramolecular hydrogen bond energy of o-chlorophenol of 1.77 kcal/mol. Taking into account the nonoptimum geometry of the intramolecular Cl- -H-O hydrogen bond, it seems very surprising that this estimated intermolecular hydrogen bond is weaker than the intramolecular hydrogen bond. Evidently there is an apparent enhancement of intramolecular hydrogen bond energy in o-chlorophenol that is not reflected in these simple model systems.

It is clear from this comparison of the intra- and intermolecular hydrogen bonding capabilities of the halogens, however, that the mesomeric, inductive, and intrinsic hydrogen bond properties of the halogens (possible explanations 4 and 5) are not the major reason for the fact that the intramolecular hydrogen bond in o-chlorophenol is stronger than the corresponding bond in o-fluorophenol.

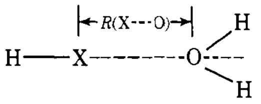
Table V. Geometries and ab Initio Hydrogen Bond Energies (ΔE) of H–X- - -H_2O Dimers (**9**)[a]

X	R(X- -O), Å	θ,[b] deg	θ',[b] deg	ΔE, kcal/mol
F[c]	2.65[e]	70[e]	0[e]	4.79
	2.65	70	50.54[g]	0.91
	2.75[f]	70	0	4.54
	2.75[f]	70	50.54[g]	1.01
Cl[d]	3.60[e]	77[e]	0[e]	1.19
	3.60	77	44.26[g]	0.66
	2.94[f]	77	0	−4.51
	2.94[f]	77	44.26[g]	−1.81

[a] H_2O experimental geometry; see ref 60. [b] See **12**. [c] HF experimental geometry; R(H–F) = 0.9170 Å, from ref 43. [d] HCl experimental geometry: R(H–Cl) = 1.2745 Å, from ref 43. [e] Minimum energy dimer geometry; θ was calculated to 1° and R(X- -O) was clculated to 0.01 Å. [f] Equal to R(X- -O) for o-X-phenol; see ref 46. [g] Equal to θ_{HOX} for *cis*-o-X-phenol; see ref 46.



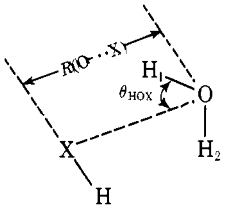
9



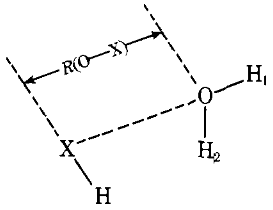
10

As an additional model system for the intramolecular hydrogen bonding of the *cis*-o-halophenols (**3**), we conducted ab initio examinations of the intermolecular hydrogen bonding of the H–X- - -H–O–H dimers (**9**, X = F or Cl). The results of these studies are presented in Table V. A "linear" dimer was assumed with the two monomer units lying in one plane. For the initial energy minimization, the X, O, and H atoms involved in the hydrogen bond were assumed to be colinear[2,57] (**9**, $\theta' = 0°$). Geometry searches were conducted simultaneously for both R(X- -O) and θ (see **9**). The θ value obtained was used in all subsequent calculations. As expected, the dimer hydrogen bond was greater for HF (4.79 kcal/mol) than for HCl (1.19 kcal/mol). Hydrogen bond energies were then calculated for the dimers upon changing either the minimum energy R(X- -O) distance to the R(X- -O) distance in the corresponding o-X-phenol and/or the minimum energy θ' angle (0°) to the θ_{HOX} angle of the corresponding *cis*-o-X-phenol. R(F- -O) for the minimum energy H–F- - -H–O–H dimer is only slightly less than R(F- -O) for o-fluorophenol. Hence, the dimer energy is only slightly decreased upon changing the R(F- -O) distance of the minimum energy dimer to that of *cis*-o-fluorophenol. Variation of θ' from 0° to θ_{HOX} for *cis*-o-fluorophenol, however, results in over 80% loss of hydrogen bond strength. Simultaneous variation of R(F- -O) and θ' to the *cis*-o-fluorophenol values results in a large hydrogen bond energy loss dominated by the θ' change but slightly compensated for by the increase in R(F- -O). The situation is quite different, however, for the H–Cl- - -H–O–H dimer. Changing θ' from 0° to the *cis*-o-chlorophenol θ_{HOX} value results in loss of 50% of the hydrogen bond strength, much less than for the fluorine case. R(Cl- -O) in the H–Cl- - -H–O–H minimum energy dimer is much greater than R(Cl- -O) for *o*-chlorophenol. Changing R(Cl- -O) to the *o*-chlorophenol value, therefore, causes a large Cl- -H repulsion that results in large net dimer repulsion. Simultaneously changing θ' and R(Y- -C) to the corresponding *cis-o*-chlorophenol values results in a net dimer repulsion dominated by the Cl- -H repulsion but significantly compensated for in part by allowing the O–H bond to move off the Cl- -O axis. Although this is a very simplified model system for the intramolecular hydrogen bonding of the *o*-fluoro- and *o*-chlorophenols, these results suggest that the deviations of the intramolecular hydrogen bond strengths from values which should be intrinsically possible may be due primarily to deviation of θ_{HOX} from 0° for *o*-fluorophenol and to H- -Cl repulsion (due to a small R(Cl- -O)) in *o*-chlorophenol. In the latter case, deviation of θ_{HOX} to larger angles actually might relieve this H- -Cl repulsion. On this basis one might intuitively predict that θ_{COH} for the *cis-o*-halophenols should increase F < Cl < Br < I, although experimental evidence is not available to test this hypothesis. As a corresponding model for the X- -O repulsions in the *trans-o*-halophenols (**4**), we calculated the repulsion energies for the H–X- - -OH_2 dimers (**10**, X = F or Cl; all atoms coplanar, H–X bond bisecting H–O–H angle, R(X- -O) = R(X- -O) for the *o*-X-phenols). The ab initio calculations surprisingly predict the repulsive energies for the two dimers to be essentially the same: 1.54 kcal/mol for HF- - -OH_2 and 1.53 kcal/mol for HCl- - -OH_2. This simple model system, however, is unable to reflect any influence that F and Cl might have on the X- -O repulsion by inductive and resonance electronic effects.

We examined one further set of geometries for the HX/H_2O dimers in order to attempt to approximate the *o*-X-phenol geometries more exactly. The geometries of the HX/H_2O dimers (**11** and **12**) were chosen such that R(X- -O) = R(X- -O) for the corresponding *o*-X-phenol,[46] the X–H, O–H_1, and O–H_2 bonds have the same vectorial orientations as the F–C, O–H, and O–C bonds for the corresponding *o*-X-phenol, and the H–O- - -X angle of **11** = θ_{HOX} for the corresponding *cis-o*-X-phenol (**3**).[46] (**11** and **12** reflect the geometries of the corresponding cis and trans conformers, respectively, of the corresponding *o*-X-phenols (**3** and **4**) and should reflect more accurately (than **9** and **10**) the spatial distributions of electron densities of the H, X, and O atoms of these phenols. This requires an H_2O θ_{HOX} of 110° and R(O–H) of 0.96 Å.) ΔE(**11**→**12**) values can then be used to estimate the intramolecular hydrogen bond strengths of the corresponding *o*-X-phenols. The ab initio calculations gave ΔE(**11**→**12**) values of −4.75 and −1.08 kcal/mol for X = F and Cl, respectively. However, the total energy for these structures was ~300 kcal/mol above the energies for the isolated monomers, so it may be that this difference only reflects a relief of H- -H repulsions in the trans conformation.



11



12

We also tried to estimate the physical forces behind these H bonds by comparing the energies of the *p*-halophenols with those of the cis and trans conformations of the corresponding *o*-halophenols. These results are presented in Table VI. It appears that one cannot use the para-ortho energy comparison as support for the importance of O- -halogen repulsion effects, since the inductive effect of two electronegative groups ortho is more destabilizing for the fluoro (more inductively withdrawing than the chloro). The mesomeric effect of F might also contribute to lowering the *o*-halophenol (cis-trans) energy difference since it makes F more positive. However, this is not the dominant effect since our calculations find that fluorobenzene is still capable of forming stronger intermolecular bonds than chlorobenzene. Additional insight into the nature of intramolecular hydrogen bonding of the *o*-halophenols and unsymmetrical 2,6-dihalophenols comes from examining the atomic populations and bond orders of these compounds.[46] In all cases, electron density is shifted from the phenolic proton to both the phenolic oxygen and the halogen upon hydrogen bond formation. With the ab initio calculations the majority of the electron density shift is from the phenolic proton to the proton-accepting halogen, with much less of the shift from the phenolic proton to the proton-donating oxygen. These same qualitative charge density shifts have been noted before.[3,9] The H, O, and halogen charge densities, as well as the H- -halogen and O- -halogen bond orders, are affected very little by the substitution of a second halogen ortho to the phenolic OH for both the CNDO/2 and ab initio calculations. This is supported by the fact that the difference between the intramolecular hydrogen bond strengths (CNDO/2 or ab initio) of any two of the *o*-halophenols (Table I) is in each case almost equal to the energy difference between the two conformations of the corresponding unsymmetrical 2,6-dihalophenol (Table II). These observations somewhat surprisingly suggest that the two halogen substituents ortho to a phenolic OH interact essentially independently with the OH group.

