THE DISSOCIATION CONSTANTS
AND SPECTRAL PROPERTIES
OF 2-HYDROXY-6-METHYLBENZOPHENONE DERIVATIVES

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The dissociation constants and chemical shifts of hydroxyl group of seven 3-, 4- and 5-substituted 2-hydroxy-6-methyl-benzophenones were measured. The effect of basic solvents on the ultraviolet and infrared spectra of these compounds has been studied. The equilibrium constants of the extinction of intramolecular hydrogen bond were determined on the basis of changes in the ultraviolet spectra of studied compounds caused by addition of pyridine. The linear correlation of the dissociation with the equilibrium constants has been found. Comparison of the corresponding quantities for 2-hydroxy-4,6-dimethylbenzophenone and 2-hydroxy-4-methylbenzophenone revealed that the introduction of methyl group into position 6 brings about a weakening of intramolecular hydrogen bond. The effect of solvents on the absorption spectra has been explained in terms of the extinction of intramolecular hydrogen bond.

Physico-chemical properties of 2-hydroxybenzophenone derivatives have attracted much attention. Their characteristic properties such as high absorption in near ultraviolet region[1−3], high photochemical stability[4] and efficiency as light stabilizers[5] have been attributed to the presence of an intramolecular hydrogen bond in their molecule. Shulgin and Kerlinger[6] observed very weak intramolecular hydrogen bond in 2-hydroxy-4,6-ditert-butylbenzophenone. On the other hand, O'Connell[7] found that photochemical stability of this compounds in various solvents is comparable with that of 2-hydroxybenzophenone.

In this paper we report on some physico-chemical quantities, and spectral properties of a series of 3-, 4- and 5-substituted 2-hydroxy-6-methylbenzophenones. As another aim of this study was to evaluate changes in intramolecular hydrogen bond caused by introduction of a substituent to position 6, the results obtained were confronted with those reported by us for 2-hydroxybenzophenone derivatives[3].

EXPERIMENTAL

The preparation of 2-hydroxy-6-methylbenzophenones studied is described elsewhere[8]. The melting points are given in Table II. The ultraviolet absorption spectra were taken on an Unicam

SP 700 A Spectrophotometer. The precise measurements of absorbance were carried out on an one-beam non-registrationing Zeiss VSU-1 Spectrophotometer (Zeiss, Jena). The NMR spectra were measured with Tesla BS 487 (80 MHz) Spectrometer (Tesla, Brno), using samples of total weight of 0·7 g containing 40—50 mg of a studied compound. Deuteriochloroform was used as the solvent and hexamethyldisiloxane as the internal standard. The infrared spectra were taken on an Unicam SP 200 Spectrophotometer using 0·1 mm cells. Chloroform and a mixture of pyridine

TABLE I

Physico-Chemical Constants of 2-Hydroxy-4-methylbenzophenone (*I*) and 2-Hydroxy-4,6-di-methylbenzophenone (*II*)

Quantity	Compound *I*	Compound *II*
pK'	10·56 ref. 11 [a]	10·08
τ_{OH}	−1·93 ref. 3	0·77
$\nu_{(C=O)}$, cm^{-1}	1 638 (1 640)[b]	1 635 (1 670)[b]
$\varepsilon(\lambda_{340}$, nm)	5 500 (5 750)[c]	3 450 (940)[c]
K, 1 mol^{-1}	—	1·70

[a] Measured in 50 v. % ethanol. [b] Measured in 50 v. % pyridine in chloroform. [c] Measured in 25 v. % pyridine in chloroform.

