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# Intramolecular and Intermolecular Hydrogen Bond Formation by Some Ortho-Substituted Phenols: Some Surprising Results from an Experimental and Theoretical Investigation

**Grzegorz Litwinienko,*,† Gino A. DiLabio,*,‡ Peter Mulder,⊥ Hans-Gert Korth,§ and K. U. Ingold‖**

*Department of Chemistry, University of Warsaw, Pasteura 1, 02-093 Warsaw, Poland, National Institute for Nanotechnology, National Research Council of Canada, 11421 Saskatchewan Drive, Edmonton, Alberta, Canada T6G 2M9, Leiden Institute of Chemistry, Leiden University, P.O. Box 9502, 2300 RA Leiden, The Netherlands, Institut für Organische Chemie, Universität Duisburg-Essen, D-45117 Essen, Germany, and Steacie Institute for Molecular Sciences, National Research Council of Canada, 100 Sussex Drive, Ottawa, ON, Canada K1A 0R6*

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The effects produced by addition of various concentrations of the strong hydrogen bond (HB) acceptor, dimethyl sulfoxide (DMSO), on the OH fundamental stretching region of the IR spectra of several *o*-methoxy, *o*-nitro, and *o*-carbonyl phenols in $CCl_4$ are reported. In most of these phenols the intramolecular HB is not broken by the DMSO. Instead, the DMSO acts as a HB acceptor to the intramolecular HB forming a bifurcated intra/intermolecular HB. For *o*-methoxyphenols the bifurcated HBs are observed as new IR bands at much lower wavenumbers ($\Delta\nu(OH) \sim -300$ cm$^{-1}$) than the band due to their intramolecular HB. The formation of bifurcated HBs and the large frequency shift of their OH bands in *o*-methoxyphenols are well reproduced by theoretical modeling. In contrast to the *o*-methoxyphenols DMSO has little effect (other than causing some broadening) on the intramolecular HB OH bands of *o*-nitro and *o*-carbonyl phenols, with the single exception of 2,4-dinitrophenol. In this case, but not for 2,4-diformylphenol, the intramolecular HB OH band decreases as the DMSO concentration increases and a new absorption grows in at lower wavenumbers, indicating that DMSO can break this intra-HB and form an inter-HB, a result well reproduced by theory. Although DMSO has little effect on the O−H stretching band of 2-nitrophenol, theory indicates extensive formation (90%) of bifurcated HBs with OH stretching bands at slightly *higher* wavenumbers ($\Delta\nu(OH) \sim +20$ cm$^{-1}$) than that for the intramolecular HB OH group and 10% of a "simple" intermolecular HB in which the intramolecular HB has been broken. Theory also indicates that, with DMSO, 2-formylphenol also forms a bifurcated HB ($\Delta\nu(OH) \sim +150$ cm$^{-1}$), whereas 2,4-diformylphenol forms both intermolecular HBs ($\Delta\nu(OH) \sim -130$ cm$^{-1}$) and bifurcated HBs ($\Delta\nu(OH) \sim +165$ cm$^{-1}$). The IR spectrum of 2-methoxymethylphenol shows that although an intramolecular HB conformer is dominant there is a small percentage of a "free" OH, non-HB conformer (2.1% in $CCl_4$, 1.5% in cyclohexane). These results are quantitatively reproduced by theory. We conclude that theory can provide important insights into the formation and structure of inter, intra, and bifurcated HBs, and into their OH stretching frequencies, that are not always revealed by IR studies alone.

In 1995 it was shown that the rate constants for hydrogen atom abstraction (HAT) by *tert*-alkoxyl radicals from phenol and *tert*-butyl hydroperoxide decreased as the hydrogen bond accepting (HBA) abilities of the solvents increased.[1] It was hypothesized that (i) a substrate molecule, XOH, could act as a hydrogen bond donor (HBD) to only a single HBA molecule, S, at any one time, (ii) the magnitude of the equilibrium constant, $K^S$, for the formation of the XOH···S hydrogen-bonded complex was independent of the medium, and (iii) *tert*-alkoxyl radicals could not abstract the hydroxylic H-atom from XOH···S complex, as shown in Scheme 1. This scheme yields the kinetic expression:

$$k^S = k^0(1 + K^S[S])^{-1} \tag{1}$$

where $k^S$ is the rate constant measured in the solvent S and $k^0$ is the measured rate constant in a saturated hydrocarbon, i.e., in a non-HBA solvent. The inability of the XOH···S complex to undergo HAT was attributed to steric factors. That is, the optimum transition state for HAT involves a linear arrangement of the italicized atoms, $[t\text{-R}O\cdots H\cdots O\text{X}]^{\ddagger}$, while the optimized intermolecular hydrogen bond also involves a linear arrangement of the italicized atoms $[S\cdots H\cdots O\text{X}]$, so the radical cannot approach the hydroxylic H-atom of H-bonded XOH molecules.

Much subsequent work[2,3] has confirmed this model of hydrogen bonding on kinetic solvent effects (KSEs) for HAT processes. The kinetic data for HAT from many substrates in many solvents have been shown to be well correlated by the simple empirical equation:

$$\log(k^S/\text{M}^{-1}\ \text{s}^{-1}) = \log(k^0/\text{M}^{-1}\ \text{s}^{-1}) - 8.3\alpha_2^H\beta_2^H \tag{2}$$

where $\alpha_2^H$ is Abraham et al.'s[4] thermodynamically related relative scale of solutes' HBD activities (of the substrate XOH, range

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* To whom correspondence should be addressed.

† University of Warsaw.

‡ National Institute for Nanotechnology, National Research Council of Canada.

⊥ Leiden University, The Netherlands.

§ Universität Duisburg-Essen.

‖ Steacie Institute for Molecular Sciences, National Research Council of Canada.

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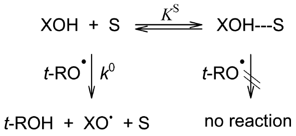
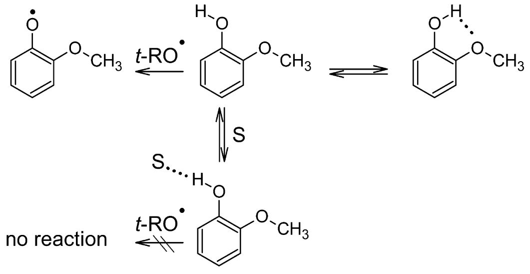
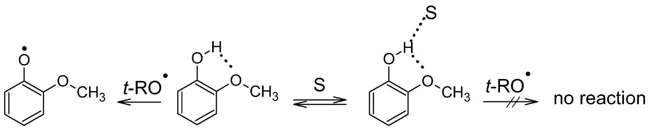
**SCHEME 1**



**SCHEME 2**



**SCHEME 3**



of 0.0 to ~1.0) and $\beta_2^H$ is Abraham et al.'s[5] thermodynamically related relative scale of solutes' HBA activities (of the solvent, S, range of 0.0−1.0). Thus, for phenols (and other substrates), plots of log($k^S$/$M^{-1}$ $s^{-1}$) against $\beta_2^H$ yield straight lines with slopes equal to $-8.3\alpha_2^H$.[3]

With this background on the complete inhibiting effect of intermolecular hydrogen bonding on HAT processes it was a surprise to discover that four *o*-methoxyphenols (2-methoxy, 2,4-dimethoxy, 2,6-dimethoxyphenol, and ubiquinol-0[6]), all of which possess an intramolecular hydrogen bond (HB), were highly reactive HAT agents to *tert*-alkoxyl radicals.[7] Moreover, the rate constants for these HAT reactions were solvent-dependent. Plots of log($k^S$/$M^{-1}$ $s^{-1}$) against $\beta_2^H$ were linear for these four *o*-methoxyphenols, and the four slopes were, within experimental error, equal to −2.0, a value significantly lower than the slopes of the corresponding lines for 4-methoxyphenols (−4.2) and phenol (−5.2). For those *o*-methoxyphenols possessing only one *o*-methoxy group these KSEs might simply be attributed to formation of a HB to a solvent molecule by the (putative) OH group not involved in an intramolecular HB. That is, the (putative) "free" OH group of 2-methoxyphenol could be a strong HAT agent to *tert*-alkoxyl radicals, and in HBA solvents, this phenol's reactivity would decrease, see Scheme 2.

However, this "explanation" cannot be correct because the magnitude of the KSE (i.e., the slope of the log($k^S$/$M^{-1}$ $s^{-1}$) versus $\beta_2^H$ plot) for 2,6-dimethoxyphenol is indistinguishable from the KSE for the three *o*-methoxyphenols which possess only a single *o*-methoxy group. It was, therefore, concluded that the KSEs for all the *o*-methoxyphenols must arise from essentially identical *intermolecular* HB interactions with HBA solvent molecules, and these must, perforce, involve *intramolecular* HBs,[7] see Scheme 3. The formation of an intermolecular HB prevents HAT in *o*-methoxyphenols[7] just as the formation of an intermolecular HB prevents HAT in all other phenols.[1−3] It was suggested that these bifurcated intra/inter HBs were possible because the five-center intramolecular HB in *o*-methoxyphenols are *nonlinear*. The formation of bifurcated HBs by *o*-methoxyphenols is supported by infrared spectroscopic measurements in $CCl_4$,[3,4,8] see also below.

Although the abilities of phenols possessing nonlinear, five-center, intramolecular HBs to form bifurcated intra/inter HBs with HBA molecules is firmly established, the abilities of phenols possessing six-center intramolecular HBs to form bifurcated intra/inter hydrogen bonds has not been established. Moreover, the available literature on this topic is extremely confusing (vide infra). In the present paper, we examine this problem using a combination of experiment and theory.

## Computational Procedures

In order to predict the properties of HB complexes it is necessary to first survey conformational space as thoroughly as possible to ensure that the relevant energy structures are found. Preliminary calculations on 2-methoxyphenol with dimethyl sulfoxide (DMSO) revealed that there are eight possible arrangements for DMSO for every orientation of the ring substituents. For 2-methoxyphenol there are three orientations of the ring substituents ($H_3CO\cdots HO$, $H_3CO\cdots OH$, $OCH_3\cdots OH$), giving 24 possible structures, see Supporting Information. These structures were used as starting points for calculations on a subset of the systems investigated experimentally. One of us has shown that the B971 functional[9] performs very well for hydrogen-bonded systems compared to more commonly used functionals, such as B3LYP.[10] This is likely because B971 has generally better long-range behavior than many common functionals.[10] To speed up the structure optimization process in several cases, calculations were initially performed using locally dense basis sets (LDBS).[11] In this approach, larger basis sets (6-311++G(2d,2p)) are used for the atoms directly involved in the HB (e.g., $OH\cdots O{=}S$) and on atoms involved in secondary interactions, whereas smaller basis sets (6-31G(d)) are used on all remaining atoms (see Supporting Information). The use of LDBSs greatly reduces computational times without sacrificing accuracy.[12] The structures obtained from the initial LDBS optimizations, were used as starting points for optimization and vibration frequencies calculations using B971 with 6-311++G(2d,2p) basis sets on all atoms. Final energies for all monomers and complexes were obtained by extrapolating the B971/aug-cc-pVDZ and B971/aug-cc-pVTZ energies to the complete basis set (CBS) limit.[13] The CBS approach allows us to avoid computing basis set superposition corrections for the HB complexes under study (see Supporting Information and ref 12). The CBS extrapolated energies were modified by the B971/6-311++G(2d,2p) derived vibrational enthalpy corrections in order to obtain $H_{298}$ for monomers and complexes. These enthalpies were used to determine relative populations of structures arising from each of the HB complexes and their respective enthalpies of hydrogen bonding. This is done with the assumption that differences in the entropy terms of the conformers is zero. In all cases, the calculations were performed using the Gaussian 03 package.[14,15]