Table VI. CNDO/2 and ab Initio Relative Energies of *o*-Halophenols (**3** and **4**) and *p*-Halophenols (**13**)

	ΔE_{calcd}(**3**→**13**), kcal/mol		ΔE_{calcd}(**4**→**13**), kcal/mol	
X	CNDO/2	Ab initio	CNDO/2	Ab initio
F	−0.17	−0.51	−1.54	−2.19
Cl	2.67	0.32	0.37	−1.45
Br	2.31		0.63	
I	1.09		0.33	

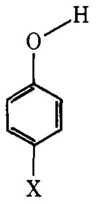
In summary, it seems that a combination of explanations 3 and 6 is the major cause of this "anomalous" hydrogen bond order in the *o*-halophenols. The fact that *o*-fluorophenol is further from an optimal hydrogen bond geometry than *o*-chlorophenol makes the hydrogen bond in the F compound weaker than one might expect. However, there also appear to be significant repulsions in the trans conformation (**4**) of *o*-chlorophenol which make its ΔE(cis→trans) unusually large when compared to the ΔE for forming an intermolecular Cl- - -H–O hydrogen bond.

(B) Intramolecular Hydrogen Bonding in Other Ortho-Substituted Phenols. We next chose to examine the intramolecular hydrogen bonds in other ortho-substituted phenols in order to compare their properties with those of the *o*-halophenols. While CNDO/2 calculations provide reasonable CH_3 rotational barriers for both the cis and trans conformers of *o*-methylphenol (Table VII), they predict that the most stable cis conformer is 0.84 kcal/mol more stable than the most stable trans conformer (each with the CH_3 group staggered with respect to the OH group). This is in contrast to the repulsive interaction that one might expect to exist between the CH_3 and OH groups in the cis conformer. Experimental evidence (Table VIII) confirms the existence of this repulsion in that it shows that the trans conformer is slightly more stable than the cis for *o*-methylphenol. Also, ΔE(cis→trans) for *o-tert*-butylphenol

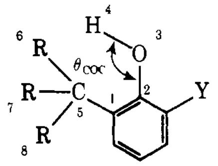
Table VII. CNDO/2 and ab Initio Conformational Dependence of Energies of *o*-Alkylphenols (**14**) (Relative Energies in kcal/mol)

					CNDO/2 for ϕ_{1234}[a]		Ab initio for ϕ_{1234}[a]	
R_6	R_7	R_8	Y	ϕ_{2156}[a]	0	180	0	180
H	H	H	H	0	1.92	0.95		
				30	0.72	0.91		
				60	0.00	0.84	1.53	0.00
H	CH_3[b]	CH_3[b]	H	0	1.64	0.60		
				30	1.56	1.69		
				60	3.80	2.10		
				90	81.2	4.81		
				120	51.5	3.42		
				150	79.2	2.47		
				180	4.52	0.00		
CH_3[b]	CH_3[b]	CH_3[b]	H	0	49.8	1.65		
				30	79.0	2.39		
				60	4.48	0.00		
H	H	H	Cl	60	1.48	0.00		
H	H	H	I	60	0.00	0.04		
F	F	F	H	0	2.97	2.50	3.09	
				25			3.02	
				30	0.02	2.53	0.04	
				33	0.00			
				35	0.02		0.00	
				40			0.15	
				45	0.32			
				60	0.64	2.50	0.84	0.12

[a] In degrees. [b] CH_3 protons in staggered conformation.



13



14

increases to a slightly *less* negative value upon substitution of a CH_3 group in the other ortho position. Our ab initio results (Table XVII, microfilm edition) agree with the experimental data; with the CH_3 group staggered with respect to the OH group, the trans conformer is found to be more stable by 1.53 kcal/mol. The spurious attractive interaction between OH and CH_3 in the CNDO/2 calculations (apparently an artifact of the approximations of the method) can be seen from the decreases in the CNDO/2 intramolecular hydrogen bond strengths of *o*-chloro- and *o*-iodophenol (Table I) upon addition of a CH_3 group in the other ortho position (Table VII). After a complete CNDO/2 geometry search of *o*-methylphenol (15° variations in the CH_3 rotation and 30° variations in the OH rotation), it was found (assuming a Boltzmann distribution between all conformers) that the net energy of the cis conformers (**3**, $X = CH_3$: $-90° < \phi_{1234} < 90°$) was still 0.57 kcal/mol less than the net energy of the trans conformers (**3**, $X = CH_3$: $90° < \phi_{1234} < 270°$).

CNDO/2 calculations on *o*-isopropylphenol and *o-tert*-butylphenol (Table VII) gave more reasonable results than were obtained for *o*-methylphenol, especially with respect to phenolic OH/*o*-alkyl repulsive interactions. The most stable trans OH conformer of the *o*-isopropylphenol was found to be 1.56 kcal/mol more stable than the most stable *cis*-OH conformer; for *o-tert*-butylphenol, this energy difference is 4.48 kcal/mol. Assuming a Boltzmann distribution between the various *cis*- and *trans*-isopropyl rotamers of Table VII, it was found that the net energy of the *trans*-OH isopropyl rotamers is 1.23 kcal/mol less than the net energy of the *cis*-OH isopropyl rotamers. The corresponding energy difference in the *tert*-butyl case was 4.31 kcal/mol. Thus, even though CNDO/2 underestimates repulsions, it still gives the correct sign for $\Delta E(\text{cis} \rightarrow \text{trans})$ for *o-tert*-butyl- and *o*-isopropylphenol.

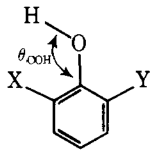
That the alkyl and phenolic OH groups of the *o*-alkylphenols interact in a repulsive and not an attractive manner is emphasized by the $\Delta\nu_{OH}$ values of various ortho-substituted phenols (Table IX). Ortho substituents that are capable of forming intramolecular hydrogen bonds with the phenolic OH cause ν_{OH} of the cis conformer to shift to lower frequencies, ν_{OH} for the trans conformer being relatively unaffected. For *o*-alkyl substituents which have repulsive interactions with the phenolic OH, ν_{OH} for the cis conformer is shifted to higher frequencies, ν_{OH} for the trans conformer being relatively unaffected. An intramolecular hydrogen bond should lengthen the O–H bond, decreasing the O–H bond energy and consequently ν_{OH}. Conversely, it has been suggested[19] that steric interactions between an *o*-alkyl substituent and the phenolic OH narrow the potential energy well of the O–H stretching mode by repelling the phenolic proton, cause the O–H bond to shorten, and increase ν_{OH}.

o-CF_3-phenol is an unusual case in which there are apparently both attractive and repulsive interactions between the CF_3 and phenolic OH groups. *o*-CF_3-phenol displays two ν_{OH} bands[16] (Table IX): a more intense band (3624.6 cm^{-1}) shifted to higher frequency from ν_{OH} for phenol (and apparently corresponding to the cis conformer) and a less intense band (3605 cm^{-1}) at about ν_{OH} for phenol (and apparently corresponding to the trans conformer). These assignments are confirmed by the two ν_{OH} bands for 2-Br-6-CF_3-phenol[16] (Table IX): one at a ν_{OH} (3510.4 cm^{-1}) about equal to ν_{OH} for the cis conformer of *o*-bromophenol (Table IX) and one of less

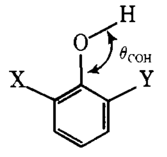
Table VIII. CNDO/2, ab Initio, and Experimental Intramolecular Hydrogen Bond Strengths of Ortho-Substituted Phenols (**15** and **16**)

		ΔE(**15**→**16**), kcal/mol		
X	Y	CNDO/2	Ab initio	Exptl
CH_3	H	0.84^f	-1.53^f	-0.86^g $-0.29^{h,i}$ $-0.51^{j,k}$
i-Pr	H	-1.56^f		
t-Bu	H	-4.48^f		$-1.38^{h,i}$ $-1.57^{j,k}$ -1.38^l -3.04^g
t-Bu	CH_3			$-1.05^{h,i}$ $-1.06^{j,k}$ -2.22^g
CF_3	H	2.50^f	0.12^f	>0 and $<\sim 2.5^{j,m}$
$NO_2{}^a$	H	8.29		6.65^o 2.1^p 4.7^q
OH^b	H	1.37	3.27	$2.29^{h,r}$
$OCH_3{}^c$	H	1.32		$2.00^{h,i}$
$C_6H_5{}^d$	H	1.66		$2.73^{h,i}$ $1.45^{s,j}$
CHO^e	H	6.02	7.44	7.09^o 1.8^p 3.6^q
CN	H	2.01		$1.73^{h,i}$

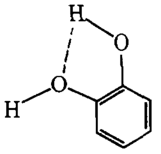
[a] Structure **18**. [b] Structure **17**. [c] Structure **19**; CH_3 group staggered. [d] Structure **20**, $\phi_{2156} = 90°$. [e] Structure **21**. [f] See Table VII. [g] Reference 65; method of study = molecular mechanics force field calculation. [h] Method of study = IR OH torsional frequency; cyclohexane solution. [i] Reference 12. [j] Method of study = IR OH stretching frequency, CCl_4 solution. [k] Reference 19. [l] Reference 65; method of study = dipole moment; CCl_4 solution. [m] Estimated from ref 16. [n] Reference 66. [o] Reference 26; method of study = OH ^{1}H chemical shift; CCl_4 solution. [p] Reference 4; method of study = EHT. [q] Reference 4; method of study = CNDO/2. [r] Estimated from ref 26 and 58. [s] Reference 67.