TABLE II

The Dissociation and Equilibrium Constants and the Chemical Shifts of Hydroxyl Group of 2-Hydroxy-6-methylbenzophenone Derivatives
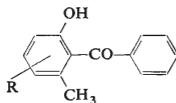
Compound	R	M.p. °C	pK'	K 1 mol^{-1}	τ_{OH} p.p.m.
1	4-CH$_3$	140	10·08	1·70	0·75
2	3-CH(CH$_3$)$_2$	104	10·43	0·63	0·89
3	3-C(CH$_3$)$_3$	125—126	10·65	0·17	0·49
4	3-C$_5$H$_{11}$	74	10·93	0·16	0·57
5	3-CH(CH$_3$)$_2$; 5-Br	74	9·61	0·94	1·62
6	3-C(CH$_3$)$_3$; 5-CH$_3$	89—90	10·47	0·28	1·28
7	3-C$_5$H$_{11}$; 5-CH$_3$	85	10·82	0·10	1·43

and chloroform, were employed as the solvents. The pH measurements were carried out on a pH-Meter 4 (Radiometer, Copenhagen) equipped with a glass electrode (Type G 200 B) and a saturated calomel electrode (Type K 100). The glass electrode was standardized with $0.05M$-$Na_2B_4O_7$ to pH 9·18 at 25°C.

Dissociation constants were determined spectrophotometrically from the absorption spectra of the compounds in $0.1M$-HCl and $0.1M$-NaOH in 40 v. % methanol, following changes in absorbance at the wavelength at which the difference between absorbances of the ionized and nonionized form is maximal. Borate buffer containing 40 v. % of methanol was used in this measurement as a medium for this determination. The concentration of a compound studied was 10^{-4} mol/l and absorbance and pH were measured at 25 ± 0.1°C. The pK's were calculated from relation (*1*) (ref.[9])

$$pK = pH - \log(A_{HA} - A)/(A - A_{A^-}) - \log \gamma \,, \qquad (1)$$

where $pK = -\log K$, A_{HA} and A_{A^-} is the absorbance of nonionized and ionized form, A is the absorbance at a given pH, and γ is the ionic strength, the effect of which we did not taken into account in the calculations. For this reason we denote the pK constants obtained as pK'. The dissociation constants were determined as an average of five measurements, the measuring accuracy being ± 0.05 pK'.

Equilibrium constants were determined from changes in absorbance of long-wavelength absorption band in mixtures of chlorofom–pyridine solutions. The concentration of pyridine varied within $0.1 - 2.5$ mol/l. The equilibrium constants were calculated according to relation (2) (ref.[10]).

$$1/(A_0 - A) = 1/(A_0 - A_D) Kd - 1/(A_0 - A_D) \,, \qquad (2)$$

where A_0 and A_D is the absorbance in chloroform and pyridine, resp., A is the absorbance in a chloroform–pyridine mixture, K is the equilibrium constant in 1/mol, and d is the concentration of pyridine in mol/l. The dependence of $1/(A_0 - A)$ on $1/d$ proves to be linear (Fig. 1) and from the ratio of the slope and its abscissa the equilibrium constant were calculated. The measurements were carried out at 25 ± 0.1°C. Both methanol and chloroform used for spectral measurements were of spectral purity. Pyridine (analytical purity grade) was distilled before use.

RESULTS AND DISCUSSION

Comparison of chemical shifts of hydroxyl group of 2-hydroxy-4-methylbenzophenone (*I*) and 2-hydroxy-4,6-dimethylbenzophenone (*II*) shows that the intramolecular hydrogen bond in compound *II* is weaker than in compound *I* (Table I). This conclusion can be extended to all 2-hydroxy-6-methylbenzophenone derivatives studied (see Table II). The comparison of dissociation constants of compounds *I* and *II* supports this conclusion.
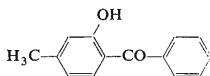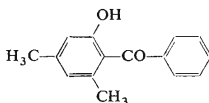

I   *II*

TABLE III

Position of Long-Wavelength Absorption Band for 2-Hydroxy-6-methylbenzophenone Derivatives

Com- pound[a]	Chloroform		Pyridine[b]		Methanol	
	λ_{max} nm	ε	λ_{max} nm	ε	λ_{max} nm	ε
1	342	3 450	—[c]	—	—[c]	—
2	350	2 880	—[c]	—	340[d]	620
3	356	1 560	—[c]	—	340	1 600
4	353	3 370	335	780	340	1 350
5	364	3 380	338	800	—[c]	—
6	353	2 490	340	550	350	1 060
7	364	2 500	340	780	345·2	1 070

[a] For numbering of compounds see Table II. [b] Pyridine contained 10 v. % of chloroform. [c] No absorption band or shoulder has been observed in the 300—400 nm region. [d] Shoulder.