## Background and Results

**Methoxyphenols.** ***Background.*** See Introduction.

***Infrared Spectra.*** The intramolecular HB in 2-methoxyphenol produces an O−H fundamental stretching band with a maximum at 3558 $cm^{-1}$ in $CCl_4$ (Figure 1A). This band occurs at a lower frequency than the band due to the O−H fundamental stretch in 4-methoxyphenol (3618 $cm^{-1}$, Figure 1B). Although the 2-methoxyphenol band is fairly narrow relative to the bands of other phenols possessing intra- (and inter-) molecular HBs it is noticeably broader than the O−H stretching band for 4-methoxyphenol. We chose DMSO to study the effect of a very strong HBA on the IR spectra of phenols possessing an intramolecular HB. This choice

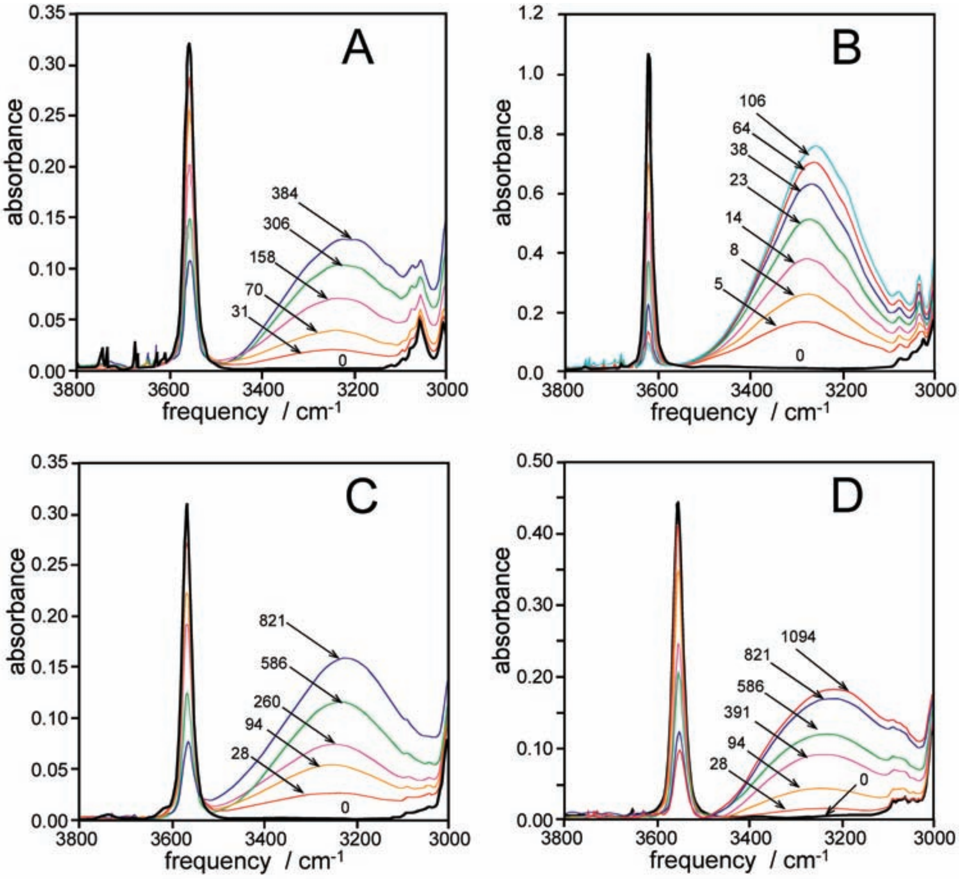


**Figure 1.** OH stretching region of the IR spectrum of (A) 2-methoxyphenol (15.3 mM), (B) 4-methoxyphenol (20.0 mM), (C) 2,4-dimethoxyphenol (14.7 mM), and (D) 2,6-dimethoxyphenol (20.3 mM) in $CCl_4$ containing DMSO (concentrations, in millimoles per liter, are indicated by numbers).

**TABLE 1: Some Phenols and Their p$K_a$'s and O−H Fundamental Stretching Band Maxima ($\nu_{max}$/cm$^{-1}$) in $CCl_4$ and in $CCl_4$ Containing DMSO at 298 K**

| substituent | p$K_a$[a] | $\nu_{max}(CCl_4)$ | $\nu_{max}(CCl_4 + DMSO)$[b] | substituent | p$K_a$[a] | $\nu_{max}(CCl_4)$ | $\nu_{max}(CCl_4 + DMSO)$[b] |
|---|---|---|---|---|---|---|---|
| 2-$OCH_3$ | 9.98 | $3558_{(intra)}$ | 3200−3260 | 2-$NO_2$ | 7.06 | $3243_{(intra)}$ | |
| 4-$OCH_3$ | 10.21 | $3618_{(free)}$ | 3257−3304 | 4-$NO_2$ | 7.14 | $3596_{(free)}$ | 3130 |
| 2,4-$(OCH_3)_2$ | 10.22[c] | $3566_{(intra)}$ | 3220−3270 | 2,4-$(NO_2)_2$ | 3.93 | $3218_{(intra)}$ | |
| 2,6-$(OCH_3)_2$ | 10.14[c] | $3554_{(intra)}$ | 3220−3250 | 2,6-$(NO_2)_2$ | 3.70 | $3175_{(intra)}$ | |
| 2,4,6-$(OCH_3)_3$ | 10.11[c] | $3563_{(intra)}$ | 3220−3250 | 7-hydroxy-indan-1-one | 8.43 | $3342_{(intra)}$ | |
| 2-$CH_3OCH_2$ | | $3614_{(free)}$ $3409_{(intra)}$ | 3175−3244 | 2-$CH_3C(O)$ | 10.1[d] | indeterminate | |
| | | | | 2-C(O)H | 8.3 | $3120−3190_{(intra)}$ | |
| | | | | 2,4-$(C(O)H)_2$ | 6.54[c] | $3050−3150_{(intra)}$ | |

[a] From Sergeant, E. P.; Dempsey, B. *Ionization Constants of Organic Acids in Aqueous Solutions*; IUPAC Chemical Data Series No. 23; Pergamon Press: Oxford, 1979. [b] When a range is given, it indicates that $\nu_{max}$ varies with [DMSO], see figures. [c] This work, using the spectrophotometric method, in water/methanol (1:1, v/v). [d] This value appears to be high, particularly since the p$K_a$ for 4-acetylphenol is 8.0 (from footnote *a*).

was made because DMSO is not only a strong HBA, $\beta_2^H$ 0.78,[5] but also because it is an extremely weak base, p$K_a$ = −2.7 (for $DMSOH^+ \rightleftarrows DMSO + H^+$)[16] that would not encourage the ionization of even highly acidic phenols, a problem that should be expected with many other strong HBAs that are also strong bases, e.g., pyridine, $\beta_2^H = 0.62$,[5] p$K_a$ = 5.14 (for pyridine$H^+ \rightleftarrows$ pyridine + $H^+$).[16] In the event, the addition of DMSO caused the O−H stretching bands in both 2- and 4-methoxyphenol to decrease in intensity and to be replaced by very much broader bands at considerably lower frequencies (Figure 1, parts A and B). The same effect is observed with 2,4-dimethoxyphenol and 2,6-dimethoxyphenol (Figure 1, parts C and D) and with 2,4,6-trimethoxyphenol (Supporting Information). Since DMSO is one of Abraham's calibrated HBAs,[4] these IR data can be used to calculate the $\alpha_2^H$ values for these four phenols. The $\alpha_2^H$ values so obtained are the following: 4-methoxyphenol, 0.55;[3] 2-methoxyphenol, 0.29;[17] 2,4-dimethoxyphenol, 0.27; 2,6-dimethoxyphenol, 0.29; 2,4,6-trimethoxyphenol, 0.26. The last four values for $\alpha_2^H$ are reasonably consistent with the values that can be calculated from the KSE slopes of −2.0 for *o*-methoxyphenols,[7] viz., $\alpha_2^H = -2.0/-8.3 = 0.24$. The O−H fundamental stretching band maxima and p$K_a$ values (when available) for these and other phenols are collected in Table 1.

***Computations.*** There are three minimum energy structures of 2-methoxyphenol. The lowest energy structure is predicted to constitute 99.8% of the Boltzmann population and has the substituents groups in the plane of the ring with an intramolecular HB between them, i.e., $O-H\cdots OCH_3$. A second structure has the OH pointing away from the methoxy group and the methyl of the methoxy group pointing toward the OH group. In this case,

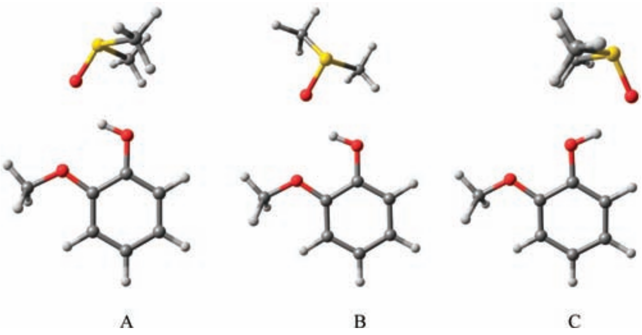


**Figure 2.** Three lowest energy structures for complexes of 2-methoxyphenol with DMSO. (A) Bifurcated intra/intermolecular HB, $\Delta H_{HB}$ = −5.7 kcal/mol, $R$(HO···OS) = 2.77 Å, $\theta$(O−H−OS) = 148.0°, $R$(SCH···OH) = 2.60 Å. (B) Bifurcated intra/intermolecular HB, $\Delta H_{HB}$ = −4.6 kcal/mol, $R$(HO···OS) = 2.81 Å, $\theta$(O−H−OS) = 146.9°, $R$(SCH···OH) = 2.60 Å. (C) "Simple" intermolecular HB, $\Delta H_{HB}$ = −4.7 kcal/mol, $R$(HO···OS) = 2.71 Å, $\theta$(O−H−OS) = 160.0°, $R$(SCH···OH) = 2.60 Å. Structure B is one of a degenerate pair, the second of which is formed by a rotation about the DMSO O−S bond of ~180°.

the OH is coplanar with the ring but the OMe group is rotated out of plane by 70.8°. This structure is predicted to make up only 0.2% of the total population of 2-methoxyphenol and is therefore not observed experimentally. This structure is higher in enthalpy than the lowest-lying complex by 3.8 kcal/mol, i.e., *3.8 kcal/mol represents the intramolecular HB strength in 2-methoxyphenol*. The least stable structure has both substituents in-plane and pointing away from each other; it is 5.4 kcal/mol higher in enthalpy than the lowest-lying structure.

The two symmetrically unique structures for 4-methoxyphenol have the substituents lying in the plane of the ring and pointing either in the same direction or in different directions. These two structures are essentially energetically degenerate.

The O−H stretching frequencies for 2- and 4-methoxyphenol are calculated to be larger than the corresponding measured values by ca. 7.2%. This error, which is fairly consistent for all of the theoretical results presented herein and is common for many computational procedures,[18] arises largely because the calculated frequencies do not incorporate anharmonicity. Despite these shortcomings, differences in O−H stretching frequencies are expected to be fairly well reproduced. This expectation is realized for the frequency difference between 2- and 4-methoxyphenol, viz., $\Delta\nu(\mathrm{OH})_{\mathrm{exptl}}$ = (3618 − 3558, Table 1) = 60 cm$^{-1}$ and $\Delta\nu_{\mathrm{calcd}}$ (OH) = 51.7 cm$^{-1}$ (averaged).

The complexes of 2-methoxyphenol with DMSO are predicted to form three low-energy structures, see Figure 2, which includes in its caption some geometric parameters. Note that all three structures have close contacts between at least one of the methyl H-atoms in DMSO and the hydroxylic O atom in 2-methoxyphenol. Similar secondary interactions are a common feature of many of the HB complexes studied in the present work.