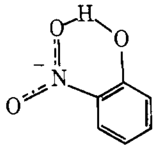
15



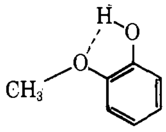
16



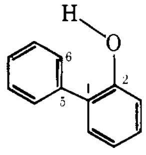
17



18



19



20

intensity (3616.9 cm^{-1}) at about the ν_{OH} assigned to the cis conformer for *o*-CF_3-phenol. Konovalov et al.[66] also observed a ν_{OH} doublet at 3605 and 3626 cm^{-1} for *o*-CF_3-phenol and assigned the higher frequency to the cis conformer. They also found that with increasing temperature the intensity of the 3605 cm^{-1} band increased while that of the 3625 cm^{-1} band decreased. This study gave a ΔH(cis→trans) value of 0.9 kcal/mol. In contrast to the above studies,[16,66] Marler and Hopkins[68] assigned the less intense 3606 cm^{-1} ν_{OH} and the more intense 3624 cm^{-1} ν_{OH} of *o*-CF_3-phenol to the cis and trans conformers, respectively. In addition, they found that the ratio of the integrated intensities of the 3624 cm^{-1} band to the 3606 cm^{-1} band *increased* with increasing temperature. Their data yield values of ΔH(cis→trans) = 1.4 kcal/mol and ΔS(cis→trans) = ~6 cal/deg/mol. This rather large ΔS for intramolecular hydrogen bond formation is inconsistent with experimental ΔS values that are essentially zero for other ortho-substituted phenols[20,22,53] and with theoretical considerations.[54] We support the assignment of the higher ν_{OH} frequency to the cis conformer based on our calculated ΔE(cis→trans) values (see below), ΔS(cis→trans) considerations, and the more abundant (although still scant) experimental evidence supporting this assignment. Further experimental studies on *o*-CF_3-substituted phenols are certainly indicated for the resolution of the previous experimental ambiguities.

That *o*-CF_3-phenol does form intramolecular hydrogen bonds is also supported by ^{19}F NMR solvent shift and dilution studies.[25] Hence, like the *o*-alkylphenols there is apparently a repulsive steric interaction between the CF_3 and the phenolic OH, causing ν_{OH} for the cis conformer to be shifted to a higher frequency. And like the *o*-halophenols there is also an attractive hydrogen bond interaction between the CF_3 and the phenolic OH, causing the cis conformer to be more stable relative to the trans conformer. The results of our CNDO/2 and ab initio calculations on *o*-CF_3-phenol are presented in Table VII. For the cis conformer, both methods of calculation predict an identical energy minimum (with one of the F cis to the OH and rotated 33° up from the ring plane), as well as nearly identical CF_3 rotational potentials. For the trans conformer, the CNDO/2 calculations predict a shallow rotational potential about 2.50 kcal/mol less stable than the cis conformer energy minimum, whereas the ab initio calculations predict the trans conformer to be only 0.12 kcal/mol less stable than the cis conformer energy minimum. The fact that the ν_{OH} intensity for the *o*-CF_3-phenol cis conformer is "several times" that for the trans conformer and the fact that the ν_{OH} intensity for the 2-Br-6-CF_3-phenol conformer with the OH cis to the Br is

Table IX. Experimental ν_{OH} and $\Delta\nu_{OH}$ Values[a] for Ortho-Substituted Phenols (**15** and **16**

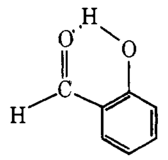
X	Y	ν_{OH}, cm^{-1} **15**	ν_{OH}, cm^{-1} **16**	$\Delta\nu_{OH}$, cm^{-1} [b]	Ref
H	H	3610.5			18
F	H	3591	*c*	*c*	18
Cl	H	3545	3608	63	18
Br	H	3522	3604	82	18
I	H	3499	3600	101	18
CH_3	H	3614	*c*	*c*	12
t-Bu	H	3647	3607	−40	12
t-Bu	CH_3	3649	3610	−39	12
i-Pr	H	3614	*c*	*c*	19
C_6H_5	H	3564.9	3606.9	40	65
CF_3	H	3624.6	3605	−19.6	16
CH_3	Br	3616.9	3510.4	−106.5	16

[a] All determined in CCl_4. [b] $\Delta\nu = \nu_{OH}(\mathbf{16}) - \nu_{OH}(\mathbf{15})$. [c] $\nu_{OH}(\mathbf{15}) \approx \nu_{OH}(\mathbf{16})$.

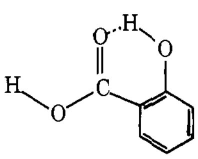
greater than that of the conformer with the OH cis to the CF_3[16] suggest that the actual intramolecular hydrogen bond strength of *o*-CF_3-phenol lies somewhere between our CNDO/2 value of about 2.50 kcal/mol and our ab initio value of 0.12 kcal/mol. This is supported by the ΔH(cis→trans) value of 0.9 kcal/mol of Konavalov et al.[66] for *o*-CF_3-phenol.

We also carried out calculations on the cis–trans isomerism of ortho-substituted phenols for a selection of ortho substituents capable of forming intramolecular hydrogen bonds with the phenolic OH. The CNDO/2 and ab initio results are presented in Table VIII. The CNDO/2 results are in fairly good agreement with the experimental data for the chelated *o*-NO_2- and *o*-CHO-phenols, for the weak intramolecular hydrogen bonding of the *o*-OH- and *o*-OCH_3-phenols, and for the weak O-H- - -π intramolecular interactions of the *o*-CN- and *o*-C_6H_5-phenols. The ab initio hydrogen bond strengths for the *o*-OH- and *o*-CHO-phenols are in slightly better agreement with the experimental data than the CNDO/2 results.

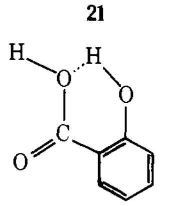
A CNDO/2 study was also conducted on the intramolecular hydrogen bonding of a salicylic acid with the relative energies of conformers **22**, **23**, and **24** predicted as 0.00, 1.38, and 4.62 kcal/mol, respectively. That **22** is actually the intramolecularly hydrogen bonded conformer that predominates is supported by the IR studies of Mori et al.[69]



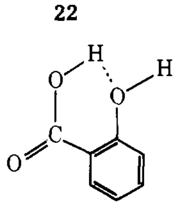
21



22



23



24

Thus, both CNDO/2 and minimal basis ab initio methods are capable of qualitatively reproducing almost all of the experimental data (except for the *o*-CH_3 with CNDO/2) for intramolecular hydrogen bonding of ortho-substituted phenols. The ab initio calculations yield semiquantitative agreement with experiment in the molecules studied and rank correctly the intramolecular "hydrogen bond" strengths in the series CHO > OH > Cl ≳ F > CF_3 > H > CH_3.

Table X. CNDO/2 and ab Initio Energy Calculations on Thiophenol and *o*-Halothiophenols (**25**, **26**, and **27**)

X	$V(90°)$,[a] kcal/mol CNDO/2	$V_1 = \Delta E(\mathbf{25}\rightarrow\mathbf{26})$, kcal/mol CNDO/2	$V_1 = \Delta E(\mathbf{25}\rightarrow\mathbf{26})$, kcal/mol Ab initio	V_2,[b] kcal/mol CNDO/2
H	0.35	0.00	0.00	0.35
F	0.89	0.75	0.82	0.51
Cl	4.00	3.53	−2.79	2.23
Br	4.16	3.46		2.43
I	2.28	1.38		1.59

[a] $V(90°) = \Delta E(\mathbf{25}\rightarrow\mathbf{27})$. [b] Calculated from $V(90°)$, V_1, and eq 3.

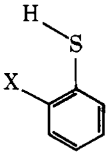
(C) Intramolecular Hydrogen Bonding in Ortho-Substituted Thiophenols. Having examined the ability of CNDO/2 and ab initio calculations to predict the interactions of the phenolic OH with the ortho substituents of ortho-substituted phenols, we next examined the abilities of the two computational methods to predict the intramolecular hydrogen bonding capabilities of ortho-substituted thiophenols. A CNDO/2 geometry search for a minimum energy θ_{CSH} in thiophenol yielded a value of 98°, which was used in all subsequent CNDO/2 and ab initio calculations on the thiophenols. As a parallel to the phenol studies, the intramolecular hydrogen bonding of the *o*-halothiophenols was examined first and the results are presented in Table X. The CNDO/2 and ab initio calculations are in agreement with *o*-fluorothiophenol forming an intramolecular hydrogen bond about half the strength of the intramolecular hydrogen bond of *o*-fluorophenol. For the other *o*-halothiophenols, however, the CNDO/2 calculations predict intramolecular hydrogen bond strengths about 150% of those for the corresponding *o*-halophenols. These CNDO/2 results for *o*-chloro-, *o*-bromo-, and *o*-iodothiophenol are inconsistent with one's intuition based on pK_a values[70] that SH is a poorer proton donor than OH. In contrast, the ab initio calculations predict the trans conformer of *o*-chlorothiophenol to be 2.79 kcal/mol more stable than the cis conformer. Experimentally two ν_{SH} bands are actually observed[71,72] for *o*-chloro- and *o*-bromothiophenol. The ν_{SH} band for the cis conformer was found[72] to represent no more than about 20% of the population for the *o*-chloro- and *o*-bromothiophenols, in agreement with the ab initio but not the CNDO/2 calculations. Some insight into the source of this discrepancy between the CNDO/2 and ab initio calculations is provided by the bond orders, atomic populations, and geometrical parameters found in these calculations.[46] Upon the trans to cis conformational transition, there is a rise in the S- -X repulsive bond order (especially for the ab initio calculations). For the cis conformer there is a positive H- -X attractive bond order in the CNDO/2 calculations on all four *o*-halothiophenols and in the ab initio calculations on *o*-fluorothiophenol. Rather

