

SUBSTITUENT EFFECTS ON CHEMICAL SHIFT OF HYDROXYL GROUP IN 2-HYDROXYBENZOPHENONE DERIVATIVES

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NMR and ultraviolet absorption spectra of sixteen 4- and 5-substituted derivatives of 2-hydroxybenzophenone were measured in carbon tetrachloride and deuteriochloroform. The effect of substituents on chemical shift of hydroxyl group was sufficiently expressed by two-parameter correlation with σ^- and σ constants. It was found that there exists a good correlation between the chemical shift of hydroxyl group and the position of ultraviolet long-wavelength absorption band maximum. Solvent effects on both the correlations are discussed.

The evidence for intramolecular hydrogen bond in 2-hydroxybenzophenone was based on the shifts of $\nu(\text{C}=\text{O})$ (ref.¹) and $\nu(\text{OH})$ (ref.²) in infrared spectra and on chemical shifts of hydroxyl group^{2,3} in NMR spectra. Merrill² compared both the methods on some of the derivatives of 2-hydroxy- and 2,2'-dihydroxybenzophenone and referred to the advantages of the nuclear magnetic resonance.

Recently, Bekárek and collaborators⁴ examined the effect of substituents on the chemical shift of hydroxyl group bonded by intramolecular hydrogen bond in various derivatives of *o*-nitrophenole, salicylaldehyde and *o*-hydroxyazobenzene. The authors observed that in polar solvents the chemical shift may be correlated with σ^- -substituent constants by simple one-parameter equation, whereas in non-polar solvents a two-parameter correlation with σ^- and σ constants should be employed.

A two-parameter correlation has been used in the evaluation of indirect effects of substituents transmitted through intramolecular hydrogen bond upon dissociation constants of salicylic acid derivatives by Dunn and Fei-lin Kung⁵ and of 2-hydroxybenzophenone derivatives by Hrdlovič and collaborators⁶. In these cases the two parameter correlation was found to be equivalent to simple Hammett-like one-parameter correlation, which was attributed^{5,6} to a weakening of intramolecular hydrogen bond in polar aqueous alcoholic medium. On the other hand, half-neutralization potential of salicylic acid derivatives in benzene has been found⁷ to be appreciably influenced by indirect effect of substituents *via* intramolecular hydrogen bond.

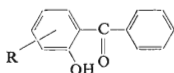
In the present work we examined the effect of substituents on chemical shift of hydroxyl group of a series of 4- and 5-substituted 2-hydroxybenzophenone derivatives, using a two-parameter equation. Since UV long-wavelength absorption band

is indicative of the existence of intramolecular hydrogen bond^{8,9} we made an attempt to correlate the absorption spectra of these derivatives with their NMR spectra.

EXPERIMENTAL

The preparation of 2-hydroxybenzophenone derivatives was described elsewhere⁶. The NMR spectra of compounds studied were recorded on a Tesla BS 487 (80 MHz) Spectrometer (Tesla, Brno). The instrument was calibrated with the aid of a RC Generator, Model BM 269 (Tesla, Brno). The samples of total weight of 0.7 g containing 40–50 mg of studied compound were used in the measurements. The solvents used, tetrachloromethane and deuteriochloroform, were of analytical purity. Hexamethyldisiloxane was used as the internal standard ($\tau = 9.95$ with respect to tetramethylsilane). The chemical shifts of hydroxyl group shown in Table I were not