Two of the three lowest energy structures form bifurcated intra/intermolecular HBs and have HB enthalpies of 5.7 and 4.6 kcal/mol (Figure 2, parts A and B, respectively). These structures are calculated to have $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$ = −312 and −224 cm$^{-1}$ relative to 2-methoxyphenol, which are in fair agreement with the measured range (−358 to −298 cm$^{-1}$). The principal "simple" intermolecular H-bonded structure (Figure 2C) has a HB enthalpy of 4.7 kcal/mol and $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$ = −405 cm$^{-1}$. Unfortunately, a complex with this structure cannot be resolved experimentally (see Figure 1A). Breaking the intramolecular HB in the HB donor does allow DMSO to approach the O−H group in 2-methoxyphenol more closely and to form a HB that is more linear, in comparison to the bifurcated intra/intermolecular HB structures. However, the enthalpic cost of breaking the intramolecular HB in 2-methoxyphenol is not fully compensated by the enthalpy of the resulting "simple" intermolecular HB (Figure 2C).

**TABLE 2: Summary of Calculated Data for H-Bonded Complexes of Phenols with DMSO**[a,b]

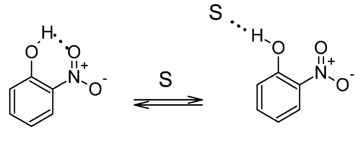
| molecule | complex type | $-\Delta H_{298}$ (HB with DMSO) | $\Delta\nu$ (OH) | $-\Delta H_{298}$ (HB intra) |
|---|---|---|---|---|
| 2-OMe phenol | Bif | 5.7 | −311.6 | 3.8 |
|  | Bif | 4.6 | −224.6 |  |
|  | Inter | 4.7 | −405.1 |  |
| 2-NO$_2$ phenol | Bif | 3.4 | +81.8 | 10.4 |
|  | Bif | 2.9 | +74.8 |  |
| 2,4-(NO$_2$)$_2$ phenol | Bif | 4.8 | +18.7 | 10.4 |
|  | Bif | 4.5 | +22.0 |  |
|  | Inter | 3.4 | −397 |  |
| 7-hydroxyindanone | Bif | 3.9 | −11.6 | 8.3 |
|  | Bif | 3.5 | −13.6 |  |
|  | Inter | 2.6 | −265.3 |  |
| 2-CHO phenol | Bif | 2.1 | +156 | 8.2 |
| 2,4-(CHO)$_2$ phenol | Bif | 3.8 | +173.5 | 8.5 |
|  | Bif | 3.0 | +160.9 |  |
|  | Inter | 3.2 | −132.4 |  |
| 2-methoxymethylphenol | Inter | 6.1 | −302.3[c] | 3.0 |
|  | Inter | 5.9 | −254.6[c] |  |
|  | Inter | 5.8 | −267.1[c] |  |

[a] The nature of the HB complex is identified (bifurcated intra/intermolecular HB = Bif, intermolecular = Inter). Complex and molecular HB strengths are in kcal/mol, and $\Delta\nu_{\mathrm{calcd}}$(O−H) values are in cm$^{-1}$. See text for details of the calculations. [b] Conversion of these $\Delta H$(298 K) values obtained by calculation (at 1 atm standard state) to $\Delta H$(298 K) values (1 M standard state) requires the subtraction of 0.4 kcal/mol (assuming ideal gas and solution behavior), see ref 19. $\Delta G$(298 K) values obtained by calculation (at 1 atm standard state) are converted to $\Delta G$(298 K) values (1 M standard state) by subtracting 1.89 kcal/mol. [c] Relative to the main, intramolecular O−H peak.

The experimental results gave global equilibrium constants of 3.71 M$^{-1}$ for DMSO and 2-methoxyphenol, which with 1 M DMSO leads to a percentage of bifurcated intra/intermolecular HB complexes of 78.7%. The present calculations are in excellent agreement with this value, predicting that 82.5% of the complexes of 2-methoxyphenol with DMSO form bifurcated intra/intermolecular HB structures.

The calculated results for all the phenols on which computations were carried out are summarized in Table 2.

**Nitrophenols.** ***Background.*** There have been several IR spectroscopic studies of the O−H fundamental stretching band of *o*-nitrophenols with comparison of this band in CCl$_4$ and in various neat HBA solvents.[20] A number of other, non-IR, studies on *o*-nitrophenols have also been employed to decide on the abilities of these phenols to form (or not form) intermolecular HBs.[21] For *o*-nitrophenols, the interpretations of the shifts in the O−H stretching band frequencies from their values in CCl$_4$ that are produced by dissolution of these phenols in neat polar solvents are confusing at best.[20,21] Frequently, experiments were done solely on 2-nitrophenol(s)[20a,c,d,f] and the results were often interpreted in terms of breaking the intramolecular HB by the HBA solvent with intermolecular HB formation, i.e.,



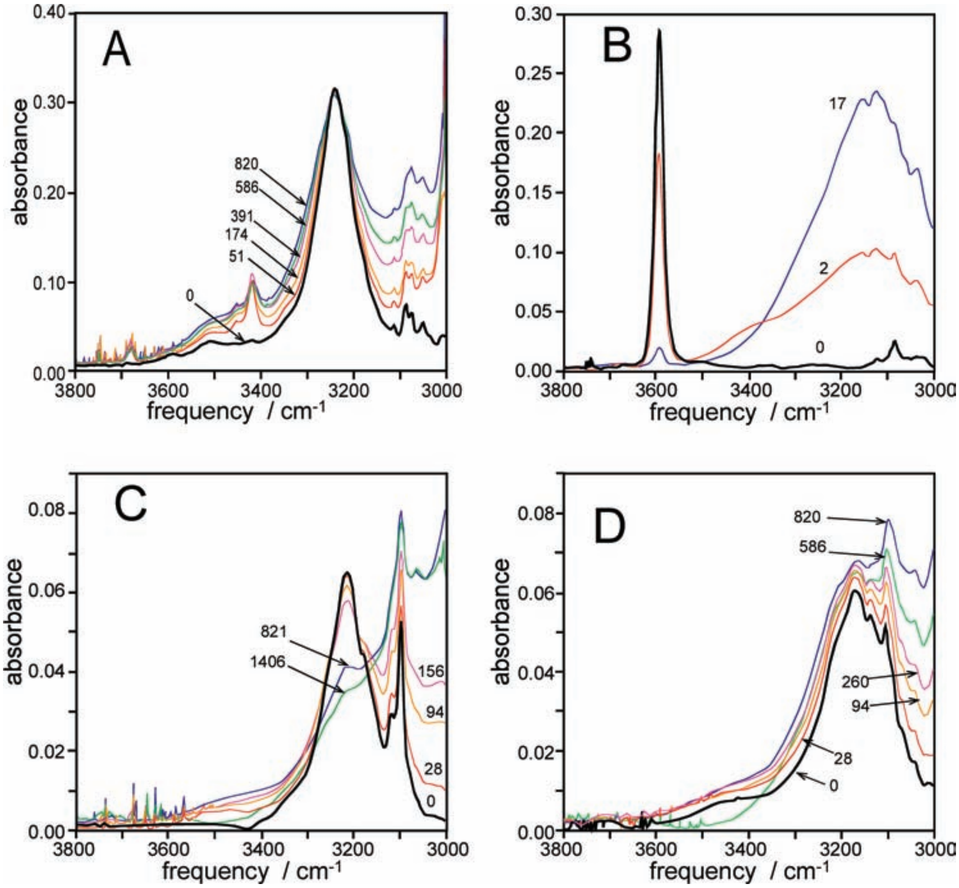
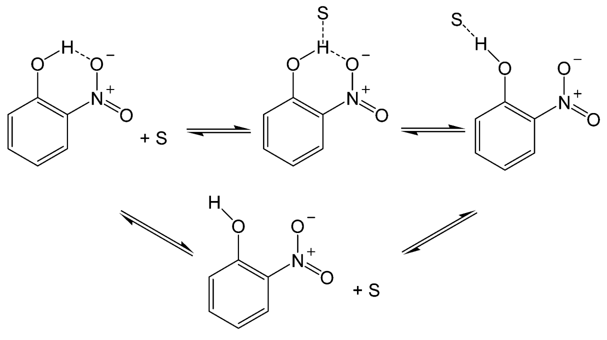


**Figure 3.** OH stretching region of the IR spectrum of (A) 2-nitrophenol (17.5 mM), (B) 4-nitrophenol (4.4 mM), (C) 2,4-dinitrophenol (7.2 mM), and (D) 2,6-dinitrophenol (10.3 mM) in $CCl_4$ containing DMSO (concentration, in millimoles per liter, are indicated by numbers).

With no data on 2,6-dinitrophenol(s), where formation of an intermolecular HB of the type shown above is not possible, such interpretations are somewhat suspect. Even when both 2-nitrophenol and 2,6-dinitrophenols were investigated the interpretations of the IR spectrum in neat polar solvents are not always easy to accept. For example, Dabrowska and Urbanski[20b] examined the IR spectra of eight *o*-nitrophenols in $CCl_4$, nitrobenzene, ethyl acetate, acetonitrile, acetone, and dioxane. For all these *o*-nitrophenols, the O−H bands occurred at higher frequencies in the polar solvents relative to $CCl_4$.[22] The results were interpreted in terms of breaking of the intramolecular HB by the polar solvents and the formation of an intermolecular HB as shown above. However, the data do not entirely support this interpretation. For example,[20b] for 2-nitrophenol $\nu(\mathrm{OH}) = 3237\ \mathrm{cm}^{-1}$ in $CCl_4$ and $3300\ \mathrm{cm}^{-1}$ in acetonitrile, a $\Delta\nu(\mathrm{OH}) = 63\ \mathrm{cm}^{-1}$, whereas for 2,6-dinitrophenol $\nu(\mathrm{OH}) = 3164\ \mathrm{cm}^{-1}$ in $CCl_4$ and $3230\ \mathrm{cm}^{-1}$ in acetonitrile, a $\Delta\nu(\mathrm{OH}) = 66\ \mathrm{cm}^{-1}$, which is equal, within experimental error, to the $\Delta\nu(\mathrm{OH})$ for 2-nitrophenol. Since an in-plane intermolecular HB with S is not possible for 2,6-dinitrophenol explaining these IR results in terms of the breaking the intramolecular HB would require the formation of intermolecular HBs that are perpendicular to the plane of the aromatic ring for both 2-nitrophenol and 2,6-dinitrophenol. Such a structure for 2-nitrophenol is much less probable than the in-plane structure because it would be about 3.5 kcal/mol higher in energy.[23] Thus, the similar effects of neat acetonitrile on the shifts of $\nu(\mathrm{OH})$ relative to $CCl_4$ for 2-nitrophenol and 2,6-dinitrophenol could be used to argue against the abilities of polar solvents to break the intramolecular HB in *o*-nitrophenols, rather than the reverse.[20b] Another example of the difficulties involved in interpreting the $\nu(\mathrm{OH})$ region of the IR spectra is provided by Schreiber's study of 2-nitrophenol in butyronitrile.[20d] It was concluded that the intramolecular HB was largely replaced by an intermolecular HB to butyronitrile ($\beta_2^{\mathrm{H}} = 0.45^5$), the relative importance of the intermolecular HB increasing as the temperature increased. However, this seems improbable, because even DMSO ($\beta_2^{\mathrm{H}} = 0.78^5$) does not appear to break the intramolecular HB in 2-nitrophenol (Figure 3A). More recently, the shifts in the $\nu_{\mathrm{intra}}(\mathrm{OH})$ for 2-nitrophenol in neat polar solvents relative to the $\nu_{\mathrm{intra}}(\mathrm{OH})$ in $CCl_4$ have been interpreted in terms of conversion of the intramolecular HB into a bifurcated HB,[20e] i.e.,