The effect of pyridine on the long-wavelength absorption band in the ultraviolet spectrum of compound II (Fig. 2) and on the position of the carbonyl group in its infrared spectra may be attributed to a weakening or extinction of intramolecular hydrogen bond (see equilibrium (A)).

(A)
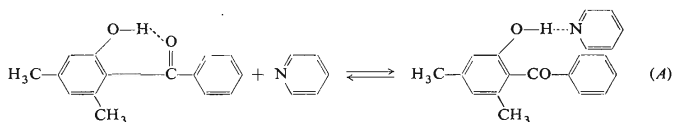
The intramolecular hydrogen bond in compound II enables the carbonyl group to interact with the hydroxyl group in the plane of the aromatic ring, and thus its extinction affects also this interaction, which leads to the decrease of intensity, respectively the extinction of the long-wavelength absorption band[1-3]. The introduction of methyl group to position 6 results in weakening of the intramolecular hydrogen bond, which is accompanied by enhanced sensitivity of the bond in compound II toward basic solvents. The above substitution affects also an electronic interaction between the carbonyl and the hydroxyl group that leads to the formation of the long-wavelength absorption band. This phenomenon has not been observed[3] in the case of compound I. A more bulky tert-butyl group in position 3 — due to its steric effect — makes the formation of intramolecular hydrogen bond impossible even in nonpolar solvents[6], which manifests itself in disappearance of long-wavelength absorption band[7].

The equilibrium constants determined on the basis of changes of absorbance of the absorption band at longest wavelength brought about by addition of pyridine show that the substituent in position 3 has a stabilizing effect on the intramolecular hydrogen bond – likely due to its steric effect. (Table II). This effect is obvious from inspection of Table III, which presents the positions of the longest-wavelength absorption bands for 2-hydroxy-6-methylbenzophenone derivatives in pyridine and methanol. In the spectra of the compounds substituted in position 3 by bulky groups the absorption band is preserved, while in 2-hydroxy-4,6-dimethylbenzophenone it disappears. In pyridine as a more basic solvent this band is strongly supressed even in the above 3-substituted derivatives.

The equilibrium constants and the chemical shifts of 2-hydroxy-6-methylbenzophenone derivatives do not change in the same way (Fig.3). Chemical shifts of hydroxyl group of studied derivatives are divided into two groups. For compounds 1−4 (Table II) the chemical shifts decrease, in accordance with decreasing values of equilibrium constants. The chemical shifts of compounds 5−7 (Table II), which are substituted also in position 5, are higher than those of compounds 1−4, which may be indicative of weakening of intramolecular hydrogen bond.

In contrast, the equilibrium constants for compounds 5−7 are comparable with those for derivatives 1−4. It seems that these contradictory results are a consequence of unequal effect exerted by substituents in position 5 of derivatives 5−7 on the chemical shift and the equilibrium constant.
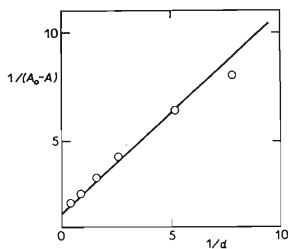

FIG. 1

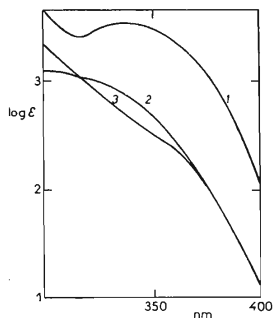Plot of $1/(A_0 - A)$ *versus* $1/d$ for a 2-Hydroxy-4,6-dimethylbenzophenone(II)– Pyridine System

FIG. 2

Ultraviolet Absorption Spectrum of 2-Hydroxy-4,6-dimethylbenzophenone (II) in Chloroform (Curve 1), 0·1M-HCl — 50 v.% Methanol (Curve 2), and Pyridine (Curve 3)