Table XI. CNDO/2 and ab Initio Relative Energies for the Conformers of *o*-Hydroxythiophenol (**28**, **29**, and **30**)

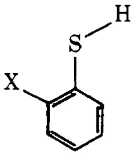
Conformer	Relative energies, kcal/mol	
	CNDO/2	Ab initio
28	0.07	2.14
29	0.98	1.20
30	0.00	0.00

dramatically, however, a large repulsive ab initio H- -X bond order occurs for the *cis-o*-chlorothiophenol conformer. As the halogen size increases, *R*(H- -X) increases very little for the *o*-halothiophenols while the sum of the van der Waals radii for H + X increases significantly. The amount of H- -X overlap of the van der Waals radii is about the same for the *o*-halophenols and *o*-halothiophenols for each X. Just as *R*(O- -X) increases more slowly for the *o*-halophenols than the sum of the van der Waals radii for O + X as the halogen size increases, so also *R*(S- -X) increases more slowly for the *o*-halothiophenols than the sum of the van der Waals radii for S + X. The amount of S- -X overlap repulsion (i.e., the amount *R*(S- -X) is less than the sum of van der Waals radii of S and X) for the *o*-halothiophenols is significantly greater, however, than the amount of O- -X repulsion for the *o*-halophenols for each X. The Cl > Br > I > F CNDO/2 attractive intramolecular hydrogen bond strengths for the *o*-halothiophenols reflect these trends, but apparently, as with the O- -X repulsions in the phenols, the CNDO/2 calculations tend to poorly represent the S- -X repulsions. The ab initio attractive intramolecular hydrogen bond strength for *o*-fluorothiophenol and repulsive intramolecular interactions for *o*-chlorothiophenol reflect not only these trends but also the ability of the ab initio calculations to correctly represent and weight the H- -X attraction and S- -X repulsion. However, they are not always completely successful in this weighting (see below).

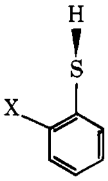
As a direct comparison of the intramolecular hydrogen bonding capabilities of the ortho-substituted phenols and thiophenols, we next looked at *o*-hydroxythiophenol. Based on the intensities of the ν_{SH} and ν_{OH} bands of the various possible conformers (**28**, **29**, and **30**) of *o*-hydroxythiophenol, David and Hallam[71] suggest that the conformations **28** and **30** are present in about equal amounts in dilute CCl_4 solution. As seen from Table XI, the CNDO/2 results appear to agree with the experimental results[71] concerning the relative stabilities of the conformers, but the ab initio results do not. While the bond orders[46] do not directly reflect these differences, they do suggest that the differences in the CNDO/2 and ab initio results are due not so much to their differences in handling the H- -S and H- -O interactions but more to their differences in handling changes in the O- -S repulsive interactions.



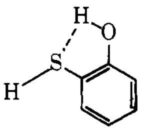
25



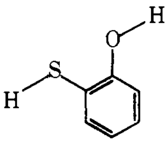
26



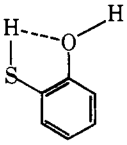
27



28



29



30

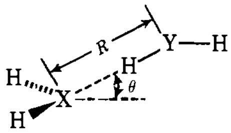
Because of these differences of the CNDO/2 and ab initio calculations in representing the intramolecular attractive and repulsive interactions of the *o*-halo- and *o*-hydroxythiophenols, we conducted CNDO/2 and ab initio calculations on the intermolecular hydrogen bonding of the H_2O/H_2S, H_2O/phenol, and H_2O/thiophenol dimers. This was done in order to provide some reference points with which to compare the CNDO/2 and ab initio calculations on the intramolecular interactions of the ortho-substituted thiophenols.

Table XII. Ab Initio Hydrogen Bond Energies (ΔE)[a] and Geometrical Parameters[b] for H_2O/H_2S Dimers (**31**)

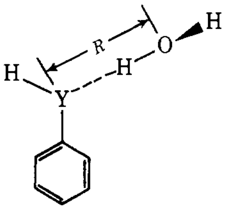
	Proton donor		
	H_2O	H_2S	
ΔE	2.54	1.86	STO-3G basis set[c]
R	3.33	3.37	
θ	76	46	
ΔE	3.9	3.8	431G basis set[d]
R	3.66	3.59	
θ	78	22	

[a] Energies in kcal/mol. [b] R = O- -S internuclear distance (in Å); θ in deg; see **31**. [c] These results from this study. [d] These results from ref 74.

For the H_2O/H_2S intermolecular hydrogen bonding, a "linear" dimer (**31**, X = S and Y = O, or vice versa) was assumed, with the two monomer units lying in perpendicular planes with the X, Y, and H atoms involved in the hydrogen bond colinear.[60,73] A geometry search was conducted simultaneously for both *R* (the O- -S internuclear distance) and θ (see **31**). The results of our ab initio calculations with an STO-3G basis set and a previous ab initio study[74] using a 431G basis set are presented in Table XII. As noted before,[74] the STO-3G basis set predicts ΔE values 1–2 kcal/mol less than the 413G basis set ΔE values. Except for slightly shorter *R* values, the STO-3G geometries are very similar to the 431G geometries for the H_2O/H_2S dimers. As would be expected, ΔE for H_2S as the proton donor is significantly less than for the H_2O as the proton donor.



31



32

We next examined with CNDO/2 and ab initio calculations the intermolecular hydrogen bonding of the H_2O/C_6H_5SH dimers. For C_6H_5YH (Y = S or O) as a proton acceptor (**32**), a "linear" dimer was assumed with Y- -H-O lying in the ring plane and on a line bisecting θ_{CYH} of C_6H_5YH. Y- -H-O-H all lie in a plane perpendicular to the ring plane in order to minimize the interactions of the second H_2O proton with C_6H_5YH. For C_6H_5YH as the proton donor (**8**, X = H) a "linear" dimer was assumed with the two monomer units lying in perpendicular planes and with the Y, O, and H atoms involved in the hydrogen bond colinear. θ (see **8**) was taken as before as 57° for Y = O (from the STO-3G H_2O dimer value)[64] and as 46° for Y = S (from the STO-3G H_2S/H_2O dimer value for H_2S as proton donor; Table XII). Only *R* (the X- -O internuclear distance) was varied in our geometry searches. Several interesting observations can be made from the CNDO/2 and ab initio results, which are presented in Table IV. The CNDO/2 calculations on the H_2O/C_6H_5OH dimer with phenol both as the proton donor and as the proton acceptor yield ΔE and *R* values very close to the CNDO/2 ΔE (5.9 kcal/mol) and *R* (3.3 Å) values for the H_2O/H_2O dimer

(**31**, X = Y = O with $\theta = 0°$ and H_2O experimental geometry).[75,76] Our ab initio calculations on the H_2O/C_6H_5OH dimer give a ΔE that is more than twice as large for phenol as the proton donor than for H_2O as the proton donor. This larger ΔE is accompanied by a smaller R value. Conversely, our ab initio calculations on the H_2O/C_6H_5SH dimer give a ΔE that is more thn twice as small for thiophenol as the proton donor than for H_2O as the proton donor. This smaller ΔE is accompanied by a larger R value. Our ab initio calculations predict C_6H_5SH to be both a poorer proton donor and a poorer proton acceptor than phenol. In each case ΔE and R correspond well with ΔE and R for the corresponding H_2O/H_2S dimer (Table XII). While our CNDO/2 calculations give a reasonable approximation for ΔE for thiophenol as a proton acceptor, they grossly overestimate the ΔE for thiophenol as a proton donor. Apparently this same error is reflected in our CNDO/2 calculations predicting very attractive hydrogen bonds for the *o*-halothiophenols (Table X).

That the ab initio calculations predict relative instability for conformer **28** of *o*-hydroxythiophenol can possibly be rationalized by inspecting the geometries of all three *o*-hydroxythiophenol conformers (**28, 29,** and **30**).[46] The O- -H van der Waals radii overlap for **30** is significantly less than the rather large S- -H overlap for **28**. In contrast to CNDO/2 underestimating O- -halogen repulsions in the *o*-halophenols, apparently ab initio may overestimate the S- -H repulsions for **28**. However, the observed relative intensities of the S-H and O-H stretches make a precise estimate of the amount of conformers **28-30** in *o*-hydroxythiophenol ambiguous.