***Infrared Spectra.*** In our opinion, all "interpretations" of the effects of neat polar solvents on the HB structures of *o*-nitrophenols that have been based on change (or lack of) in $\nu_{\mathrm{intra}}(\mathrm{OH})$[20,21] rest on shaky ground. Many of the HBA solvents employed were also HBDs and are likely to form hydrogen bonds to the nitro group(s) and indirectly influence $\nu_{\mathrm{intra}}(\mathrm{OH})$

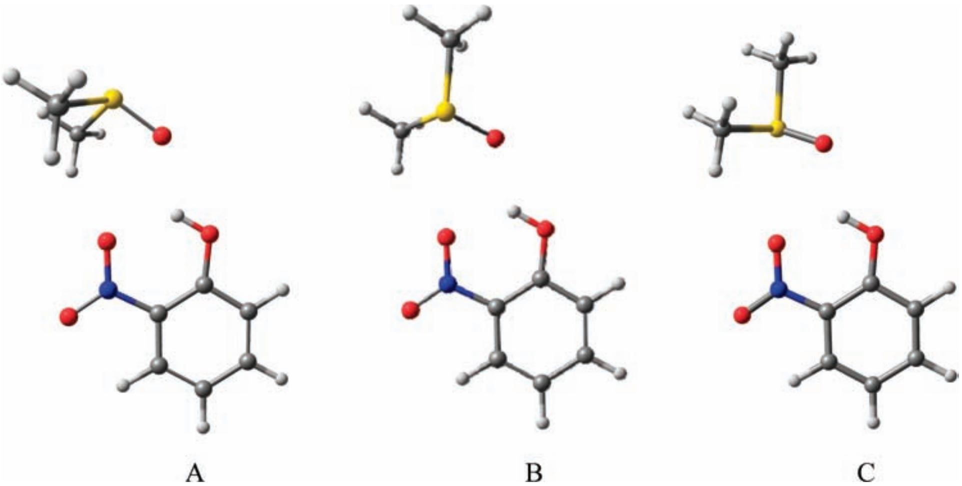


**Figure 4.** Lowest energy structures for complexes of 2-nitrophenol with DMSO. (A) Bifurcated intra/intermolecular HB, $\Delta H_{HB} = -3.4$ kcal/mol, $R$(HO···OS) = 2.79 Å, $\theta$(O−H−OS) = 131.0°, $R$(SCH···ON) = 2.52 Å. (B) Bifurcated intra/intermolecular HB, $\Delta H_{HB} = -2.9$ kcal/mol, $R$(HO···OS) = 2.80 Å, $\theta$(O−H−OS) = 134.0°, $R$(SCH···ON) = 2.53 Å. (C) This structure is degenerate with that shown in structure B and differs by a rotation about the DMSO O−S bond of ≈180°.

in this way. In addition, there must be dipole−dipole interactions between the polar solvents and the nitro group(s) which are also likely to change $\nu_{intra}$(OH). Furthermore, many of the solvents employed were sufficiently strong bases that the nitrophenols were probably partially ionized. Finally, the IR bands in question are extremely broad (see Figure 3, parts A and D) and shifts in the band maximum have generally been rather small.

The O−H fundamental stretching region of the IR spectra of 2-nitro-, 4-nitro-, 2,4-dinitro-, and 2,6-dinitrophenol in $CCl_4$ are shown in Figure 3, together with the effect of added DMSO on these bands. (The results with 2,4,6-trinitrophenol are shown in the Supporting Information.) The intramolecular HB in 2-nitrophenol exhibits a rather broad band with a maximum at ~3243 cm$^{-1}$ (Figure 3A). Neither the position nor the intensity at the band maximum was altered by the added DMSO. However, the DMSO did induce considerable band broadening, particularly on the band's low-frequency side. Indeed, the apparently unchanged intensity of the band is an artifact that arises from a reduced intramolecular HB band intensity "sitting" on the side of a broad absorption that "grows in" as the DMSO concentration is increased. A roughly comparable situation seems to exist with 2,6-dinitrophenol (Figure 3D) and 2,4,6-trinitrophenol.[25] However, with 2,4-dinitrophenol the intramolecular O−H band (maximum ~3218 cm$^{-1}$) actually decreases in intensity as the DMSO concentration is increased and again, a broad new absorption band grows in at lower frequencies (Figure 3C).[25] The difference between the behavior of this phenol and 2-nitrophenol is striking. Thus, and in contrast to all the *o*-methoxyphenols with their five-center intramolecular HBs, the 2-, 2,6-, and 2,4,6-nitrophenols with their six-center intramolecular HBs might, *at first sight*, *appear* not to form bifurcated intra/inter HBs with DMSO. This *implies* that the DMSO-induced shift of the O−H stretching band in 2,4-dinitrophenol arises because the DMSO induces breaking of the intramolecular HB with the formation of a "simple" intermolecular HB to a DMSO molecule. The results in Figure 3C yield an equilibrium constant of 5.7 M$^{-1}$ for 2,4-dinitrophenol's intramolecular HB versus its intermolecular HB with DMSO. The effects of the added DMSO on 4-nitrophenol's fundamental O−H stretching band are consistent with its $\alpha_2^H$ value of 0.824.[4]

The different behavior toward DMSO of the intramolecular HBs in 2-nitrophenol and 2,4-dinitrophenol can be understood qualitatively as arising from a combination of two factors. First, the intermolecular HB donor activity of 2,4-dinitrophenol will be higher than that of 2-nitrophenol because the former phenol is a much stronger acid than the latter (p$K_a$ = 3.93 and 7.06, respectively, cf. 7.14 for 4-nitrophenol). The second factor arises because the HBA activity of the *o*-nitro group in 2,4-dinitrophenol will be reduced relative to that in 2-nitrophenol. That is, because of the strong electron-withdrawing ability of nitro groups, it can be predicted that two nitro groups on a benzene ring will reduce the HB acceptor activities of one another compared with the HB acceptor ability of a single nitro group on a benzene ring. To check this prediction, the value of $\beta_2^H$ for 1,3-dinitrobenzene was determined (see Supporting Information) to be 0.30 (i.e., smaller than the $\beta_2^H$ value for nitrobenzene, 0.34)[5] and corresponding to a $\beta_2^H$ value per nitro group of only 0.23. These facts imply that there is a significant reduction in HB acceptor activity of the 2-nitro group in 2,4-dinitrophenol relative to 2-nitrophenol. Together, these two factors allow the intramolecular HB in 2,4-dinitrophenol to be broken by DMSO, but not the corresponding bond in 2-nitrophenol.

***Computations.*** These show that the actual situation for *o*-nitrophenols in the presence of DMSO is even more complicated and interesting than was, at first sight, suggested by their IR spectra. Thus, for 2-nitrophenol plus DMSO, bifurcated intra/intermolecular HB complexes comprise ca. 90% of the total population (see Supporting Information), while the remaining 10% exists as a "simple" intermolecular HB complex. This latter structure has a calculated binding enthalpy of 1.7 kcal/mol, which is not enough to overcome the 1.8 kcal/mol (3*RT*) of entropy associated with the degrees of freedom lost upon HB formation. This weak intermolecular binding is partly due to the strength of the intramolecular HB in 2-nitrophenol, calculated to be 10.4 kcal/mol, so that 2-nitrophenol and DMSO do not form stable "simple" intermolecular HB complexes.

The bifurcated intra/intermolecular complexes involving 2-nitrophenol, shown in Figure 4, somewhat resemble those formed by 2-methoxyphenol (see Figure 2, parts B and C) in that there are significant secondary interactions between a DMSO methyl group and an oxygen atom in the phenol. However, in 2-nitrophenol this interaction involves an oxygen in the nitro group, whereas in 2-methoxyphenol it involves the phenolic oxygen. The proximity of the atoms involved in the six-centered intramolecular HB of 2-nitrophenol prevents DMSO from forming a well-aligned HB and from approaching as closely as it can in the case of 2-methoxyphenol. This is evident from the geometries of the lowest energy HB complexes with DMSO, viz., 2-methoxyphenol, $R$(HO···OS) = 2.77 Å, $\theta$(O−H−OS) = 148.0°, $R$(SCH···OH) = 2.60 Å (see Figure 2A); 2-nitrophenol, $R$(HO···OS) = 2.79 Å, $\theta$(O−H−OS) = 131.0°, $R$(SCH···ON) = 2.52 Å (see Figure 4A). Consequently, the strengths of the bifurcated intra/intermolecular HBs in the complexes involving 2-nitrophenol are as much as 2.3 kcal/mol lower in enthalpy than those involving 2-methoxyphenol complexes. Moreover, although the formation of bifurcated HBs between 2-methoxyphenol and DMSO is experimentally very obvious (Figure 1A), the only sign of bifurcated HBs between 2-nitrophenol and DMSO is some band broadening, there being no shift in the position of the band maximum (Figure 3A).

Interestingly, the 2-nitrophenol bifurcated intra/intermolecular HB complexes have $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$ values in the range of +74 to +82 cm$^{-1}$ which implies that the strength of the O−H bond in 2-nitrophenol is increased by the interaction with DMSO. It has been reported, vide supra, that the difference in the OH band maximum for 2-nitrophenol in acetonitrile and in CCl$_4$, $\nu_{\mathrm{MeCN}} - \nu_{\mathrm{CCl4}} = \Delta\nu(\mathrm{OH})_{\mathrm{exptl}} = +63$ cm$^{-1}$.[20b] Our calculations on the 2-nitrophenol + acetonitrile complex gave $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}} = +112.5$ cm$^{-1}$, indicating that we are overestimating the increase in O−H stretching frequency. It seems likely that we are also overestimating $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$ in the bifurcated intra/intermolecular HB complexes of 2-nitrophenol (and other species) with DMSO. We propose that the positive values of $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$, which are computed for all bifurcated intra/intermolecular HB complexes involving six-membered intermolecular HBs (except for 7-hydroxyindanone, see Table 2), are related to a collinear arrangement of the HB-donating and -accepting group dipoles, i.e.,

$$\mathrm{O}\overleftarrow{-}\mathrm{H}\cdots\mathrm{O}\overleftarrow{-}\mathrm{S}$$

In the case of the HB structure of 7-hydroxyindanone with DMSO in which the HB-donating and -accepting dipoles are collinear, $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$ is slightly less than 0 (see below).

Despite its lower p$K_a$ (see Table 1), the strength of the intramolecular HB in 2,4-dinitrophenol is calculated to be the same as that in 2-nitrophenol, whereas $\nu$(OH) for 2,4-dinitrophenol is computed to be only 16.3 cm$^{-1}$ (exptl 25 cm$^{-1}$) lower than in 2-nitrophenol. These results are explained by the fact that the stability of 2,4-dinitrophenol with the OH group pointing away from the ortho-substituent, i.e., the non-HB structure, is higher by ca. 1.4 kcal/mol than the analogous structure for 2-nitrophenol and this cancels the greater strength of the intramolecular HB in 2,4-dinitrophenol, as computed to a first approximation.[26−28]

The bifurcated intra/intermolecular HB complexes formed by 2,4-dinitrophenol and DMSO have the same general structure as those formed by 2-nitrophenol (see Figure 4), but HB strengths are ca. 1.5 kcal/mol higher in the former complexes. The $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$ values for these complexes are only +20 ± 2 cm$^{-1}$, which accounts for the fact that there is no IR evidence for their formation. However, our calculations predict that 10.2% of the 2,4-dinitrophenol/DMSO HB complexes are "simple" intermolecular HBs (two symmetrically related conformers with secondary interactions between a methyl of DMSO and the *hydroxylic* oxygen, see Figure 5). Although the fractions of "simple" intermolecular complexes with DMSO formed by 2-nitrophenol and 2,4-dinitrophenol are essentially identical, the latter complexes are more strongly H-bonded than the former (viz., 3.4 vs 1.7 kcal/mol). For the 2,4-dinitrophenol plus DMSO intermolecular HB, $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}}$ is calculated to be −397 cm$^{-1}$. Unfortunately, this is outside of the spectroscopic range examined experimentally because of complications arising from overlap with the C−H stretching modes. Nevertheless, our calculations are fully consistent with experiment (Figure 3C) and further support the formation of "simple" intermolecular HB complexes between 2,4-dinitrophenol and DMSO.

