BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3259—3262 (1969)

Intermolecular Hydrogen Bond Involving a π Base as the Proton Acceptor. VII. Substituents and Steric Effects in the Hydrogen Bonding of 2,6-Xylenols to Mesitylene

Zen-ichi YOSHIDA, and Nobuyuki ISHIBE[*1]

Department of Synthetic Chemistry, Kyoto University, Yoshida, Sakyo-ku, Kyoto

(Received April 30, 1969)

Hydrogen bonding of 4-substituted-2,6-xylenols to mesitylene has been investigated by measurement of the hydroxyl stretching vibration. A linear relationship between the electronic effects of *para* substituents (Hammett σ_p constant) and the frequency shifts of the hydroxyl stretching vibration was obtained. A similar correlation was also observed with the free energy change associated with the formation of the hydrogen-bonded complex. The thermodynamic sutdies on the hydrogen bonding of 2,6-xylenol and phenol with both mesitylene and acetonitrile demonstrated the steric effect of 2- and 6-methyl groups on hydrogen bond formation. The free energy change for hydrogen bond formation with 2,6-xylenols as the proton donor was lower than with phenol. This is explained in terms of both entropy and enthalpy factors.

Many workers have investigated the substituent effects of proton donors such as phenols on the intramolecular hydrogen bond[1] and reported that usually there was a correlation between the electronic effects of substituents and the frequency shifts of hydroxyl stretching vibration due to hydrogen bond formation. Recent studies of the substitutent effects on the intermolecular hydrogen bond[2] show that the proton donors having typical substituents auch as nitro, acetyl, or alkoxyl groups are subject to self association.[3] This phenomenon is explained in terms of the proton accepting ability of these substituentents. In order to resolve this experimental difficulty, the sterically hindered phenols were used as the proton donor[2] because they are less associated than the simple hydroxyl compounds.[4-6]

Singh and Rao[2a] reported that in the hydrogen bonding of *para* substutited-2,6-di-*t*-butylphenols with tetrahydrofuran neither the equilibrium constantsnor the values of frequency shifts show a linear relationship with the Hammett σ_p constants. Both values of pK_a[7] and OH stretching vibration[8,9] in the infrared are, however, correlated with σ_p. The substituent effects of the proton donor on weak hydrogen bonding involving benzenes as a π base have not been investigated. We report the effect in the system of the 4-substituted-2,6-xylenols and mesitylene by measurement of the stretching frequencies of the OH group. In order to reveal whether the decrease of the equilibrium constant is due to the steric effect of 2- and 6-methyl groups on the enthalpy change and/or on the entropy change, the thermodynamic measurements of hydrogen bonding of phenol and 2,6-xylenol with both mesitylene and acetonitrile were carried out. These experiments are important because there is some discrepancy in the explanation of the smaller frequency shifts and free energy changes in hydrogen bonding of the hindered phenols to various proton acceptors involving a lone pair electron.[2a,5]

[*1] Present address: Department of Chemistry, University of Illinois at Chicago Circle, Chicago, Illinois 60680, U.S.A.

1) L. L. Ingraham, J. Corse, G. F. Bailey and F. Stiff, *J. Am. Chem. Soc.*, **74**, 2297 (1952); M. Ōki and H. Iwamura, This Bulletin, **32**, 955 (1959); *ibid.*, **34**, 1395 (1961); C. K. Hancock and A. D. H. Clague, *J. Am. Chem. Soc.*, **86**, 4942 (1964); Z. Yoshida and M. Haruta, *Tetrahedron Letters*, **1964**, 263; *ibid.*, **1965**, 3745.

2) a) S. Singh and C. N. R. Rao, *J. Am. Chem. Soc.*, **88**, 2142 (1966). b) S. Singh, A. S. M. Murth and C. N. R. Rao, *Trans. Faraday Soc.*, **62**, 1056 (1966).

3) P. J. Stone and H. W. Thompson, *Spectrochim. Acta*, **10**, 17 (1957).

4) a) B. G. Somers and H. S. Gutowsky, *J. Am. Chem. Soc.*, **85**, 3065 (1963). b) I. Yamaguchi, This Bulletin, **34**, 744 (1961).