We found that there exists a good correlation between equilibrium and dissociation constants. In both cases we deal here with an equilibrium including the extinction of intramolecular hydrogen bond. In the case of equilibrium constants the extinction of intramolecular hydrogen bond is connected with the formation of a complex the two components of which are bonded by intermolecular hydrogen bond. In the case of dissociation constants the extinction is connected with the dissociation of proton. The fact that the spectrum of 2-hydroxy-6-methylbenzophenone in aqueous–methanolic alkaline solution differs from that measured in pyridine clearly shows that in pyridine the intramolecular hydrogen bond is broken and further that the ionization does not take place. The equilibrium and dissociation constants of studied derivatives reflect mainly the steric effect of substituents in position 3. However, derivative 5 does not fit this correlation (Table II), likely due to operation of electronic effect of bromine attached to position 5. This indicates that while substituents affect by its steric effects both constants in the same way their electronic effect may operate in different way. If the effect of substituents were at least in part transferred *via* intramolecular hydrogen bond, then substituents should have exterted essentially the same effect on equilibrium constant as on the chemical shift of 2-hydroxybenzophenone derivatives[3].

Comparison of chemical shifts of the hydroxyl group with data on solvent effects on the ultraviolet absorption spectra of 2-hydroxybenzophenone[3] and 2-hydroxy-6-methylbenzophenone derivatives leads to the following sequence of the strength of intramolecular hydrogen bond in various solvents. 2-Hydroxybenzophenone derivatives possess a strong intramolecular hydrogen bond in nonpolar media. In polar solvents the bond is weakened, the ultraviolet spectra are, however, only little affected. The introduction of methyl group into position 6 results in a weakening of intramolecular hydrogen bond. In polar solvents this bond disappears, which exhibits itself in the ultraviolet absorption spectra of these compounds.

The study of chemical shifts of the hydroxyl group and of spectral properties
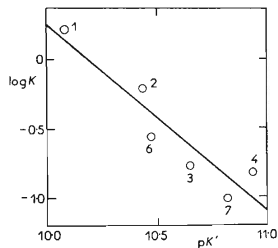

FIG. 3

Dependence of log K on pK' for 2-Hydroxy-6-methylbenzophenone Derivatives (*I*).

For numbering of compounds see Table II

of 2-hydroxybenzophenone[3] and 2-hydroxy-6-methylbenzophenone revealed that there is an interrelation between intramolecular hydrogen bond and absorption properties of studied derivatives. This interrelation sheds some light on the correlation found between the strength of intramolecular hydrogen bond of 2-hydroxybenzophenone derivatives and their efficiency as light stabilizers[5]. However, according to O'Connel[7] the intramolecular hydrogen bond does not play a role in the desactivation of excited state. This conclusion has been drawn from comparable photochemical stability of 2-hydroxy-4,6-ditert-butylbenzophenone with 2-hydroxybenzophenone. However, data available do not allow to predict conclusively as to how the extinction of intramolecular hydrogen bond will affect the photochemical properties of 2-hydroxy-6-methylbenzophenone in a polar solvent.

REFERENCES

1. Dilling W. L.: J. Org. Chem. *31*, 1045 (1966).
2. Hrdlovič P., Belluš D.: Chem. zvesti *22*, 508 (1968).
3. Hrdlovič P., Schubertová N., Palovčík R.: This Journal *36*, 1942 (1971).
4. Beckett A., Porter G.: Trans. Faraday Soc. *59*, 2051 (1963).
5. Chaudet J. H., Tamblyn J. W.: Soc. Plastics Eng. Trans. *1*, 57 (1961).
6. Shulgin A. T., Kerlinger H. O.: Chem. Commun. *1966*, 249.
7. O'Connell E. J., jr.: J. Am. Chem. Soc. *90*, 6550 (1968).
8. Arventiev B., Singurel L., Offenberg H., Nicolaescu T.: Analen, Stiint. Univ. Al. I. Cuza Sect. I c *13*, 135 (1967); Chem. Abstr. *69*, 86153 (1968).
9. Albert A., Sergeant I. P.: *Ionization Constants of Acids and Bases.* Methuen, London 1962.
10. Takahashi F., Karoly W. J., Greenhields J. B., Li N. C.: Can. J. Chem. *45*, 2034 (1967).
11. Hrdlovič P., Belluš D., Lazár M.: This Journal *33*, 59 (1968).