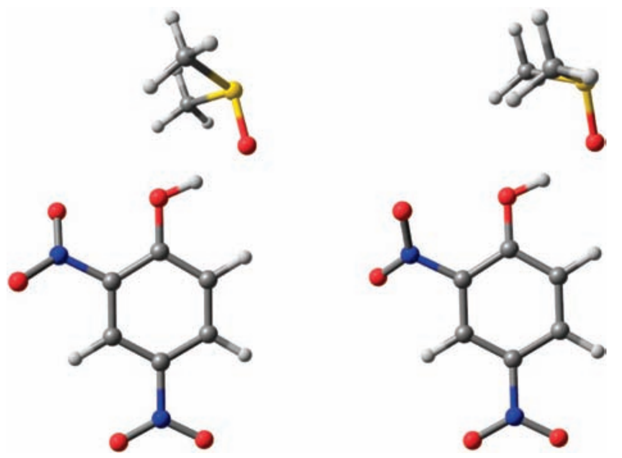


**Figure 5.** Two symmetrically related structures for "simple" intermolecular HB complexes between 2,4-dinitrophenol and DMSO, $\Delta H_{\mathrm{HB}}$ = −3.4 kcal/mol, $R$(HO···OS) = 2.59 Å, $\theta$(O−H−OS) = 167.5°, $R$(SCH···OH) = 2.70 Å.

**Phenols with *o*-Carbonyl Groups.** ***Background.*** There have been a number of IR investigations of 2-formylphenol (salicaldehyde),[29,30] 2-acetylphenol,[30] and methylsalicylate.[20b,30b] Both the O−H stretching band frequencies[20b] and the C=O stretching band frequencies[30] in CCl$_4$ and in some neat polar solvents have been employed to draw conclusions about the formation of intermolecular HBs between these phenols and the HBA solvents. Thus, Dabrowska and Urbanski[20b] reported that the $\nu_{\mathrm{intra}}$(OH) in methyl salicylate occurs at the same frequency (3197 cm$^{-1}$) in the following neat solvents: CCl$_4$, nitrobenzene, ethyl acetate, acetonitrile, acetone, and 1,4-dioxane. In contrast, Berthelot et al.[30b] concluded, from an IR study of the C=O stretching band of this phenol in neat CCl$_4$ and in neat DMSO, that in the latter solvent an intermolecular HB to a DMSO molecule was formed to the extent of 25%. Similarly, DMSO was claimed to break the intramolecular H-bond to the extend of 15% in 2-hydroxyacetophenone and 70% in 2-formylphenol.[30b]

The conclusions of Berthelot et al.[30b] are at odds with those of Dabrowska and Urbanski,[20b] but neither group of authors report any bifurcated HB formation.[31] However, the O−H stretching bands in 2-acylphenols are broad (see Figure 6A−C), so the formation of intermolecular HBs and bifurcated HBs might not be easy to observe. Although an aromatic nitro group is not as strong an acceptor of *intermolecular* HBs as an aromatic carbonyl group[32] the situation for *intramolecular* HBs in ortho-substituted phenols is less certain. Despite the geometrical restrictions on intramolecular HBs, there is evidence that the shifts in O−H band frequencies (relative to phenol) for over 20 ortho-substituted phenols also give a fairly good linear correlation with the strengths of their intramolecular HBs, as estimated from their OH $^1$H NMR chemical shifts.[33] This would be expected on the basis of Badger and Bauer's proposal[34] that the shift in the IR frequency of an OH group on forming a HB to a base would be linearly related to the enthalpy of HB formation. On the other hand, B3LYP/6-31G(d,p)-computed frequencies and intramolecular HB strengths for an even greater number of ortho-substituted phenols revealed "at best a crude relationship."[35] The intramolecular HBs in 2-nitro-, 2-formyl,

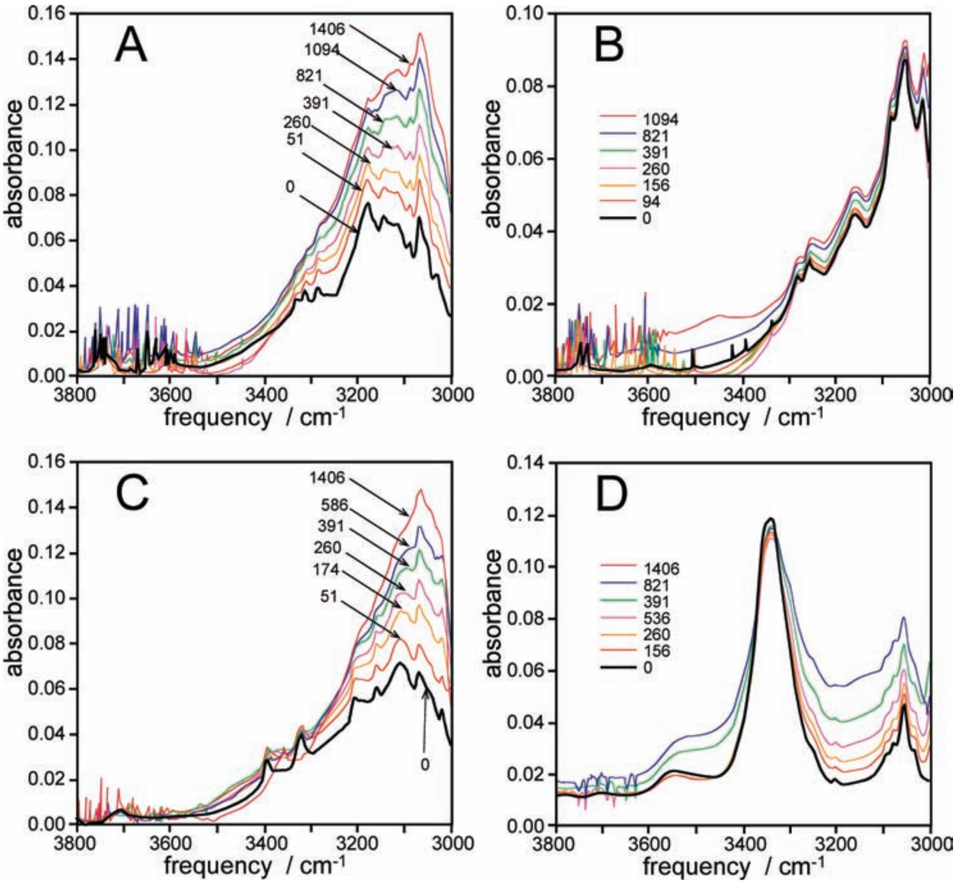


**Figure 6.** OH stretching region of the IR spectrum of (A) 2-formylphenol (salicylaldehyde, 20.3 mM), (B) 2-acetylphenol (17.9 mM), (C) 2,4-diformyphenol (16.1 mM), and (D) 7-hydroxyindanone (16.0 mM) in $CCl_4$ containing DMSO (concentrations, in millimoles per liter, are indicated by numbers).

and 2-acetyl-phenol produce six-membered rings with conjugation in the heavy atom skeleton, a conjugation that is believed to add to the HB strengths.[36a] Although these intramolecular HB strengths may not correlate linearly with the quoted (intermolecular HB) $\beta_2^{\mathrm{H}}$ values, it would be surprising if the intramolecular HBs to *o*-carbonyl groups were not approximately as strong as those to *o*-nitro groups.

***Infrared Spectra.*** The O−H fundamental stretching region of the IR spectra in $CCl_4$ of 2-formylphenol, 2-acetylphenol, 2,4-diformylphenol, and 7-hydroxyindan-1-one are shown in Figure 6, together with the effect of added DMSO on these spectra. The first three of these phenols show very broad O−H stretching bands, broader than the bands of the *o*-nitrophenols; indeed, the present spectrum does not allow the band maximum for 2-acetylphenol to be assigned.[36b] However, the maximum for 2-formylphenol appears to be in the range of ∼3120−3190 $cm^{-1}$, i.e., at a lower frequency than the 2-nitrophenol band at ∼3243 $cm^{-1}$.[36b] These results would be consistent with a weaker intramolecular HB in 2-nitrophenol than in 2-formylphenol, vide supra, but calculations show that this is not the case, vide infra.

The broad bands in Figure 3, parts A, C, and D, and Figure 6A−C imply that the six-membered HB rings are, in contrast to the five-membered HB rings in *o*-methoxyphenols (Figure 1), highly flexible and have a considerable range of structures. The very broadness of these bands makes it difficult to determine whether the added DMSO does, or does not, affect these intramolecular HBs (with the single exception of 2,4-dinitrophenol, Figure 3C). Nevertheless, the contrast in the behavior of DMSO on the IR spectra of 2,4-dinitrophenol (HB obviously broken by DMSO, Figure 3C) and 2,4-diformylphenol (HB apparently not broken by DMSO, Figure 6C) is noteworthy.

DMSO induces a broadening and an increase in the intensities of the OH bands of 2-formylphenol and 2,4-diformylphenol (Figure 6, parts A and C), indicating an increase in the local O−H dipole moment. However, DMSO has no significant effect on the OH band of 2-acetylphenol (Figure 6B). At first sight, this difference is surprising. However, the reported OH band maximum for 2-acetylphenol (3050 $cm^{-1}$)[36] is at the end of the 3800−3000 $cm^{-1}$ frequency range examined experimentally (because of overlap with C−H stretching bands). The expected DMSO-induced shift of this band to significantly lower frequencies would not, therefore, be detected.

7-Hydroxyindan-1-one was chosen in the hope that the near planarity of the six-membered H-bonded ring that is enforced by the indanone's geometry would both weaken the intramolecular HB relative to those in 2-formyl- and 2-acetyl-phenol and greatly reduce the flexibility of the HB ring, with a consequent sharpening of the O−H band. This hope was realized insofar as bandwidth is concerned (Figure 6D). Also, to judge by its 3342 $cm^{-1}$ band maximum, this phenol would appear to have a *weaker* intramolecular HB than any of the six-membered intramolecular HB phenols considered so far. However, appearances can be deceptive, see computational results below. The experimental spectra also *suggest* that added DMSO does not break the intramolecular H-bond in 7-hydroxyindan-1-one but it does induce significant band broadening both at higher and at lower frequencies than the main band.