(D) Infrared Spectral Properties of Ortho-Substituted Phenols. The *o*-halophenols (except for *o*-fluorophenol) exhibit in "inert" solvents two O-H stretching frequencies, ν_{OH}: one approximately equal to ν_{OH} of phenol and corresponding to the trans non-hydrogen-bonded conformer; the other shifted to a lower frequency and corresponding to the cis intramolecularly hydrogen-bonded conformer. (*o*-Fluorophenol exhibits only a single (but broad) ν_{OH} because ν_{OH} for the cis conformer is ca. ν_{OH} for the trans conformer.) The difference ($\Delta\nu_{OH}$) between the two frequencies is of the order $F < Cl < Br < I$ (Table IX). Both the experimental data and our CNDO/2 and ab initio calculations indicate that the order of intramolecular hydrogen bond strengths of the *o*-halophenols is most likely $Cl \approx F > Br > I$ or $Cl > Br > F > I$ (depending on which studies are cited). This is in conflict with the Badger-Bauer rule[77] which states that $\Delta\nu_{OH}$ (the shift to lower frequencies upon hydrogen bond formation) is directly proportional to the hydrogen bond strength. This discrepancy has been attributed[15,23,55] to these intramolecular hydrogen bonds being highly bent from an ideal colinear geometry for O-H- -X and to the H- -X distances being fixed by the molecular geometry of the phenols at values not necessarily equal to the preferred interacting distances.[78] It appears[23] that for the ortho-substituted phenols $\Delta\nu_{OH}$ is a measure of the amount of H- -X overlap and not the net energy of the OH and X interactions, which, for example, will include the O- -X repulsion. Both our CNDO/2 and ab initio calculations support this hypothesis. The cis conformer H- -X bond orders[46] (providing some measure of the H- -X interaction) correlate well with the $\Delta\nu_{OH}$ values (Table IX) but not with the intramolecular hydrogen bond strengths. The experimental $\Delta\nu_{OH}$ shifts to lower frequencies should be paralleled by similar decreases in the *o*-halophenol O-H bond orders upon hydrogen bond formation. The CNDO/2 phenol and *trans-o*-halophenol O-H bond orders are all essentially the same, just as the experimental phenol and trans *o*-halophenol $\Delta\nu_{OH}$ values are essentially the same. In addition, the CNDO/2 calculated O-H bond order decreases upon hydrogen bond formation for the *o*-halophenols closely parallel the corresponding experimental $\Delta\nu_{OH}$ values (except for the I O-H bond order which is slightly out of line). While the ab initio calculated O-H bond orders are also fairly constant for phenol and the *trans-o*-halophenols, the ab initio O-H bond order decreases of the two *o*-halophenols upon hydrogen bond formation do not correlate with the corresponding experimental $\Delta\nu_{OH}$ values.

In order to see whether either the CNDO/2 or ab initio calculations could predict the experimental $\Delta\nu_{OH}$ values for the *o*-halophenols, we conducted geometry searches for the minimum energy O-H bond lengths for phenol and the *o*-halophenols. Assuming a harmonic oscillator model for changes in energy with R(O-H) variation near the minimum energy R(O-H), force constants (k) and hence the ν_{OH} values were calculated for the O-H stretch (Table XIII). The CNDO/2 calculations overestimate the "expected" equilibrium R(O-H), k, and ν_{OH} values. The CNDO/2 *o*-halophenol ν_{OH} values, even though slightly overestimated, are in reasonable agreement with the experimental data both in magnitude and ordering (except for I which is slightly out of line). The CNDO/2 *cis-o*-halophenol equilibrium R(O-H) values vary in essentially the same manner as ν_{OH} for the halogens. The ab initio calculations give reasonable estimates for the *o*-halophenol $R(\text{O-H})_{\min}$ values and ν_{OH} values that are less overestimated than for the CNDO/2 calculations. However, the ab initio calculations do very poorly in predicting the magnitude of $\Delta\nu_{OH}$ for the *o*-halophenols.

Because of this insensitivity of the ab initio calculations to $\Delta\nu_{OH}$ for the *o*-halophenols, we decided to investigate this area further. Assuming again a harmonic oscillator model for the O-H stretch:

$$\tfrac{1}{2}k\langle x^2\rangle_n = \langle V\rangle_n = \tfrac{1}{2}E_n$$

where $\langle x^2\rangle_n$ = the expectation value of x^2 of the nth O-H stretching energy level; $x = |R(\text{O-H}) - R(\text{O-H})_{\min}|$; $\langle V\rangle_n$ = expectation value for V (the potential energy of the O-H bond) in the nth O-H stretching energy level; and E_n = energy of the nth O-H stretching energy level = $(n + \tfrac{1}{2})h\nu_{OH}$. Then

$$\langle x^2\rangle_n = E_n/k \qquad (1)$$

Assuming $\nu_{OH} \approx 3600\ \text{cm}^{-1}$ gives: $k = 7.65 \times 10^5\ \text{ergs/cm}^2$; $E_0 = \tfrac{1}{2}\,h\nu_{OH} = 1800\ \text{cm}^{-1}$; $E_1 = \tfrac{3}{2}\,h\nu_{OH} = 5400\ \text{cm}^{-1}$. Equation 1 then gives

$$\langle x^2\rangle_0{}^{1/2} = 0.068\ \text{Å}$$

$$\langle x^2\rangle_1{}^{1/2} = 0.118\ \text{Å}$$

We expected that for a phenol the energy difference between these two R(O-H) geometries might give a better indication of the H- -X interactions than the harmonic oscillator ν_{OH} for two reasons. First, the comparison occurs on a portion of the O-H stretch curve that is steeper and hence more sensitive to variations in the environment around the O-H bond, compared to the less steep portion of the curve around $R(\text{O-H})_{\min}$. Second, by comparing energies at the respective E_0 and E_1 values of x correspondings to $\langle x^2\rangle_n{}^{1/2}$, we would be looking at the portions of the curve where the proton spends a good portion of its time in the ground and vibrationally excited state. The results, given as $\Delta E(\langle x^2\rangle_0{}^{1/2} \rightarrow \langle x^2\rangle_1{}^{1/2})$, are presented in Table XIV. Although the ab initio results do qualitatively suggest shifts to lower O-H stretching frequencies for the *cis-o*-fluoro- and *o*-chlorophenols, the sensitivity of the model is poor and it does not predict the correct order for X = H, F, and Cl.

As stated earlier, the *o*-CF_3-phenol is unusual in that the hydrogen bonded (cis) O-H stretching peak is larger than the trans but shifted to higher frequencies from the trans O-H stretch. A CNDO/2 geometry search for a minimum energy O-H bond length for *o*-CF_3-phenol (Table XIII) gives a $R(\text{O-H})_{\min}$ value which is longer than the CNDO/2 calculated $R(\text{O-H})_{\min}$ value for phenol. From the data points used

Table XIII. CNDO/2 and ab Initio O–H Stretching Minimum Energy Bond Lengths, Force Constants, Frequencies, and Frequency Shifts for Phenol and Various Ortho-Substituted Phenols (**3**)

	$R(\text{O–H})_{\text{min}}$, Å		k, ×10^6 ergs/cm^2		ν_{OH},[c] cm^{-1}		$\Delta\nu_{\text{OH}}$,[c] cm^{-1}	
X	CNDO/2[a]	Ab initio[b]	CNDO/2[a]	Ab initio	CNDO/2	Ab initio	CNDO/2	Ab initio
H	1.0323	0.985	1.6662	0.9992	5318	4118		
F	1.0328	0.987	1.6524	1.0003	5296	4121	22	−3
Cl	1.0378	0.985	1.5841	0.9996	5185	4119	133	−1
Br	1.0387		1.5664		5156		162	
I	1.0374		1.5881		5192		126	
CH_3[d]	1.0347		1.6224		5248		70	
CHO[e]	1.048	0.990	1.4234	0.9541	4915	4024	403	94
OH[f]	1.033	0.986	1.6406	0.9977	5277	4115	41	3
CF_3[g]	1.0381		1.6043		5218		100	
CF_3[h]		0.981		0.9984		4117		1

[a] Calculated using least-squares quadratic fit using 7 to 14 points evenly spaced from R(O–H) = 1.01 to 1.06 Å. [b] Calculated using a three-point quadratic fit (R(O–H) = 0.98, 0.99, and 1.00 Å). Least-squares quadratic fits to five points at 0.01 Å intervals of R(O–H) from 0.96 to 1.01 Å gave poor results due to anharmonicity over this R(O–H) range. [c] ν_{OH}(phenol) was assumed to be equal to ν_{OH} for the trans conformers (**4**) of each of the *o*-halophenols. The ν_{OH} values in this table therefore refer to the *o*-halophenol cis conformers. Also, $\Delta\nu_{\text{OH}} = \nu_{\text{OH}}(\text{trans}) - \nu_{\text{OH}}(\text{cis}) \approx \nu_{\text{OH}}(\text{phenol}) - \nu_{\text{OH}}(\text{cis})$. [d] Structure **14**; $R_6 = R_7 = R_8 = Y = H$; $\phi_{2156} = 60°$. [e] Structure **21**. [f] Structure **17**. [g] Structure **14**; $R_6 = R_7 = R_8 = F$; $Y = H$; $\phi_{2156} = 33°$. [h] Structure **14**; $R_6 = R_7 = R_8 = F$; $Y = H$; $\phi_{2156} = 30°$.

Table XIV. Ab Initio Calculations on the O–H Stretching Potential Energy Curve for Various Phenols (**3**)

X	$\Delta E(\langle x^2\rangle_0{}^{1/2} \rightarrow \langle x^2\rangle_1{}^{1/2})$,[a] kcal/mol
H	5.32
F	5.25
Cl	5.30
CF_3[b]	5.40
CHO[c]	4.76
OH[d]	5.30

[a] See text for derivation of $\langle x^2\rangle_n{}^{1/2}$ values. [b] Structure **14**; $R_6 = R_7 = R_8 = F$; $Y = H$; $\phi_{2156} = 30°$. [c] Structure **21**. [d] Structure **17**.

in the search, a ν_{OH} was obtained which incorrectly predicts a shift to lower frequency for ν_{OH} for the cis conformer of about 100 cm^{-1}. A similar ab initio geometry search yielded a $R(\text{O–H})_{\text{min}}$ value that is *shorter* than the ab initio calculated $R(\text{O–H})_{\text{min}}$ value for phenol and a ν_{OH} for the cis conformer that is about equal to the ab initio calculated ν_{OH} value for phenol (Table XIII). For *o*-CF_3-phenol the ab initio $\Delta E(\langle x^2\rangle_0 \rightarrow \langle x^2\rangle_1{}^{1/2})$ value, in contrast to the *o*-fluoro- and chlorophenol cases, is *larger* than for phenol, suggesting a steeper O–H bond stretch potential for *o*-CF_3-phenol than for phenol. This in turn suggests that this steric repulsion between the hydrogen-bonded CF_3 and OH groups causes the ν_{OH} shift to higher frequency observed for the cis conformer of *o*-CF_3-phenol.