5) F. Takahashi and N. C. Li, *J. Phys. Chem.*, **69**, 1622 (1965).

6) a) W. Heinen, *Rec. Trav. Chim.*, **82**, 859 (1963). b) L. J. Bellamy, G. Eglinton and J. F. Morman, *J. Chem. Soc.*, **1961**, 4762; L. J. Bellamy and R. L. Williams, *Proc. Roy. Soc. (London)*, A**254**, 119 (1960).

7) L. A. Cohen and W. M. Jones, *J. Am. Chem. Soc.*, **85**, 3402 (1963).

8) K. U. Ingold, *Can. J. Chem.*, **38**, 1092 (1960).

9) Z. Yoshida, N. Ishibe and K. Shobatake, *Kogyo Kagaku Zasshi (J. Chem. Soc. Japan, Ind. Chem. Sect.)*, **68**, 808 (1965).

Experimental

Materials. Carbon tetrachloride as a solvent, mesitylene and acetonitrile as the proton acceptors, and phenol as a proton donor were purified by known methods.[10] 4-Substituted-2,6-xylenols were prepared by known methods.[9] The details of the preparative method were reported previously.[9]

Determination and Analysis of Spectra. All spectra of the hydroxyl stretching vibration, ν_{OH}, were obtained with a double pass grating infrared spectrophotometer JASCO DS-402G. The scanning conditions for determination of the spectra were the same as in the previous report.[11] Two liquid cells of 2 and 10 mm thickness (window material: NaCl), were used. Concentration ranged from 0.001 to 0.04 mol/l for the proton donors and from 1.5 to 4 mol/l for mesitylene. The cells were placed in a thermostated air-bath[12] to adjust the sample to an appropriate temperature. Analysis of the spectra and calculation of the equilibrium constants have been described previously.[13]

When thermodynamic values were estimated from a linear plot of log K *vs.* $1/T$, concentrations of free phenol and 2,6-xylenol were corrected. This was necessary because the integrated absorption intensities of phenol[14] and 2,6-xylenol in the absence of base depend not only on their concentration but also on temperature. In the range of -10 to 50° C the integrated molar absorption intensities of phenol[14] and 2,6-xylenol (A_p and A_x, l/mol cm) (whose band shape are assumed to be represented by Lorentzian function) correlate with the sample temperature (T) as follows:

$$A_p = 18200 - 26.50 \times T$$

$$A_x = 13700 - 18.09 \times T$$

Results

The OH stretching frequency of 4-substituted-2,6-xylenols (ν^f), the frequency shifts ($\Delta\nu$), the relative frequency shifts ($\Delta\nu/\nu^f$), and the free energy changes for hydrogen bonding between 4-substituted-2,6-xylenols and mesitylene are summarized in Table 1. The thermodynamic values of hydrogen bonding of phenol and 2,6-xylenol to both mesitylene and acetonitrile are given in Table 2. The values of frequency shifts in the hydrogen bond involving mesitylene remain constant with the change of concentration of π base and the temperature. In the case of acetonitrile, however, they depend not only on the concentration of acetonitrile[15] but also on the temperature. The frequency shifts decrease with increase of temperature.[14] This behavior could be explained as a specific solvent effect (dipole-dipole interaction).[16]

TABLE 1. FREQUENCY SHIFTS AND FREE ENERGY CHANGES FOR THE HYDROGEN BOND BETWEEN 4-SUBSTITUTED-2,6-XYLENOLS AND MESITYLENE