***Computations.*** The strength of the intramolecular HB in 2-formylphenol is calculated to be 8.2 kcal/mol,[37] which is 2.2 kcal/mol *weaker* than the intramolecular HB in 2-nitrophenol (10.4 kcal/mol, vide supra), a result that is consistent with the higher $pK_a$ of 2-formylphenol (see Table 1). Nevertheless, the

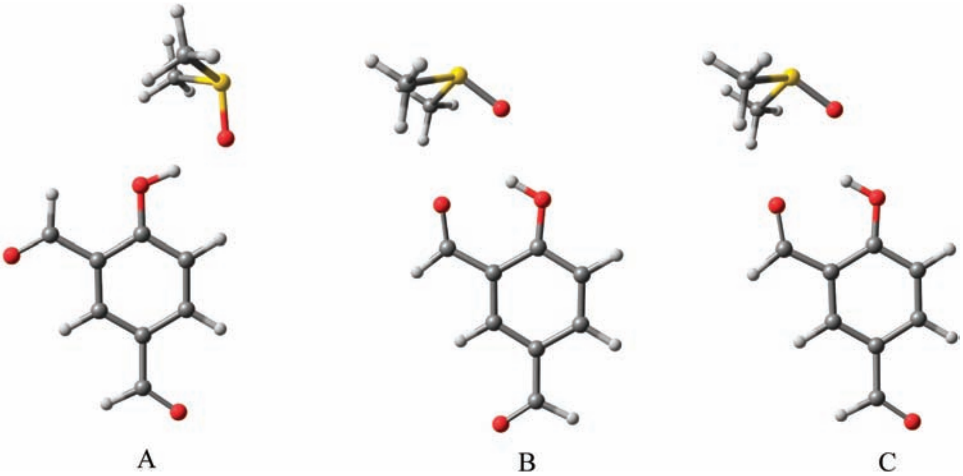


**Figure 7.** Three lowest energy structures for complexes of 2,4-diformylphenol with DMSO. (A) Intermolecular $\Delta H_{HB} = -3.2$ kcal/mol, $R(HO\cdots OS) = 2.65$ Å, $\theta(O-H-OS) = 171.5°$, $R(CH\cdots OH) = 2.98$ Å. (B) Bifurcated intra/intermolecular $\Delta H_{HB} = -3.0$ kcal/mol, $R(HO\cdots OS) = 2.75$ Å, $\theta(O-H-OS) = 128.2°$, $R(CH\cdots OH) = 2.48$ Å. (C) Bifurcated intra/intermolecular $\Delta H_{HB} = -2.8$ kcal/mol, $R(HO\cdots OS) = 2.75$ Å, $\theta(O-H-OS) = 128.3°$, $R(CH\cdots OH) = 2.49$ Å.

frequency difference, $\nu(OH)_{2\text{-nitrophenol}} - \nu(OH)_{2\text{-formylphenol}}$ [$= 123 - 53$ cm$^{-1}$ (experiment) and $= 35.9$ cm$^{-1}$ (calculation)], is *positive* despite the weaker intramolecular HB in 2-formylphenol. This result is *inconsistent* with the Badger−Bauer rule,[34] as noted previously for intramolecular HBs by Korth et al.[35] However, it is intriguing to note that decomposition of the enthalpy of 2-formylphenol into stabilization enthalpies indicates that its intramolecular HB strength, as computed to a first approximation,[26−28] is indeed *higher* than that of 2-nitrophenol (viz., 7.1 vs 4.4 kcal/mol). In addition, the non-HB structure of 2-formylphenol is stabilized by an attractive interaction between the formyl CH and the hydroxyl O atom. This means that the computed strength of the intramolecular HB is smaller for 2-formylphenol than for 2-nitrophenol, in which this interaction is absent.[26] If this CH···OH interaction were not present, the intramolecular HB strength in 2-formylphenol would be 10.4 kcal/mol. Calculations indicate that several complexes can be formed between 2-formylphenol and DMSO. However, only one structure is predicted to have a binding enthalpy that exceeds the 1.8 kcal/mol entropic cost of complex formation. This is a bifurcated intra/intermolecular HB complex analogous to the lowest enthalpy structure for the complex of 2-nitrophenol with DMSO (see Figure 4A), which has a HB strength of 2.1 kcal/mol. The $\Delta\nu(OH)$ value for this 2-formylphenol plus DMSO complex is calculated to be $+156.1$ cm$^{-1}$ (expected to be somewhat overestimated). Such a DMSO-induced shift in frequency may well explain the DMSO-induced change in shape of the O−H stretching band (see Figure 6A).

The lowest energy complexes of 2,4-diformylphenol and DMSO are computed to be of the *intermolecular* type, although a few complexes of the *bifurcated* type were also found. With the 2,4-diformylphenol in the "away" configuration, DMSO is able to approach the phenol fairly closely and is able to form linear H-bonds, see Figure 7. The HB strengths for the all of the complexes range from 2.0 to 3.2 kcal/mol. The $\Delta\nu(OH)_{calcd}$ values for the structures shown in Figure 7 are quite variable, viz., Figure 7A, $-132.4$ cm$^{-1}$; Figure 7B, $+160.9$ cm$^{-1}$; Figure 7C, $+173.5$ cm$^{-1}$. All three of these structures would lead to bands lying within the observed, broad, O−H band, Figure 6C, *which explains why formation of these intermolecular HBs is not observed experimentally.*

The expectation that the intramolecular HB strength in 7-hydroxyindanone would be weaker than in 2-formylphenol is not supported by calculations which gave HB strengths for these two phenols of 8.3 and 8.2 kcal/mol, respectively. Nevertheless, the calculated frequency difference, $\nu(OH)_{7\text{-hydroxyindanone}} - \nu(OH)_{2\text{-formylphenol}} = 152.5$ cm$^{-1}$, is in excellent agreement with the 152−222 cm$^{-1}$ found experimentally. Similarly, the calculated frequency difference, $\nu(OH)_{7\text{-hydroxyindanone}} - \nu(OH)_{2\text{-nitrophenol}} = 116.8$ cm$^{-1}$, is in satisfactory agreement with the experimental value of 99 cm$^{-1}$.

The complexes of 7-hydroxyindanone with DMSO are predicted to be mainly (94.2%) of the bifurcated intra/intermolecular HB type. Two complexes of this type (Figure 8, parts A and B) were calculated to have HB strengths of 3.9 and 3.5 kcal/mol and to have structures somewhat similar to the 2-nitrophenol complexes shown in Figure 4, parts A and B. There is also a "simple" intermolecular complex (Figure 8C) with a calculated HB strength of 2.6 kcal/mol that is similar to the HB structure formed between 2-methoxyphenol and DMSO, see Figure 2C. As has been found in other HB complexes, a collinear arrangement of the HB-donating and -accepting group dipoles (Figure 8, parts A and B) causes $\Delta\nu(O-H)_{calcd}$ values to be "unexpected" relative to the strengths of the HBs, viz., $\Delta\nu(O-H)_{calcd} = \sim -12$ cm$^{-1}$ for the structures shown in Figure 8, parts A and B. This means, of course, that these HB complexes will not be observed by IR studies of the O−H stretching band, see Figure 6D. The "simple" intramolecular HB structure (Figure 8C) has $\Delta\nu_{calcd} =$ ca. $-265$ cm$^{-1}$ and is quite consistent with the DMSO-induced grow-in of a broad absorbance between 3200 and 3000 cm$^{-1}$ (Figure 6D). Note that the sharp band at ~3050 cm$^{-1}$ is unrelated to complex formation between 7-hydroxyindanone and DMSO because it is present at [DMSO] = 0 and is presumably due to a C−H stretching mode.

***o*-Methoxymethylphenol.** ***Background.*** Another functional group that accepts intermolecular H-bond with a facility approximately equal to the formyl group in benzaldehyde is dimethyl ether, $\beta_2^H = 0.43$.[5] The six-membered intramolecular HB in 2-methoxymethylphenol is not stabilized by conjugation in its heavy atom skeleton. The IR spectrum of 2-methoxymethylphenol in $CCl_4$ has been reported.[39] Two O−H stretching bands were observed, a relatively narrow, weak band at 3612 cm$^{-1}$ and a much broader and more intense band with a maximum at 3409 cm$^{-1}$. The latter was attributed to the intramolecular HB and the former to the "free" phenol, i.e., to a conformer in which the OH group points "away" from the methoxymethyl group. The estimated "population distri-

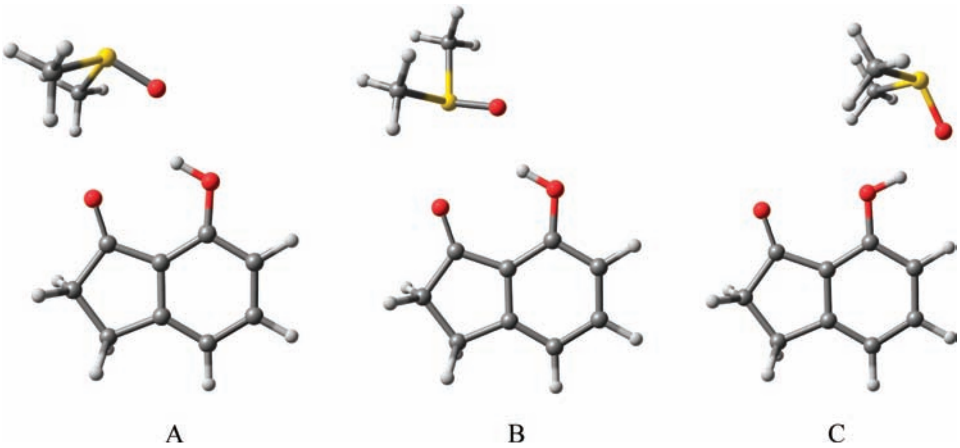


**Figure 8.** Lowest energy structures for complexes of 7-hydroxyindanone with DMSO. (A) Bifurcated intra/intermolecular HB. $\Delta H_{HB} = -3.9$ kcal/mol, $R$(HO···OS) = 2.73 Å, $\theta$(O−H−OS) = 134.5°, $R$(SCH···O=C) = 2.38 Å. (B) Bifurcated intra/intermolecular HB. $\Delta H_{HB} = -3.5$ kcal/mol, $R$(HO···OS) = 2.72 Å, $\theta$(O−H−OS) = 141.2°, $R$(SCH···O=C) = 2.42 Å. (C) "Simple" intramolecular HB. $\Delta H_{HB} = -2.6$ kcal/mol, $R$(HO···OS) = 2.65 Å, $\theta$(O−H−OS) = 158.7°, $R$(SCH···O=C) = 2.56 Å. Structure B is one of a degenerate pair, the second of which is formed by a rotation about the DMSO O−S bond of ≈180°.

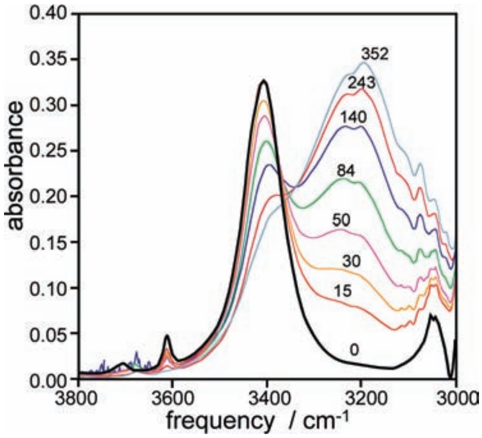


**Figure 9.** OH stretching region of the IR spectrum of 2-methoxymethylphenol (20.3 mM) in $CCl_4$ containing DMSO, concentration of DMSO (mM) is indicated by the numbers.

bution of the OH groups [was] 4% free and 96% hydrogen-bonded."[39] We were somewhat skeptical about the presence of the "free" phenol for two reasons. First, calculations of the intramolecular HB strength in the structurally related 2-hydroxybenzyl alcohol[35] implied that the "free" phenol concentration in 2-methoxymethylphenol should be negligible. Second, the synthesis[40] of this phenol has been shown to give *o*-cresol as a major side product, together with other products that would also show "free" OH groups.[41]

***Infrared Spectrum.*** Synthesis of this phenol, an oily liquid, followed by high-vacuum distillation gave a material that was pure, as judged by $^1$H NMR and by gas chromatography. This material gave an IR spectrum quite similar to that reported by Langoor and van der Maas.[39] The original synthesis of this compound gave it a melting point of −1 °C.[40] A single crystal was eventually obtained by prolonged storage at −80 °C. The O−H stretching region of the IR spectrum of this undoubtedly pure 2-methoxymethylphenol in $CCl_4$ is shown in Figure 9. That the small band at 3614 cm$^{-1}$ (rather than 3612 cm$^{-1}$) really was due to an O−H stretch was confirmed by adding a drop of $D_2O$ to the $CCl_4$ solution of this phenol. This caused the disappearance of both the small (3614) and large (3409 cm$^{-1}$) IR bands and formation of an O−D stretching band with a maximum at ~2530 cm$^{-1}$, which presumably arises from the intramolecular D-bond (see Supporting Information, the "free" O−D stretching band was too weak to identify with certainty). Figure 9 also shows that the addition of DMSO to the $CCl_4$ solution of 2-methoxymethylphenol leads to the loss of both of its O−H stretching bands and their replacement by an intermolecular HB band with a maximum at ~3170 cm$^{-1}$. These data yield $\alpha_2^H = 0.53$ for 2-methoxymethylphenol, a value quite similar to that for phenol itself, viz.,[3] $\alpha_2^H = 0.59$.