TABLE I
Spectral Properties of 2-Hydroxybenzophenone Derivatives



Compound	R	λ_{\max}^a nm	ϵ $\text{l mol}^{-1} \text{cm}^{-1}$	τ_{OH}^a	σ_p^- (lit. ⁶)	σ_m^- (lit. ⁶)
1	H	338.7	4 860	-1.85	0.00	0.00
					σ_p^-	σ_m^-
2	5-NO ₂	305.2 ^b	12 570	-2.62 ^c	1.24	0.71
3	5-COCH ₃	335.2	4 760	-2.32	0.84	0.31
4	5-COC ₆ H ₅	331.5 ^b	4 860	-2.45 ^c	0.80	0.34
5	5-Cl	351.9	4 860	-1.80	0.23	0.37
6	5-CH ₃	352.0	5 280	-1.68	-0.15	-0.07
7	5-OCH ₃	376.5	7 810	-1.35	-0.26	0.12
8	5-CH(CH ₃) ₂	350.6	6 700	-1.63	-0.15 ^d	-0.07 ^d
					σ_m^-	σ_p^-
9	4-NO ₂	362.6 ^b	4 760	-1.73 ^c	0.69	0.78
10	4-Cl	331.3	6 140	-2.16	0.37	0.23
11	4-CH ₃	337.1	6 810	-1.95	-0.08	-0.17
12	4-OCH ₃	328.7	10 550	-2.61	0.12	-0.26
13	4-OCOCH ₃	331.3	6 260	-2.11	0.38	0.32
14	4-OCOC ₆ H ₅	331.3	6 920	-2.26	0.33	0.27
15	4-O(CH ₂) ₇ CH ₃	328.4	10 350	-2.30	0.12 ^d	-0.26 ^d
16	4-OCH ₂ CH(C ₂ H ₅)C ₄ H ₉	326.4	10 560	-2.35	0.12 ^d	-0.26 ^d

^a Measured in tetrachloromethane. ^b Measured in chloroform. ^c Measured in deuteriochloroform.

^d Estimated value based on the values for similar substituents.

corrected to this difference. The accuracy of the measurement was ± 0.02 p.p.m.. The spectra were measured at 25°C. The absorption spectra of solutions of studied compounds in carbon tetrachloride and chloroform were measured with an Unicam Spectrophotometer, Model SP 700 A. The solvents used were of spectral purity. The position and extinction of long-wavelength absorption band, together with σ^- and σ constants used are given in Table I.

RESULTS AND DISCUSSION

We have found that both strong electron-acceptor substituents in position 5 and strong electron-donor groups in position 4 affect the chemical shift of the hydroxyl group of 2-hydroxybenzophenone derivatives in the same way. This characteristic feature of the effect of substituents can be expressed by the two-parameter equation (1)

$$\tau_{\text{OH}} = a + b\sigma^- + c\sigma \quad (1)$$

The $b\sigma^-$ term is the measure of the direct effect of substituents on the chemical shift of hydroxyl group. The σ^- constants used were derived from the dissociation constants of substituted phenols. The term $c\sigma$ is the measure of the indirect effect of substituents on the chemical shift, which is caused by the change in electron density on the oxygen of the carbonyl group and transmitted *via* hydrogen bond. The constants which relate to the carbonyl group are the ones usually derived from the dissociation constants of substituted benzoic acid.

The treatment of the data by a least square method yielded¹⁰ the following correlation (Fig. 1)

$$\tau_{\text{OH}} = -1.887 - 1.273\sigma^- + 1.228\sigma; \quad s' = \pm 0.15, \quad (2)$$

where the deviation s' is defined as $s' = \pm [\sum \Delta\tau^2 / (n - 3)]^{1/2}$ and $\Delta\tau = \tau_{\text{exp}} - \tau_{\text{calc}}$. The effect of substituents on the chemical shift of 2-hydroxybenzophenone derivatives proves to be in quite a marked contrast with regard to that on the dissociation constants which could be expressed by one-parameter correlation. The introduction of the second parameter did not result in an essential improvement of this correlation⁶. This shows that in the latter case substituents affect mainly the O—H bond, and do not exert an appreciable indirect effect *via* hydrogen bond.

In the case of 2,6-ditert-butylphenol derivatives a good correlation has been found between chemical shifts and dissociation constants¹¹. The chemical shifts of substituted phenols in dimethyl sulfoxide correlate well with σ^- constants of substituents¹².

The different effect of substituents on chemical shift and on dissociation constants may be attributed to weakening or extinction of intramolecular hydrogen bond in polar aqueous alcoholic medium. This conclusion is also supported by the results of the study¹³ on the effect of substituents on the chemical shift of *o*-nitroaniline in a polar and non-polar medium.

On the other hand, the difference in dissociation constants of 2-hydroxy- and 4-hydroxybenzophenone may be regarded as indicating the preservation of an intramolecular hydrogen bond¹⁴ even in polar aqueous-alcoholic medium. The effect of substituents on the dissociation of the hydroxyl group is not, however, significantly transferred through this hydrogen bond.

The value of the chemical shift of hydroxyl group may be taken as the relative measure of intramolecular hydrogen bond strength. The long-wavelength absorption band in the spectra of 2-hydroxybenzophenone derivatives is influenced by the presence of intramolecular hydrogen bond in their molecule^{8,9}.