Substituent	$\nu^{f\,a)}$ (cm^{-1})	$\Delta\nu^{b)}$ (cm^{-1})	$\Delta\nu/\nu^f$ ($\times 10^3$)	$-\Delta F^{c)}$ (kcal/mol)	$\sigma^{d)}$
t-C_4H_9	3623.3	42.6	11.7_5	-1.04	-0.197
CH_3	3623.6	42.8	11.8_1	-0.99	-0.170
C_2H_5	3623.4	43.1	11.8_9	-0.94	-0.151
i-C_3H_7	3624.3	42.9	11.8_3	-0.95	-0.151
Cyclo-C_6H_{11}	3623.2	42.8	11.8_1	-0.94	—
H	3622.5	44.0	12.1_4	-0.92	0
Cl	3620.1	47.0	12.9_7	-0.80	0.227
Br	3619.9	47.3	13.0_7	-0.74	0.232
I	3617.9	47.9	13.2_3	-0.72	0.276
CH_3CO	3611.9	50.8	14.0_6	-0.54	0.87
NO_2	3606.5	53.4	14.8_0	-0.41	1.27

a) ν_{OH} in dilute solution of carbon tetrachloride.
b) The maximum error is within ±0.5 cm^{-1}.
c) The maximum error is within ±0.07 kcal/mol.
d) See Ref. 23.

Discussion

Steric Effects on Hydrogen Bonding. A linear relationship was obtained in a plot of pK_a values of unhindered phenols (alkylphenols and naphthols) *vs.* the free energy changes for hydrogen bond of these phenols to mesitylene.[17] If this correlation also holds in the hydrogen-bonded system involving 2,6-xylenol as the proton donor, the value for $-\Delta F$ is expected to be -0.60 kcal/mol when the pK_a of 2,6-xylenol is 10.58.[18] This value is much larger than the observed one of -0.94 kcal/mol. Introduction of alkyl groups to the 2 and 6 positions of phenol causes a decrease of the equilibrium constant in the hydrogen bond with a lone pair electron in amides,[5] ethers,[2a,4a] ketones,[2a,6a] nitro compounds,[2a] and other compounds.[2a] A similar decrease ($-\Delta F$) was also found in the hydrogen bond interaction with the delocalized π electrons of mesitylene. Introduction of the methyl groups (into phenol) causes a decrease of $-\Delta F$ value, which is larger in the hydrogen bond with acetone and acetonitrile than with mesitylene. The differences in $-\Delta F$ are about 0.8 kcal/mol with mesitylene (Table 2). Table 2 shows that the hydro-

---

[10] A. Weissberger, "Technique of Organic Chemistry," Vol. 7, Organic Solvent, Interscience Publ., New York (1955).

[11] Z. Yoshida and E. Ōsawa, *J. Am. Chem. Soc.*, **88**, 4019 (1966).

[12] Z. Yoshida and N. Ishibe, unpublished result.

[13] Z. Yoshida and E. Ōsawa, *J. Am. Chem. Soc.*, **87**, 1467 (1965).

[14] Z. Yoshida adn N. Ishibe, *Spectrochim. Acta*, **24A**, 893 (1968).

[15] S. S. Mitra, *J. Chem. Phys.*, **36**, 3286 (1962).

[16] E. Ōsawa and Z. Yoshida *Spectrochim. Acta*, **23A**, 2029 (1967).

[17] Z. Yoshida and N. Ishibe, unpublished result.

[18] G. W. Wheland, R. M. Brownell and E. C. Mays, *J. Am. Chem. Soc.*, **70**, 2492 (1948).

TABLE 2. FREQUENCY SHIFTS AND THERMODYNAMIC VALUES OF HYDROGEN BOND FORMATION

Proton Donors	Proton Acceptor	$\Delta\nu$ (cm^{-1})	$-\Delta H$ (kcal/mol)	$-\Delta F^\circ$ (kcal/mol)	$-\Delta S^\circ$ (e.u.)
Phenol	Mesitylene	73	1.92 ± 0.16	-0.38	7.8
	Acetonitrile	154[a]	4.74 ± 0.08	1.12	12.2
	Acetone[b]			1.47	
2,6-Xylenol	Mesitylene	44	1.26 ± 0.20	-0.92	7.3
	Acetonitrile	112[a]	2.88 ± 0.10	0.33	8.6
	Acetone[b]			0.66	
p-Cresol	Mesitylene	74.8		-0.39	
	Acetone[b]			1.35	
2,4,6-Trimethylphenol	Mesitylene	42.8		-0.99	
	Acetone[b]			0.53	

a) These values are measured at 25°C.

b) Ref. 6a. These values were obtained at 23°C.

gen bond energy and the frequency shift are much smaller in hydrogen bond of acetonitrile with 2,6-xylenol than with phenol, but the entropy change (ΔS°) increases with introduction of methyl substituents into phenol. Mesitylene behaves in a similar way, although the entropy changes for these proton donors are nearly equal.