From the geometry of our calculations, the internuclear distance between the phenolic proton and the closest F of the CF_3 group for the minimum energy CF_3 rotamer of the cis conformer of *o*-CF_3-phenol is calculated to be only 1.70 Å. Comparison of this value with the H- -F internuclear distances for the cis conformer of *o*-fluorophenol (2.26 Å)[46] and for the equilibrium H_2O/fluorobenzene dimer (1.50 Å, ab initio; Table III) and with the sum of van der Waals radii for H + F (2.67 Å)[46] suggests that for *o*-CF_3-phenol: (1) the intramolecular hydrogen bond strength is due to the expected attractive interaction of the phenolic proton with the F atom; (2) the repulsive interaction of the phenolic proton with the F atoms is due to the latter being forced (because of geometrical constraints) into very close proximity with the former in order to maximize the attractive interaction of the two; (3) this repulsive interaction due to the H- -F internuclear distance being forced to be so small is reflected in our ab initio calculations by a shortened O–H bond length, an increased O–H bond stretching force constant, and a shift in ν_{OH} to higher frequency. This shortened H- -F internuclear distance for the closest F atom in the minimum energy *cis*-CF_3-phenol conformer is reflected in the H- -F bond order (0.0169, CNDO/2; 0.0264, ab initio), which is significantly greater than the value for the *cis*-*o*-fluorophenol conformer (0.0021, CNDO/2; 0.0046, ab initio). In addition, θ_{HOF} for the most stable *cis*-*o*-CF_3-phenol conformer is only 23.4°, a much more favorable value than for the *o*-halophenols.

In a series of articles[11,24,56] Fateley et al. have assigned phenolic OH torsional frequencies to the cis and trans conformations of a number of ortho-substituted phenols and then used these to calculate the enthalpy difference between the two conformations for each (Table XV). They assumed the potential associated with the internal rotation of the phenolic OH to be adequately represented by the Fourier cosine series

$$V(\alpha) = \tfrac{1}{2} \sum_n V_n\,(1 - \cos n\alpha) \tag{2}$$

which could be truncated at $n = 2$ for most ortho-substituted phenols. (Approximate calculations have shown that higher terms are negligibly small.[80]) Equating $V(\alpha)$ with our ϕ_{1234} of **15**,

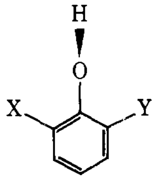
$$V(\phi_{1234}) = V_1(1 - \cos \phi_{1234})/2 + V_2(1 - \cos 2\phi_{1234})/2 \tag{3}$$

For an ortho-substituted phenol, V_1 is equal to the energy difference between the cis and trans conformations and V_2 corresponds to the OH rotational barrier with the V_1 (cis/trans) contribution factored out; i.e., V_2 is essentially the energy required to rotate the phenolic OH out of conjugation with the aromatic ring; differences in V_2 reflect differences in the inductive and resonance interactions of the different ortho substituents with the phenolic OH. From our MO calculations we can derive values for V_1 and V_2, which, together with corresponding experimental values, are presented in Table XV. For phenol itself the ab initio calculations overestimate the experimental V_2 rotational barrier by a much larger amount than the CNDO/2 underestimation of V_2. The ab initio calculations, however, agree extremely well with both the magnitudes and ordering of V_1 and V_2 for *o*-fluoro- and *o*-chlorophenol in the vapor state but are higher than the values of V_1 and V_2 in cyclohexane. This suggests an explanation for part of the overestimation by ab initio of V_2 for phenol itself since this experimental value was also measured in cyclohexane

Table XV. CNDO/2, ab Initio, and Experimental OH Rotational Energies for Phenols and Ortho-Substituted Phenols (**15**, **16**, and **33**)

		$V(90°)$,[a] kcal/mol		V_1,[b] kcal/mol			V_2,[c] kcal/mol		
X	Y	CNDO/2	Ab initio	CNDO/2	Ab initio	Exptl	CNDO/2	Ab initio	Exptl
H	H	2.88	5.13	0^{l}	0^{l}	0^{l}	2.88	5.13	$3.56^{o,u}$
F	H	3.52	5.59	1.37	1.68	$1.63^{m,n}$ $1.44^{n,o}$	2.84	4.75	$4.72^{m,n}$ $4.44^{n,o}$
Cl	H	4.65	6.15	2.30	1.77	$1.63^{m,n}$ $1.62^{n,o}$	3.50	5.26	$5.46^{m,n}$ $5.16^{n,o}$
Br	H	4.26		1.68		$1.53^{m,n}$ $1.57^{n,o}$	3.42		$5.40^{m,n}$ $5.15^{n,o}$
I	H	3.53		0.75		$1.32^{m,n}$ $1.45^{n,o}$	3.15		$4.97^{m,n}$ $4.74^{n,o}$
CH_3[d]	H	3.53		0.84	−1.53	-0.86^{p} $-0.29^{o,q}$ $-0.85^{o,q}$	3.11		$\sim 3.29^{o,q}$
CH_3[d]	CH_3[e]	3.28		0^{l}		0^{l}	3.28		$3.41,^{o,q}$ 2.31^{p}
CF_3[f]	H	5.12		~2.50		$\sim 0.9^{r}$	~3.87		$\sim 3.34^{o,p}$
CHO[g]	H	8.84		6.02	7.44	7.09^{s}	5.83		
NO_2[h]	H	11.05		8.29		6.65^{s}	6.91		
OH[i]	H	3.28		1.37	3.27	$\sim 2.29^{o,t}$	2.60		
OCH_3[j]	H	3.37		1.32		$2.00^{o,q}$	2.71		$5.94^{o,q}$
C_6H_5[k]	H	4.09		1.66		$2.73^{o,q}$	3.26		$4.52^{o,q}$

[a] $V(90°) = \Delta E(\mathbf{15} \rightarrow \mathbf{33})$. [b] $V_1 = \Delta E(\mathbf{15} \rightarrow \mathbf{16})$. [c] Calculated from $V(90°)$, V_1, and eq 3. [d] Structure **14**; $R_6 = R_7 = R_8 = H$; $\phi_{2156} = 60°$. [e] Second CH_3 staggered the same as the first with respect to the OH. [f] Structure **14**; $R_6 = R_7 = R_8 = F$; Y = H $\phi_{2156} = 33°$. [g] Structure **21**. [h] Structure **18**. [i] Structure **17**. [j] Structure **19**; CH_3 group staggered. [k] Structure **20**; $\phi_{2156} = 90°$, i.e., with the two rings perpendicular. [l] By definition. [m] Method of study = IR OH torsional frequency; vapor state. [n] Reference 24. [o] Method of study = IR OH torsional frequency; cyclohexane solution. [p] Reference 65; method of study = force field molecular mechanics calculations. [q] Reference 12. [r] Reference 66; method of study = IR OH stretching frequency; CCl_4 solution. [s] Reference 26; method of study = OH ^1H chemical shift; CCl_4 solution. [t] Estimated from ref 26 and 56. [u] Reference 79.



33

solution and not in the vapor state. The agreement of the CNDO/2 calculations with the experimental V_1 values for the four *o*-halophenols is moderately good. Interestingly, the ordering of V_2 for the ortho substituents of the *o*-halophenols and phenol itself is Cl > Br > I > H > F for CNDO/2, Cl > H > F for ab initio, and Cl > Br > I > F > H experimentally. Apparently, changes in V_2 of the *o*-halophenols (as compared to phenol) are determined by two factors. First, the greater the electronegativity of the ortho substituent (F > Cl > Br > I > H), the better it is able to inductively withdraw electron density from the phenolic ring, causing the phenolic oxygen to donate electron density into the ring, thus increasing the phenolic C–O double bond character and hence V_2. Second, the greater the ability of the ortho substituent (F ≫ Cl, Br, I > H) to donate lone pair electron density by resonance into the aromatic ring, the better it is able to oppose the delocalization of the phenolic oxygen lone pair electrons into the ring, hence decreasing V_2. The interpretation of our results is consistent with a study[79] on *p*-fluorophenol in which it was found that the *p*-fluoro substituent actually decreased V_2 (as compared to phenol) by 0.60 and 0.53 kcal/mol in experimental and ab initio studies, respectively. As seen in Table XV, the CNDO/2 and ab initio calculations generally give reasonable predictions for V_2 for the *o*-OH-, NO_2-, CN-, CHO-, C_6H_5-, CF_3-, and OCH_3-phenols, although the CNDO/2 results tend to underestimate the experimental V_2 values (where available for comparison) slightly more than the ab initio results.

Fateley and Carlson[12] found that the phenolic OH torsional frequency region was more complicated than at first expected for *o*-methylphenol. This apparently is due to the CH_3 rotational potential being superimposed upon the phenolic OH rotational potential. With the CH_3 group staggered with respect to the phenolic OH, CNDO/2 gave a value for V_2 of 3.11 kcal/mol (Table XV) in good agreement with Fateley and Carlson's experimental value of 3.29 kcal/mol.[12] With the addition of a second *o*-methyl group, the CNDO/2 V_2 value rises slightly to 3.28 kcal/mol, paralleling a rise in the experimental V_2 value to 3.41 kcal/mol.[12]

In order to test the validity of truncating the Fourier cosine series, eq 2, at $n = 2$ to give eq 3 for the potential associated with the internal rotation of the phenolic OH group, we calculated with CNDO/2 the variation of the energy of phenol and of *o*-chlorophenol at 15° increments of rotation of the OH group. Multiple least-squares linear regression analyses were then conducted, using the CNDO/2 energies with eq 2, including various combinations of the higher order terms. The results[46] lead to the following conclusions concerning these calculations. Although the inclusion of V_n terms with $n > 2$ is statistically justifiable, the changes in V_1 and V_2 induced by these inclusions are small enough so that quite accurate approximations of V_1 and V_2 can be obtained from eq 3. As theoretically expected, the changes induced in V_1 and V_2 by the inclusion of V_n terms with $n > 2$ are such that V_1 is affected only by inclusion of V_n terms with n odd and V_2 is affected only by inclusion of V_n terms with n even. The magnitude of any V_{n+2} term is only between 5 and 20% of the V_n term.