This can be qualitatively proved on the basis of the linear correlation of the chemical shift of the hydroxyl group with the position of the absorption band maxima (Fig. 2). The correlation calculated by the least square method takes the form

$$\tau_{\text{OH}} = 4.825 - 0.233\nu_{\text{max}} \cdot 10^{-3}; \quad r = 0.90, \quad s = \pm 0.14, \quad s' = \pm 0.16. \quad (3)$$

The correlation coefficient r and the standard deviation s were calculated according to Jaffé¹⁵. The s' deviation is defined by the relation $s' = \pm [\sum \Delta\tau^2 / (n - 2)]^{1/2}$ and $\Delta\tau = \tau_{\text{exp}} - \tau_{\text{calc}}$. From the linear correlation (3) between chemical shift of the hydroxyl group and the position of the long-wavelength absorption band maxima of 2-hydroxybenzophenone derivatives it is obvious that increase in the strength of intramolecular hydrogen bond results in hypsochromic shift of the position of the absorption band. The analogical shift has been observed also for the $n - \pi^*$ band

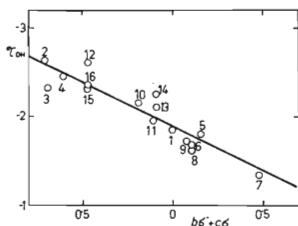


FIG. 1

Dependence of τ_{OH} of 2-Hydroxybenzophenone Derivatives on Their Structure (Eq. (1))

For numbering of compounds see Table I.

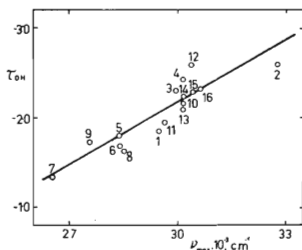


FIG. 2

The Plot of the Long-Wavelength Absorption Maximum, ν_{max} , vs. the Chemical Shift of the Hydroxyl Group, τ_{OH} , for 2-Hydroxybenzophenone Derivatives

For numbering of compounds see Table I.

of benzophenone on increasing polarity and ability of a solvent to form an intermolecular hydrogen bond⁸. Although the character of transitions corresponding to long-wavelength absorption bands of 2-hydroxybenzophenone and of benzophenone is not the same^{8,9}, the effect of specific interaction of the carbonyl group with the hydroxyl group, which leads in the former case to the formation of intramolecular hydrogen bond and in the latter to the formation of the intermolecular one, is essentially the same. Such specific interactions have been called¹⁶ "internal solvent effect" (in the case of 2-hydroxybenzophenone) or "external solvent effect" (in the case of benzophenone). The position of longwavelength absorption band of 2-hydroxybenzophenone⁸ and its derivatives⁹ is little influenced by external solvent effect, though the formation of this band is connected with charge transfer^{8,9} (CT-band) and such bands are usually sensitive to external solvent effects¹⁶. It means that the presence of intramolecular hydrogen bond reduces the sensibility of the band to external solvent effect.

The above findings show that in the case of 2-hydroxybenzophenone derivatives the effect of substituents is transferred only *via* strong intramolecular hydrogen bond, which exists only in non-polar solvents. In polar solvents this bond is weakened and thus no more capable of transferring substituent effects. The long-wavelength absorption band in the spectra of 2-hydroxybenzophenone derivatives originates from the interaction between the carbonyl and the hydroxyl group in the plane of the aromatic ring^{8,9}. Polar solvents weaken intramolecular hydrogen bond but do not affect the interaction of these groups *via* the aromatic ring. As a result small external solvent effect has been observed.

Substituents in position 6 of 2-hydroxybenzophenone derivatives affect by their steric effects both the interaction between the carbonyl and the hydroxyl group *via* the aromatic nucleus and the interaction leading to the formation of intramolecular hydrogen bond. One can thus expect that in such a case external solvent effect will be more pronounced. The solvent and substituent effects on the chemical shift and other spectral properties of 2-hydroxy-6-methylbenzophenone derivatives will be the subject of a subsequent paper¹⁷.

The conclusions on solvent effects upon the strength of intramolecular hydrogen bond are only of qualitative character. The absolute value of intramolecular hydrogen bond energy in individual solvents cannot be estimated on the basis of the spectral measurements described in this paper.

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