Our results are consistent with those of Takahashi and Li[5] who studied hydrogen bonding in amides. However, our results are not consistent with those of Singh and Rao[2a] who reported that the enthalpies of hydrogen bonding are nearly equal for both phenols and hindered phenols. The thermodynamic values reported here should be more accurate than those of Singh and Rao,[2a] because the dependence of the intensity of ν_{OH} of the free phenol on the sample temperature was considered in the calculation of the equilibrium constant. These authors[2a] stated that the increase in barrier height in the double minimum potential with increasing bulkiness of the substituent could be used to explain both the invariance of the enthalpies and the decrease of the frequency shifts in the hydrogen-bonded system involving the hindered phenols. They assumed there is little or no variation of the distance, $R_{\mathrm{x}\cdots\mathrm{y}}$, in the hydrogen bond $\mathrm{X{-}H\cdots Y}$. A more reasonable explanation is that $R_{\mathrm{x}\cdots\mathrm{y}}$ increases with the bulkiness of the alkyl substituents of the proton donors; therefore, the enthalpies decrease with introduction of the methyl substituents to 2 and 6 positions of phenol. As expected from this consideration, the frequency shift of the hydrogen bond between 2,6-xylenol and mesitylene is less than the values calculated from the $\Delta\nu-\mathrm{p}K_a$ relationship,[17] where the steric effects were not detected. This decrease is, therefore, explained by the larger distance $R_{\mathrm{x}\cdots\mathrm{y}}$ and the higher OH stretching frequency of 2,6-xylenol.[9] Qualitatively this could be supported by the correlation between the frequency shift and the $\mathrm{X\cdots Y}$ bond distance in the hydrogen-bonded solid.[19] The values of entropy changes support these considerations; the steric effect of the methyl substituent causes an increase of $R_{\mathrm{x}\cdots\mathrm{y}}$ in the hydrogen-bonded complex so that to some extent the rotational and vibrational movement of the complex is less restricted. The same trend apparently occurs in the complex involving acetonitrile as the proton acceptor. For mesitylene the entropy change in both phenol and 2,6-xylenol are nearly equal. $R_{\mathrm{x}\cdots\mathrm{y}}$ in the hydrogen-bonding of phenol with acetonitrile may be shorter than in the case of phenol with mesitylene. When the methyl groups are introduced into phenol, there seemingly occurs a greater increase of $R_{\mathrm{x}\cdots\mathrm{y}}$ with acetonitrile than with mesitylene, resulting in the differences in entropy changes mentioned above. It should be noted that the entropy anomaly observed in the hydrogen bonding of phenol with aromatic hydrocarbons[13] was obtained in the hydrogen-bonded system involving the hindered phenols.

From these considerations, steric effects on hydrogen bonding could influence not only the enthalpy but also the entropy changes associated with the formation of the hydrogen-bonded complex. Although a large steric effect was not observed in hydrogen bonding of phenol with di-*t*-butyl ether and di-*t*-butyl sulfide,[20] it is interesting that introduction of bulky groups into the proton donor causes a steric effect.

Substituent effects on hydrogen bonding: From Table 1 it is clear that both the frequency shifts and the free energy changes increase with enhance-

---

[19] G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco and London (1960), p. 85; W. C. Hamiton and J. A. Iber, "Hydrogen Bonding in Solids," W. A. Benjamin, New York (1968), p. 85.

[20] R. West, D. L. Powell, M. K. T. Lee and L. S. Whatley, *J. Am. Chem. Soc.*, **86**, 3227 (1964).