***Computations.*** There are a large number of H-bonded structures of 2-methoxymethylphenol with DMSO. The three lowest energy structures are shown in Figure 10, and the caption contains some geometric information about these complexes. The steric bulk associated with the methoxymethyl group prevents the formation of a bifurcated intra/molecular HB complex, and so all three lowest energy structures form intermolecular HBs. The lowest energy H-bonded structure (Figure 10A) has a computed $\Delta H_{HB} = -6.1$ kcal/mol. In addition to the HB, this structure has additional stabilizing interactions between a methoxymethyl substituent C−H and the phenolic O−H group and a DMSO C−H and the phenolic O−H group. These additional interactions contribute to making this complex the most strongly bound of all of the complexes studied computationally in this work. The high HB strength can also be attributed to the fact that the intramolecular HB strength in free 2-methoxymethylphenol is calculated to be quite low at 3.0 kcal/mol (vide infra). Similarly, the intramolecular HB in free 2-methoxyphenol is low (viz., 3.8 kcal/mol), and it forms complexes with DMSO that are strongly H-bonded (viz., 5.8 kcal/mol, see Table 2.) The HB complexes have $\Delta\nu(\mathrm{OH})_{\mathrm{calcd}} = -254.6$ to $-302.3$ cm$^{-1}$ relative to 2-methoxymethylphenol, which are in fair agreement with the measured range (−165 to −234 cm$^{-1}$).

**Kinetics.** Highly reactive *tert*-alkoxyl radicals can abstract the phenolic H-atom from *o*-methoxyphenols despite the involvement of these hydrogen atoms in five-center intramolecular HBs.[7] This is also the case for the much less reactive 2,2-diphenyl-1-picrylhydrazyl radical, **dpph**$^\bullet$. Rate constants for reaction 3 were determined by

$$\mathrm{ArOH} + \mathbf{dpph}^\bullet \rightarrow \mathrm{ArO}^\bullet + \mathbf{dpph} - \mathrm{H} \qquad (3)$$

monitoring the loss of **dpph**$^\bullet$ spectrophotometrically at 517 nm ($\varepsilon \sim 11\,000$ M$^{-1}$ cm$^{-1}$) in the presence of an excess of the phenol using a rapid-mixing, stopped-flow apparatus, as described in earlier work.[2k,17] The reactions were run at room temperature in *n*-heptane (to avoid complications arising from intermolecular HB formation by the phenols). The results are summarized in Table 3. Similar measurements were attempted

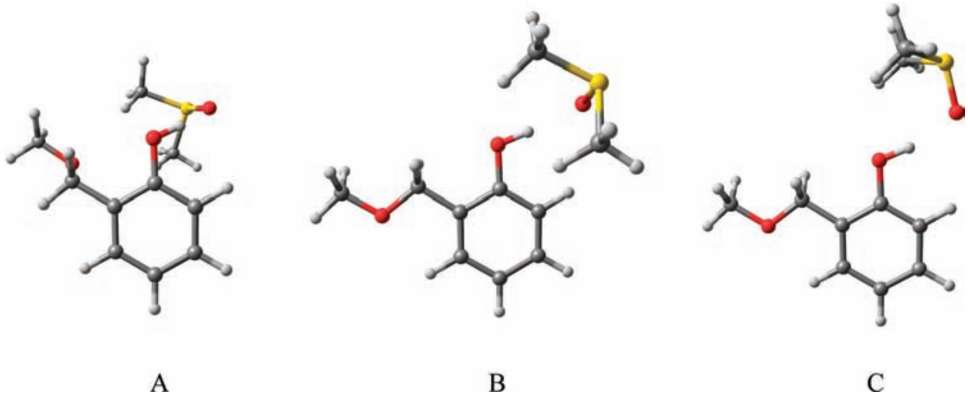


**Figure 10.** Lowest energy structures for complexes of 2-methoxymethylphenol with DMSO. (A) Intermolecular HB, $\Delta H_{HB} = -6.1$ kcal/mol, $R$(HO···OS) = 2.69 Å, $R$(OCH···O) = 2.57 Å, $\theta$(O−H−OS) = 160.9°, $R$(SCH···O(H)C) = 2.60 Å. (B) Intermolecular HB, $\Delta H_{HB} = -5.9$ kcal/mol, $R$(HO···OS) = 2.72 Å, $\theta$(O−H−OS) = 165.5°, $R$(SCH···O(H)C) = 2.75 Å. (C) Intermolecular HB, $\Delta H_{HB} = -5.8$ kcal/mol, $R$(HO···OS) = 2.72 Å, $\theta$(O−H−OS) = 165.4°, $R$(SCH···O(H)C) = 2.78 Å. Structure B is one of a degenerate pair, the second of which is formed by a rotation about the DMSO O−S bond of ≈180°.

**TABLE 3: Rate Constants for H-Atom Abstraction by dpph• from Some Phenols in *n*-Heptane at Room Temperature**

| substituent | $k_3$/M$^{-1}$ s$^{-1}$ | substituent | $k_3$/M$^{-1}$ s$^{-1}$ |
|---|---|---|---|
| none | 0.22[a] | | |
| 2-OCH$_3$ | 0.82 | 2,6-(OCH$_3$)$_2$ | 35.5 |
| 4-OCH$_3$ | 240 | 2,4,6-(OCH$_3$)$_3$ | 321 |
| 2,4-(OCH$_3$)$_2$ | 293 | 2-CH$_3$OCH$_2$ | 0.05 |

[a] From ref 3.

with the other phenols studied in this work. However, contrary to popular opinion, solutions of **dpph•** are not stable indefinitely at ambient (or even at low)[42] temperatures, particularly in the presence of strong acids (like some of the present phenols, see Table 1). The slow decomposition of **dpph•** combined with the limited solubility of many of the phenols in heptane meant that only those rate constants >10$^{-2}$ M$^{-1}$ s$^{-1}$ could be considered reliable. This limited the determination of reliable rate constants for H-atom abstraction from phenols possessing six-membered HB rings to 2-methoxymethylphenol which, of course, has a small amount of "free" OH. The negligible reactivities of the *o*-nitro-, *o*-formyl-, and *o*-acetyl-phenols are presumably due to a combination of intramolecular HB-induced steric protection of their phenolic H-atoms and the O−H bond strengthening effects of these electron-withdrawing groups.

## Discussion

For over half a century, infrared spectroscopy has been the favored method for studying hydrogen bonds. The spectra are readily measured and have, heretofore, been assumed to provide rather detailed and accurate pictures of the hydrogen bonds formed between HB donors and acceptors. It was therefore a shock to discover that modern computational methods can give a very different HB picture from that deduced by an examination of the O−H fundamental stretching bands. To cite just two examples from the present work: (1) The spectra imply that DMSO can break the intramolecular HB in 2,4-dinitrophenol to form a "simple" intermolecular HB (Figure 3C) but that DMSO cannot break the intramolecular HB in 2,4-diformylphenol (Figure 6C). However, computations indicate that DMSO can break the intramolecular HBs in both phenols. (2) Although the spectra of *o*-methoxyphenols clearly show that bifurcated intra/intermolecular HBs are formed upon addition of DMSO (Figure 1, parts A, C, and D), the spectra of *o*-nitrophenols and *o*-carbonyl-substituted phenols show no sign of the formation of bifurcated intra/intermolecular HBs upon the addition of DMSO (Figure 3, parts A and D and Figure 6 A−D). This is true even for 7-hydroxyindanone which has a remarkably narrow O−H stretching band leading one to anticipate that it would be easy to observe bifurcated HBs if they were formed. However, our computations indicate that both *o*-nitro and *o*-carbonyl phenols do form bifurcated intra/intermolecular HBs. These computations also indicate that *if* such bifurcated HBs are formed by these two classes of phenols, they would be invisible by IR spectroscopy. This is because the formation of bifurcated HBs between DMSO and *o*-nitro and *o*-carbonyl phenols is computed to induce only relatively small shifts in O−H stretching band frequencies.

The foregoing raises the vital question: *Can we trust theory to give reliable information about those HB structures, HB energies, and O−H stretching frequencies that cannot be confirmed experimentally?* We believe that, *at the level of theory we have employed*, we can answer, *yes*, to this question with a high degree of confidence. This confidence is based on the ability of theory to closely match a number of experimental observations and its ability to account for our failure to observe the formation of bifurcated intra/intermolecular HB complexes between DMSO and *o*-nitro and *o*-carbonyl phenols, vide supra. Three, quite different, examples where theory closely mirrors experimental facts are given below.

**Interaction 2-Methoxyphenol and DMSO.** The phenolic H-atoms in *o*-methoxyphenols participate in five-membered HB rings, and presumably because the *O−H···O*Me HBs are far from linear, their phenolic H-atoms can form rather strong bifurcated intra/intermolecular HBs with DMSO. These are observed experimentally. That is, the relatively sharp, intramolecular H-bonded O−H stretching bands observed for these phenols in CCl$_4$ are replaced by much broader bands with maxima at considerably lower frequencies upon the addition of DMSO (see Figure 1, parts A, C, and D). These new bands are assigned to bifurcated intra/intermolecular HBs. The magnitude of the DMSO-induced frequency shift for 2-methoxyphenol (−358 to −298 cm$^{-1}$) is relatively well reproduced by theory, viz., −312 and −224 cm$^{-1}$ for the structures shown in Figure 2, parts A and B, respectively. These two structures not only show bifurcated intra/intermolecular HBs but also indicate that there are secondary stabilizing interactions between a methyl group on the DMSO and the phenol. The DMSO-induced decrease in the intensity of 2-methoxyphenol's sharp intramolecular HB band yields an equilibrium constant for complex formation by these two substrates in $CCl_4$ equal to 2.71 $M^{-1}$, corresponding to 78.7% complex formation with 1 M DMSO. The calculations yield results in outstanding agreement with experiment, viz., 82.5% complex formation of the bifurcated inter/intramolecular type.

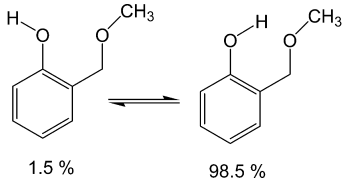
The accessibility of the phenolic H-atoms in *o*-methoxyphenols to reactants other than HB acceptor molecules like DMSO is in full accord with the experimental fact that these H-atoms can be abstracted by the HB acceptor radicals, *tert*-alkoxyl[7] and **dpph**$^\bullet$. Indeed, 2-methoxyphenol is slightly more reactive toward **dpph**$^\bullet$ than phenol (Table 3), indicating that the activating effect of the ortho-substituent is mitigated, but not completely, by the intramolecular H-bond. The reactivities of the methoxyphenols increase along the series 2 ≪ 2,6 ≪ 4 < 2,4 < 2,4,6 reflecting the well-known activating effects on H-atom abstraction by methoxy groups at the 4- and 6-positions.