Assuming a Boltzmann distribution between the conformers used for these regressions, it was found that the net energy of the cis conformers (**3**: $-90° > \phi_{1234} > 90°$) of *o*-chlorophenol was 2.33 kcal/mol less than the net energy of the trans conformers (**3**: $90° > \phi_{1234} > 270°$), in very good agreement with the value of 2.30 kcal/mol obtained for V_1 considering only ΔE(cis→trans). That this complete an analysis gives almost identical results with the simple ΔE(cis→trans) type of analysis provides additional justification for the latter's use in analyzing such cis/trans isomerisms. However, this ΔE (2.3

kcal/mol) is not the same as the V_1 derived from the least-squares fit to the Fourier series (1.93 kcal/mol). Thus, the experimental values derived from the V_1 (the torsional frequencies in the IR) may not be quantitatively comparable to the ΔE values derived by other methods, such as relative intensities of the O–H stretching peaks in the near IR.

Conclusions

With a few exceptions, the CNDO/2 MO method generally does a fairly reasonable job in reproducing the experimental intramolecular interactions (and in particular the experimental ΔE values) for ortho-substituted phenols. The probable underestimation by CNDO/2 of the intramolecular hdrogen bond strength for *o*-fluorophenol can be viewed as only a minor deficiency in the method. That the cis conformer of *o*-methylphenol is found by CNDO/2 to be more stable than the trans is, however, a more serious error. For most of the phenols studied in this article, the ab initio MO method does at least as well and often better than CNDO/2 in reproducing the experimental intramolecular interactions of ortho-substituted phenols, especially of *o*-fluoro- and *o*-methylphenol. Both the CNDO/2 and ab initio calculations do well in predicting and providing some insight into the physical origins of the "anomalous" ordering of the experimental intramolecular hydrogen bond strengths of the *o*-halophenols. These studies suggest that the intramolecular interactions of the *o*-halophenols are mainly determined by a competition between the attractive and repulsive H- -halogen interactions in the cis conformer as well as the O- -halogen repulsions in the cis and trans conformers. In addition, these interactions are a strong function of the H–O- -X angle. The calculations suggest that the magnitudes of the ν_{OH} shifts for the cis conformers of the *o*-halophenols are determined by the magnitudes of the H- -halogen interactions, which do not necessary reflect the net intramolecular hydrogen bond energies. Similar physical effects are apparently operative in *o*-CF_3-phenol. In this compound, the H- -F distance is forced to be sufficiently close in the more stable cis conformer, so that one observes a shift to higher frequency for the O–H stretch, as well as predicts (ab initio) a shortened O–H bond length in this conformer. Low-temperature neutron diffraction might be used to test this prediction.

The ab initio calculations are successful in reproducing the limited experimental data for the *o*-halothiophenols. The importance of considering X- -S repulsion effects, which should be greater than X- -O repulsion, is clear from these studies and experiments. The prediction that *o*-fluorothiophenol favors the cis hydrogen-bonded conformer and *o*-chlorothiophenol the trans (the opposite trend in cis stability from the *o*-halophenols) is a clear indication of the greater repulsive forces involved in ortho interactions when both substituents are from the second row.

Our calculations indicate that the theoretical methods we have employed are capable of yielding a better understanding of the important forces determining the near and far IR properties of ortho-substituted phenols and thiophenols.

This study suggests a number of avenues for further work:

1. In the area of semiempirical MO theory, we have done a very limited variation of the parameters of the I atom, but clearly more systematic variations in the spirit of Dewar et al.[81] are possible and would likely lead to a set of parameters which can better predict both intramolecular and intermolecular hydrogen bonding effects of I (as well as Br, Cl, and F) than the parameters we used in this study.

2. We have also used model *ntermolecular* H-bond potentials to gain insight into the nature of intramolecular H bonding. This should prove of utility in studying intramolecular H-bonded systems with more conformational flexibility, such as 1,3-propanediol,[9] where one can use such calculations to separate conformation and H-bond effects in determining the final minimum energy structure.

3. The ab initio calculations with a minimal basis set do a very good job in predicting the hydrogen-bonding properties of the ortho-substituted phenols and thiophenols, with the possible exception of *o*-hydroxythiophenol. The Mulliken populations for the thiophenols are strange (S δ^+ and H δ^-), but the net dipole moment has the opposite direction, indicating that the wave function represents the polarity in a satisfactory manner. The intermolecular potential surfaces for the H_2O/C_6H_5SH dimers (thiophenol as the proton donor or acceptor) also support the net S δ^-/H δ^+ polarity in the wave function. However, more accurate calculations on *o*-hydroxythiophenol would probably be instructive, in order to see if they can reproduce the qualitative relative conformational stabilities determined by David and Hallam.[71]

4. We have also examined some of these ortho-substituted phenols and thiophenols for which there are no direct quantitative ΔE(cis→trans) data. So we hope the calculations presented here will be an impetus for further experimental physical chemical studies.

5. Our results suggest that to reproduce $\Delta\nu$ for the X–H stretch in H-bonded systems may require a careful analysis of the anharmonic part of the proton potential. For a crude estimate of relative frequency shifts, $E(\langle x^2\rangle_1{}^{1/2}) - E(\langle x^2\rangle_0{}^{1/2})$ may be a better guide than directly calculated $\Delta\nu_{XH}$.

We are continuing our studies on the relative intermolecular and intramolecular hydrogen bonding properties of ortho-substituted phenols, with the view of using these results to interpret relative biological activities in the thyroid hormone analogues.

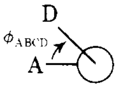
Acknowledgment. This work was supported by Grants AM-17576 (E.C.J.) from the National Institute of Arthritis, Metabolism and Digestive Diseases and GM-20564 (P.A.K.) from the National Institute of General Medical Sciences. P.A.K. is grateful to the NIH for support from Career Development Award GM-70718. We would like to acknowledge the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Supplementary Material Available: Tables XVI–XXIX, containing additional computational results (10 pages). Ordering information is given on any current masthead.

References and Notes

(1) (a) University of California; (b) Information Systems Design.
(2) P. A. Kollman and L. C. Allen, *Chem. Rev.*, **72,** 283 (1972).
(3) A. S. N. Murthy, S. N. Bhat, and C. N. R. Rao, *J. Chem. Soc. A*, 1251 (1970).
(4) P. Schuster, *Chem. Phys. Lett.*, **3,** 433 (1969).
(5) A. S. N. Murthy, R. E. Davis, and C. N. R. Rao, *Theor. Chim. Acta*, **13,** 81 (1969).
(6) A. D. Isaacson and K. Morokuma, *J. Am. Chem. Soc.*, **97,** 4453 (1975).
(7) M. S. Gordon and R. D. Koob, *J. Am. Chem. Soc.*, **95,** 5863 (1973).
(8) G. Karlstrom, H. Wennerström, B. Jönsson, S. Forsén, J. Almlöf, and B. Roos, *J. Am. Chem. Soc.*, **97**, 4188 (1975).
(9) A. Johansson, P. A. Kollman, and S. Rothenberg, *Chem. Phys. Lett.*, **18,** 276 (1973).
(10) L. Pauling, *J. Am. Chem. Soc.*, **58,** 94 (1936).
(11) O. R. Wulf, U. Liddel, and S. B. Hendricks, *J. Am. Chem. Soc.*, **58,** 2287 (1936).
(12) G. L. Carlson and W. G. Fateley, *J. Phys. Chem.*, **77,** 1157 (1973).
(13) A. W. Baker, *J. Am. Chem. Soc.*, **80,** 3598 (1958).
(14) A. W. Baker and A. T. Shulgin, *Spectrochim. Acta*, **19,** 1611 (1963).
(15) A. W. Baker and A. T. Shulgin, *Can. J. Chem.*, **43,** 650 (1965).
(16) A. W. Baker and A. T. Shulgin, *Nature (London)*, **206,** 712 (1965).
(17) A. W. Baker and A. T. Shulgin, *Spectrochim. Acta*, **22**, 95 (1966).
(18) H. Bourassa-Bataille, P. Sauvageau, and C. Sandorfy, *Can. J. Chem.*, **41,** 2240 (1963).
(19) K. U. Ingold and D. R. Taylor, *Can. J. Chem.*, **39**, 471 (1961).
(20) K. U. Ingold and D. R. Taylor, *Can. J. Chem.*, **39,** 481 (1961).
(21) I. Brown, G. Eglinton, and M. Martin-Smith, *Spectrochim. Acta*, **18,** 1593 (1962).