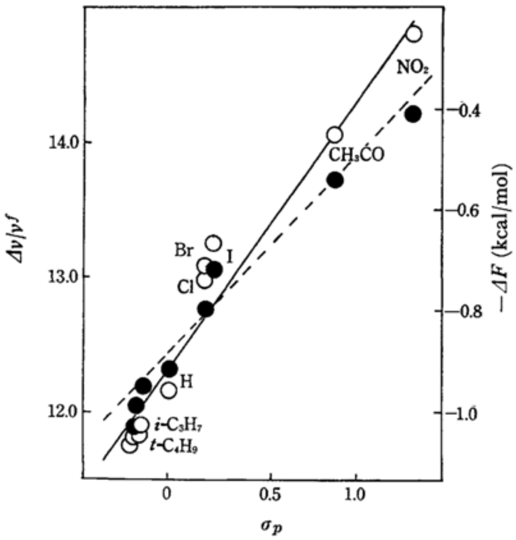

Fig. 1. $\Delta\nu/\nu^f$ and $-\Delta F$ *vs.* Hammett σ_p plots in hydrogen bonding of 2,6-xylenol with mesitylene. (—○— $\Delta\nu/\nu^f$ *vs.* σ_p, ---●--- $-\Delta F$ *vs.* σ_p)

ment of the proton donating ability of the 4-substituents in 2,6-xylenols. A similar trend was also observed in some other hydrogen bonded systems, *e.g.* alkyl phenols-aromatic hydrocarbons,[17] alcohols-diethyl amine or -ethyl ether.[21] As shown in Fig. 1, both the relative frequency shift, $\Delta\nu/\nu^f$,[22] and the free energy change vary linearly with the Hammett σ_p constants.[23] In these plots the best linear relationship was obtained when σ_p[23] was used for the substituent constants of nitro and acetyl groups. This suggests the coplanarity of the OH group of 2,6-xylenols with the benzene ring in the hydrogen-bonded complexes, as well as in free 2,6-xylenols.[9] In the hydrogen bond between *para* substituted-2,6-di-*t*-butylphenols and tetrahydrofuran, however, neither the equilibrium constants nor the frequency shifts vary linearly with the Hammett σ constants.[2a] This discrepancy cannot be explained adequately, but in the latter system, steric interaction of the *t*-butyl groups with the hydrogen atom of tetrahydrofuran causes bending of the OH group out of the plane of the benzene ring.

The slope of $\Delta\nu/\nu$ *vs.* pK_a for the hydrogen bonding of 2,6-xylenols with mesitylene is smaller than that of phenols with mesitylene.[17] The slope of $\Delta\nu/\nu$ *vs.* Hammett σ constant for the hydrogen bonding of 2,6-xylenols with mesitylene is larger than that of the intramolecular hydrogen bonding of 2-hydroxylbiphenyl derivatives.[24] The OH stretching frequencies of 4-substituted-2,6-xylenols are higher than those of the corresponding phenols,[17] so that the transmission of electronic effects of *para* substituents to the reaction center becomes more difficult in the hydrogen-bonded complexes with 4-substituted-2,6-xylenols than those with phenols. In the intramolecular hydrogen bonding of 4 (or 5)-substituted-2-hydroxylbiphenyls, the electronic effects of the substituent transmit the the reaction center not only through the benzene ring involving the OH group but also through the other ring because of conjugation between the two aromatic nuclei. The substituent effects on the OH group, therefore, cancel each other, thereby reducing the slope in the relationship $\Delta\nu/\nu^f$ *vs.* Hammett σ constants.

It is concluded that investigation of the hydrogen bond involving the hindered phenols might present interesting information about the transition states involving the hydrogen bond.

---

[21] G. Barrow, *J. Phys. Chem.*, **59**, 1129 (1954); J. Hine and M. Hine, *J. Am. Chem. Soc.*, **74**, 5266 (1952).

[22] L. J. Bellamy and R. L. Williams, *Trans. Faraday Soc.*, **55**, 14 (1959).

[23] R. W. Taft, Jr., "Steric Effects in Organic Chemistry," ed. by M. S. Newman, Chapter 13, John Wiley & Sons, New York (1956); H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

[24] M. Ōki and H. Iwamura, This Bulletin, **32**, 955 (1959).