**Interaction of 2,4-Dinitrophenol with DMSO.** The phenolic H-atoms in *o*-nitrophenols participate in six-membered HB rings and have O−H stretching bands that occur at much lower frequencies than those of the *o*-methoxyphenols. The *o*-nitrophenols also have very much broader bands which we attribute to the greater flexibility of six-membered rings relative to five-membered rings. The great width of the *o*-nitrophenols' O−H stretching bands make any DMSO-induced changes to these bands difficult to identify, except *in the case of 2,4-dinitrophenol*. For this phenol, there can be no doubt that DMSO induces a significant decrease in the intensity of its 3218 $cm^{-1}$ intramolecular HB O−H band with a concomitant increase in absorption intensities at frequencies below ca. 3150 $cm^{-1}$ (see Figure 3C). From the DMSO-induced decrease in the 3218 $cm^{-1}$ band at the lower DMSO concentrations employed, the equilibrium constant for complex formation between DMSO and 2,4-dinitrophenol in $CCl_4$ was calculated to be 5.7 $M^{-1}$.

The obvious interpretation of the experimental results shown in Figure 3C is that DMSO breaks 2,4-dinitrophenol's intramolecular HB to form an intermolecular HB. The computations indicate that this is true, but only in part. They indicate that ca. 90% of the DMSO/2,4-dinitrophenol complexes are of the bifurcated intra/intermolecular HB type with frequencies that are within ca. 20 $cm^{-1}$ of the frequency of the O−H stretching band of the phenol itself. These computational results provide a neat explanation for the fact that even 1.4 M DMSO induces only a ca. 40% decrease in the absorption intensity at 3218 $cm^{-1}$ (see Figure 3C).

Thus, it would appear that it is the computed ca. 10% of the nonbifurcated intermolecular HB complexes between DMSO and 2,4-dinitrophenol, see Figure 5, that is responsible for the DMSO-induced decrease in the 3218 $cm^{-1}$ band. This band is computed to be replaced by a dramatically shifted ($\Delta\nu = -397$ $cm^{-1}$) band at lower frequencies, a truly huge shift in frequency compared with the negligible shift for the DMSO/2,4-dinitrophenol bifurcated intra/intermolecular HB O−H bands. The value of 10% is in good agreement with a population of 15% computed from the equilibrium constant of 5.7 $M^{-1}$ for complex formation.

**2-Methoxymethylphenol: Populations of "Free" OH and Intramolecular HB Forms.** Langoor and van der Maas reported[39] that in $CCl_4$ the IR spectrum of 2-methoxymethylphenol shows a small band at ∼3612 $cm^{-1}$ and a much larger and broader band with a maximum at 3409 $cm^{-1}$. This result was interpreted as showing that a small fraction of this phenol (estimated as 4%)[43] did not have an intramolecular HB. We have confirmed the essentials of this report using extremely pure 2-methoxymethylphenol, see Figure 9. The best method for determining the quantity of "free" 2-methoxymethylphenol is to use an *appropriate* phenol and construct a peak height versus concentration calibration curve.[44] This curve allows the concentration of "free" phenol to be calculated from the "free" phenol peak height since the total concentration of 2-methoxymethylphenol is known. The integrated intensities of the fundamental O−H stretching bands of meta- and para-substituted phenols have been shown to correlate linearly with the substituents' Hammett $\sigma$ constants with intensities increasing substantially from electron-donating to electron-withdrawing substituents.[45] Since $\sigma_p(MeOCH_2) = 0.01$,[46] phenol will be a much better model for the intensity of the "free" OH band of 2-methoxymethylphenol than a cresol, $\sigma_p(Me) = -0.16$. This procedure yielded a "free"/intra-HB ratio of 2.1:97.9 in $CCl_4$ at 298 K. However, $CCl_4$ is a weak HB acceptor ($\beta_2^H = 0.05$)[3] and will slightly stabilize the "free" phenol.[47] The IR spectrum of 2-methoxymethylphenol was, therefore, also recorded in the non-HB acceptor solvent, cyclohexane (see Supporting Information). Using a calibration curve for phenol in cyclohexane, the "free"/intra-HB ratio in cyclohexane at 298 K was found to be 1.5:98.5. This ratio, which should be very close to the 298 K ratio in the gas phase, yields the free energy of formation of the intramolecular HB: $\Delta G_{298K} = -2.48$ kcal $mol^{-1}$. Since rotation about the $CH_2$−OMe bond is "frozen out" in the intramolecular HB form, the "free" OH form is entropically favored. We estimate that $T\Delta S_{298K} = RT = -0.59$ kcal $mol^{-1}$, and hence $\Delta H_{298K} = -3.1$ kcal $mol^{-1}$. To our knowledge, this is by far the most reliable experimental intramolecular phenol O−H···OR HB strength, and as such, it provides a gold standard for theory to reproduce. Fortunately, theory also meets this third test. Our calculations predict that the intramolecular H-bond strength in 2-methoxymethylphenol is −3.0 kcal/mol, which reproduces the "free"/intra-HB ratio of 1.5:98.5. Furthermore, the averaged $\Delta\nu_{calcd}$ for this compound was found to be 182 $cm^{-1}$, in very good agreement with the measured value of 205 $cm^{-1}$.



In conclusion, theory can beautifully complement experimental work on HB formation by ortho-substituted phenols by providing new insights into the formation, structure, and O−H stretching frequencies of the HBs. The level of theory employed in the present study of inter, intra, and bifurcated intra/intermolecular HBs does a truly exceptional job of quantitatively reproducing quite a variety of experimental observations. The calculations explain why certain changes in the O−H stretching region of the IR spectra of ortho-substituted phenols are observed, or not observed, upon addition of the strong HB acceptor, DMSO, and help us to understand the complex interplay of intramolecular, intermolecular, and bifurcated intra/intermolecular HBs. We are confident that appropriately high-level theory will become an integral part of all future experimental studies on HBs.

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**Supporting Information Available:** Parameters used for calculation of equilibrium constants for HB formation, values $K_{A}^{H_i}$, log $K_{A}^{H_i}$, and $\alpha_2^H$ for methoxyphenols calculated from IR measurements of HB complex formation with DMSO, kinetic data for reactions with dpph$^\bullet$, OH stretching spectra obtained in $CCl_4$, various plots of $[ArOH]_o/[ArOH]_{free}$ versus $[DMSO]_{free}$, OD stretching band of *O*-deuterio 2-methoxymethylphenol, examples of LDBS partitioning, and optimized Cartesian coordinates for various HB complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) The sharp IR band at ca. 3100 cm$^{-1}$ is due to a $C_3$−H stretching mode, see ref 20f.

(26) Intramolecular HB strengths were computed (ref 27), to a first approximation (ref 28), by taking the difference in enthalpy between the OH “toward the ortho substituent” H-bonded minimum enthalpy structure and the OH “away” minimum enthalpy structure following a 180° rotation of the OH group about the HO−C bond.

(27) By calculating the stabilization enthalpies for $2\text{-}XC_6H_4OH$ ($2,4\text{-}X_2C_6H_4OH$) + $C_6H_6 \rightarrow 2\text{-}XC_6H_5$ ($2,4\text{-}X_2C_6H_5$) + $C_6H_5OH$ at the B971/6-311++G(2d,2p) level of theory.

(28) This is only a first approximation of the intramolecular HB strength because it incorporates enthalpies associated with resonance and inductive interactions between the OH group and the other substituents on the ring.

(29) Chiorboli, P.; Mirone, P. *Ann. Chim. (Rome)* **1958**, *48*, 363–379.

(30) See, e.g.: (a) Brooks, C. J. W.; Morman, J. F. *J. Chem. Soc* **1961**, 3372–3381. (b) Berthelot, M.; Laurence, C.; Lucon, M.; Rossignol, C.; Taft, R. W. *J. Phys. Org. Chem.* **1996**, *9*, 626–630.

(31) There would appear to be no 2,6-diacylphenols commercially available, and no easy synthesis of any of them was discovered in the literature. It was not possible, therefore, to look for a bifurcated hydrogen bond with DMSO using such a phenol.

(32) For example, the $\beta_2^H$ value for nitrobenzene is 0.34, whereas the values for benzaldehyde and acetophenone are significantly greater, 0.42 and 0.51, respectively (ref 5).

(33) Takasuka, M.; Matsui, Y. *J. Chem. Soc., Perkin Trans 2* **1979**, 1743–1750.

(34) (a) Badger, R. M.; Bauer, S. H. *J. Chem. Phys.* **1937**, *5*, 839–851. See also: (b) Joesten, M. D.; Drago, R. S. *J. Am. Chem. Soc.* **1962**, *84*, 3817–3821. (c) Yoshida, Z.; Osawa, E. *J. Am. Chem. Soc.* **1966**, *88*, 4019–4026. (d) Drago, R. S.; Epley, T. D. *J. Am. Chem. Soc.* **1969**, *91*, 2883−2890 and references therein.

(35) Korth, H.-G.; de Heer, M. I.; Mulder, P. *J. Phys. Chem. A* **2002**, *106*, 8779–8789.

(36) (a) Detoni, S.; Hadzi, D.; Juranji, M. *Spectrochim. Acta* **1974**, *30A*, 249–253. (b) In this paper, the band maxima for 2-acetyl-, 2-formyl-, and 2-nitro-phenol were reported to be 3050, 3150, and 3240 cm$^{-1}$, respectively.

(37) The “ortho−para method” (ref 38) for estimating the enthalpy of this intramolecular HB from the difference in the calculated ground-state energies of 2-hydroxybenzaldehyde and 4-hydroxybenzaldehyde yielded values of 5.5 (CBS-QB3) and 5.6 (B3LYP/6-311+G(dp)) kcal/mol (ref 38b). As appears to be usual (ref 38), the ortho−para method gives lower (often much lower) intramolecular HB strengths than the “cis−trans method” we employed. There appears to be no compelling reason for choosing one method over the other. The ortho−para method yielded intramolecular HB strengths in 2-acetylphenol of 5.9 (CBS-QB3) and 6.3 (B3LYP/6-311+G(dp)) kcal/mol (ref 38b).

(38) (a) Estacio, S. G.; Cabral do Couto, P.; Costa Cobral, B. J.; Minas da Piedade, M. E.; Martinho Simoes, J. A. *J. Phys. Chem. A* **2004**, *108*, 10834–10843. (b) Bernardes, C. E. S.; Minas da Piedade, M. E. *J. Phys. Chem. A* **2008**, *112*, 10029–10039.

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(41) Dorrestijn, E.; Kranenburg, M.; Ciriano, M. V.; Mulder, P. *J. Org. Chem.* **1999**, *64*, 3012–3018.

(42) Mendenhall, G. D. Private communication.

(43) The ratio of the "free" phenol to the HB form was estimated (ref 39) to be 4:96, possibly from peak heights (our own peak height ratio is 5:95, Figure 9). However, this ratio *overestimates* the amount of the "free" phenol because HB bands are broader and generally of lower height than an equal quantity of a "free" phenol. A better measure of "free" phenol is given by the ratio of the integrated areas of the two bands, viz., 1.9:98.1. However, this ratio will *underestimate* the amount of "free" phenol because the integrated areas of the O−H stretching bands of phenols are greater when the phenol forms a HB than when it is "free".

(44) See, for example: Amorati, R.; Catarzi, F.; Menichetti, S.; Pedulli, G. F.; Viglianisi, C. *J. Am. Chem. Soc.* **2008**, *130*, 237–244.

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(46) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195.

(47) The "free"/intra-HB ratio for 2-methoxymethylphenol at 298 K is 2.1:97.9 in $CCl_4$ (see text) from which an equilibrium constant of ~0.026 $M^{-1}$ can be derived for formation of an intermolecular HB between 2-methoxymethylphenol and $CCl_4$. A very similar equilibrium constant should apply to phenol (see text), indicating that for phenol in neat $CCl_4$ about 20% of the hydroxyl groups will be hydrogen-bonded to a solvent molecule. This phenomenon is not distinguishable by IR, but it is in excellent agreement with earlier kinetic measurements (ref 3).

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