(22) I. Brown, G. Eglinton, and M. Martin-Smith, *Spectrochim. Acta*, **19**, 463 (1963).
(23) A. W. Baker and W. W. Kaeding, *J. Am. Chem. Soc.*, **81**, 5904 (1959).
(24) G. L. Carlson, W. G. Fateley, A. S. Manocha, and F. F. Bentley, *J. Phys. Chem.*, **76**, 1553 (1972).
(25) D. Doddrell, E. Wenkert, and P. V. Demarco, *J. Mol. Spectrosc.*, **32**, 162 (1969).
(26) T. Schaefer, *J. Phys. Chem.*, **79**, 1888 (1975).
(27) E. A. Allan and L. W. Reeves, *J. Phys. Chem.*, **66**, 613 (1962).
(28) E. A. Allan and L. W. Reeves, *J. Phys. Chem.*, **67**, 591 (1963).
(29) P. A. Kollman, W. J. Murray, M. E. Nuss, E. C. Jorgensen, and S. Rothenberg, *J. Am. Chem. Soc.*, **95**, 8518 (1973).
(30) E. C. Jorgensen, W. J. Murray, and P. Block, Jr., *J. Med. Chem.*, **17**, 434 (1974).
(31) E. C. Jorgensen, S. W. Dietrich, D. Koerner, M. I. Surks, and J. H. Oppenheimer, *Proc. West. Pharmacol. Soc.*, **18**, 389 (1975).
(32) In in vivo studies the phenolic 4′-OH may be replaced by functional groups which can be metabolically converted to it. Such compounds exhibit significant but not full thyromimetic activity as compared to the corresponding free phenolic compounds. See ref 33–36.
(33) K. Tomita, H. A. Lardy, D. Johnson, and A. Kent, *J. Biol. Chem.*, **236**, 2981 (1961).
(34) R. Bennett, A. Burger, and C. L. Gemmill, *J. Med. Pharm. Chem.*, **2**, 493 (1960).
(35) E. C. Jorgensen and J. A. W. Reid, *J. Med. Chem.*, **8**, 533 (1965).
(36) S. B. Barker and M. Shimada, *Mayo Clin. Proc.*, **39**, 609 (1964).
(37) E. C. Jorgensen, "Medicinal Chemistry", A. Burger, Ed., 3rd ed, Part II, Wiley, New York, N.Y., 1970, p 838.
(38) D. Koerner, H. L. Schwartz, M. I. Surks, J. H. Oppenheimer, and E. C. Jorgensen, *J. Biol. Chem.*, **250**, 6417 (1975).
(39) J. A. Pople, D. P. Santry, and G. A. Segal, *J. Chem. Phys.*, **43**, S129 (1965).
(40) J. A. Pople and G. A. Segal, *J. Chem. Phys.*, **43**, S136 (1965).
(41) The CNDO/2 calculations were carried out with Quantum Chemistry Program Exchange, Program No. 91, Indiana University.
(42) J. A. Pople and M. Gordon, *J. Am. Chem. Soc.*, **89**, 4253 (1967).
(43) *Chem. Soc. Spec. Publ.*, **No. 18** (1965).
(44) W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, and J. A. Pople, Quantum Chemistry Program Exchange, Program No. 236, Indiana University, 1973.
(45) W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, **51**, 2657 (1968).
(46) More complete computational results included as supplementary material (see paragraph at end of this paper) and to be included in Ph.D. Thesis (S.W.D.), University of California, San Francisco, Calif.
(47) The following abbreviations are used in this paper: *R*(A–B) = A–B bond length; *R*(A- -C) = A- -C internuclear distance; θ_{ABC} = A–B–C angle; ϕ_{ABCO} = the dihedral angle between the C–D bond and the A–B bond. Changes in ϕ_{ABCD} are further defined by a clockwise rotation of the C–D bond relative to the A–B bond, when observed down the C–B bond from C toward B:



$\Delta E(\text{I}\rightarrow\text{II}) = E_{\text{II}} - E_{\text{I}}$.
(48) M. N. Frey, T. F. Koetzle, M. S. Lehmann, and W. C. Hamilton, *J. Chem. Phys.*, **58**, 2547 (1973).
(49) W. S. Benedict, N. Gailar, and E. K. Plyler, *J. Chem. Phys.*, **24**, 1139 (1956).
(50) S. A. Arora, R. B. Bates, R. A. Grady, and N. E. Delfel, *J. Am. Chem. Soc.*, **97**, 5752 (1975).
(51) L. Farnell, W. G. Richards, and C. R. Ganellin, *J. Theor. Biol.*, **43**, 389 (1974).
(52) G. H. Loew and D. S. Berkowitz, *J. Med. Chem.*, **18**, 656 (1975).
(53) G. Rossmy, W. Lüttke, and R. Mecke, *J. Chem. Phys.*, **21**, 1606 (1953).
(54) H. H. Jaffe, *J. Am. Chem. Soc.*, **79**, 2373 (1957).
(55) E. A. Robinson, H. D. Schreiber, and J. N. Spencer, *Spectrochim. Acta, Part A*, **28**, 397 (1972).
(56) W. G. Fateley, G. L. Carlson, and F. F. Bentley, *J. Phys. Chem.*, **79**, 199 (1975).
(57) J. Del Bene and J. A. Pople [*J. Chem. Phys.*, **52**, 4858 (1970); **55**, 2296 (1971)] find that $(HF)_2$ and $(H_2O)_2$ have geometries "very near linear". References 58 and 59 find a similar result for $(HCl)_2$ with small deviations from linearity (10°) making a 0.1–0.2 kcal/mol difference in energy.
(58) P. Kollman and L. C. Allen, *J. Am. Chem. Soc.*, **93**, 4991 (1971).
(59) P. Kollman, A. Johansson, and S. Rothenberg, *Chem. Phys. Lett.*, **24**, 199 (1974).
(60) H_2O geometry: $\theta_{HOH} = 104.52°$ and $R(H–O) = 0.9572$ Å; from ref 49.
(61) M-L. Josien, *Pure Appl. Chem.*, **4**, 33 (1962).
(62) R. West, D. L. Powell, L. S. Whatley, M. K. T. Lee, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **84**, 3221 (1962).
(63) D. A. K. Jones and J. G. Watkinson, *J. Chem. Soc.*, 2366 (1964).
(64) J. E. Del Bene [*J. Chem. Phys.*, **57**, 1899 (1972)] gives $\theta = 57°$ for ab initio calculations with an STO-3G basis set for the H_2O/H_2O dimer, the H_2O monomer geometry having first been optimized. Hence, our use of the H_2O experimental monomer geometry is not directly comparable with the use of an ab initio/STO-3G optimized H_2O monomer geometry. In addition, our C_6H_5XH/H_2O dimer system is not necessarily directly comparable with the H_2X/H_2O dimer; various ab initio H_2O/H_2O dimer studies have shown that the dimer energy changes very little with θ variation (see ref 2). Hence, any energy change due to our not using optimized θ values for the C_6H_5XH/H_2O dimers should be negligibly small.
(65) N. L. Allinger, J. J. Maul, and M. J. Hickey, *J. Org. Chem.*, **36**, 2747 (1971).
(66) E. V. Konovalov, Yu. P. Egorov, R. V. Belinskaya, V. N. Boiko, and L. M. Yagupol'skii, *Zh. Prikl. Specktrosk.*, **14**, 484 (1971); *Chem. Abstr.*, **75**, 42673a (1971).
(67) M. Oki and H. Iwamura, *Bull. Chem. Soc. Jpn.*, **33**, 717 (1960).
(68) F. C. Marler, III, and Harry P. Hopkins, Jr., *J. Phys. Chem.*, **74**, 4164 (1970).
(69) N. Mori, Y. Asano, T. Irie, and Y. Tsuzuki, *Bull. Chem. Soc. Jpn.*, **42**, 482 (1969).
(70) But pK_a values may not necessarily correspond to weak hydrogen bond strengths.
(71) J. G. David and H. E. Hallam, *Spectrochim. Acta*, **21**, 841 (1965).
(72) M-L. Josien, P. Dizabo, and P. Saumagne, *Bull. Soc. Chim. Fr.*, 648 (1957).
(73) H_2S geometry: $\theta_{HSH} = 92.2°$ and $R(H–S) = 1.335$ Å; from ref 43.
(74) P. Kollman, J. McKelvey, A. Johansson, and S. Rothenberg, *J. Am. Chem. Soc.*, **97**, 955 (1975).
(75) P. A. Kollman and L. C. Allen, *J. Am. Chem. Soc.*, **92**, 753 (1970).
(76) J. R. Hoyland and L. B. Kier, *Theor. Chim. Acta*, **15**, 1 (1969).
(77) R. M. Badger and S. H. Bauer, *J. Chem. Phys.*, **5**, 839 (1937).
(78) Interestingly, for the phenol/cyclohexyl halide dimers[62] and for the phenol/*n*-pentyl halide dimers[63] $\Delta\nu_{OH}$ is of the order F < Cl < Br < I while ΔH of intermolecular hydrogen bond formation is of the order F > Cl > Br > I. This suggests that the lack of correlation between $\Delta\nu_{OH}$ and intramolecular hydrogen bond strength in the *o*-halophenols might in part be due to intrinsic properties of the halogens as proton acceptors and not solely due to factors uniquely present in the *o*-halophenols.
(79) L. Radom, W. J. Hehre, J. A. Pople, G. L. Carlson, and W. G. Fateley, *J. Chem. Soc., Chem. Commun.*, 308 (1972).
(80) W. G. Fateley, F. A. Miller, and R. E. Witkowski, Technical Documentary Report No. AFML-TR-66-408, Jan. 1967.
(81) R. C. Bingham, M. J. S. Dewar, and D. H. Lo, *J. Am. Chem. Soc.*, **97**, 1285 (1975), and following articles.