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Spectrophotometric Studies of the Acidities of Dichlorophene and Hexachlorophene

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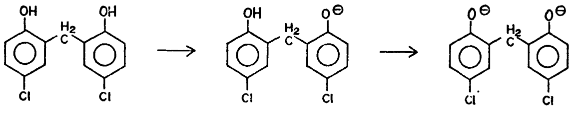
It has been found that dichlorophene (bis-(2-hydroxy-5-chlorophenyl)methane) and hexachlorophene (bis-(2-hydroxy-3,5,6-trichlorophenyl)methane) have abnormally high acidities as compared with the corresponding reference compounds, *i.e.*, 2-methyl-4-chlorophenol and 2,4,5-trichlorophenol respectively. The values of pK_a for the first and second ionizations of dichlorophene in a mixed solvent of ethanol and water (1 : 1) were determined to be 9.10 and 13.1, and those of hexachlorophene, to be 5.87 and 11.9, at 18 °C. On the basis of the infrared spectra, these observations could be interpreted in terms of the additional stabilization of the resulting mono-anions of these bis-phenolmethanes by means of the intramolecular hydrogen bondings between the OH and O$^-$ groups.

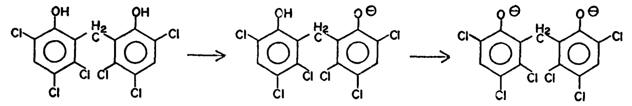
The acidities of organic compounds are more or less influenced by various types of intra- and intermolecular interactions. For many substituted phenols, the effects of intra- and intermolecular hydrogen bondings on their acidities have been widely studied.[1] It is well known that salicylic acid is a stronger acid than *o*-methoxybenzoic acid, and this has been attributed to the additional stabilization of the resulting mono-anion of salicylic acid by the intramolecular hydrogen-bonding between the COO$^-$ and OH groups.[2-6]

In the present investigation, the acidities of two bis-phenolmethanes, dichlorophene (bis-(2-hydroxy-5-chloro phenyl)methane), and hexachlorophene (bis-(2-hydroxy-3,5,6-trichlorophenyl)methane), are compared with those of 2-methyl-4-chlorophenol and 2,4,5-trichlorophenol respectively, which can be regarded as reference compounds for the above bis-phenolmethanes because their ultraviolet spectra resemble well those of the respective bis-phenolmethanes. If, in the bis-phenolmethanes, there take place some intramolecular interactions between the two moieties separated by the methylene group, their acidities may be expected to be different from those of the reference compounds. In fact, when water is added to a solution of hexachlorophene in ethanol, a new absorption band appears at 320 nm, with an intensity depending upon the concentration of the added water; this band disappears when the solution is made acidic, thus suggesting that hexachlorophene ionizes partly even in a neutral aqueous solution. On the other hand, this is not the case for 2,4,5-trichlorophenol. Accordingly, we will deal with the factors accounting for the abnormally high acidities of the bis-phenolmethanes as studied by means of ultraviolet and infrared spectroscopies.

Results and Discussion

Figures 1 and 2 show the spectral changes on the variation in the pH values of solutions of dichlorophene and hexachlorophene respectively in a mixed solvent of ethanol and water (1 : 1 in volume). These spectral changes can safely be attributed to the first and second ionizations of the phenolic hydroxyl groups of these bis-phenolmethanes. In Figs. 1 and 2 the solid and the broken lines represent the spectral changes due to the first and the second ionizations respectively. The absorption intensities of the newly-appearing bands change with a change in the pH value of the solutions, as is shown in Fig. 3. As may be seen from this figure, the second ionization of each compound occurs in a distinctly higher pH region than the first ionization.





Therefore, the pK_a values for the first and second ionizations of these bis-phenolmethanes can be determined from the absorbances of the newly-appeared bands by the application of the usual equation. The results are summarized in Table 1, in which the results for 2-methyl-4-chlorophenol and 2,4,5-trichlorophenol obtained in the same manner are also presented for the sake of comparison. As may be seen from this table, the pK_a values for the first ionizations of the bis-phenolmethanes are significantly smaller than those of the

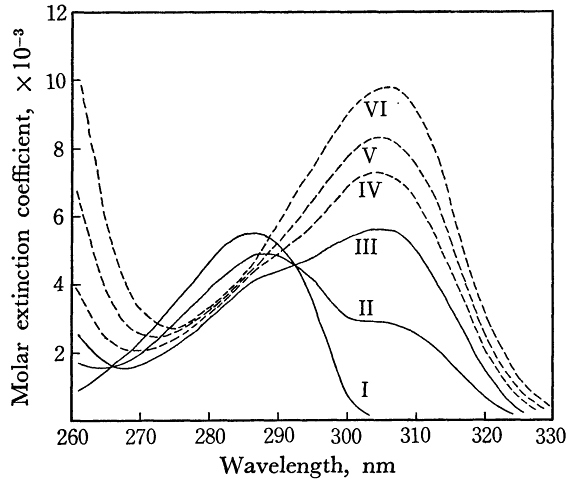


Fig. 1. Spectral change of the solution of dichlorophene in mixed solvent of ethanol and water (1 : 1) on variation of pH.

pH; I: 6.8, II: 8.9, III: 9.9, IV: 12.4, V: 13.1, VI: 13.7

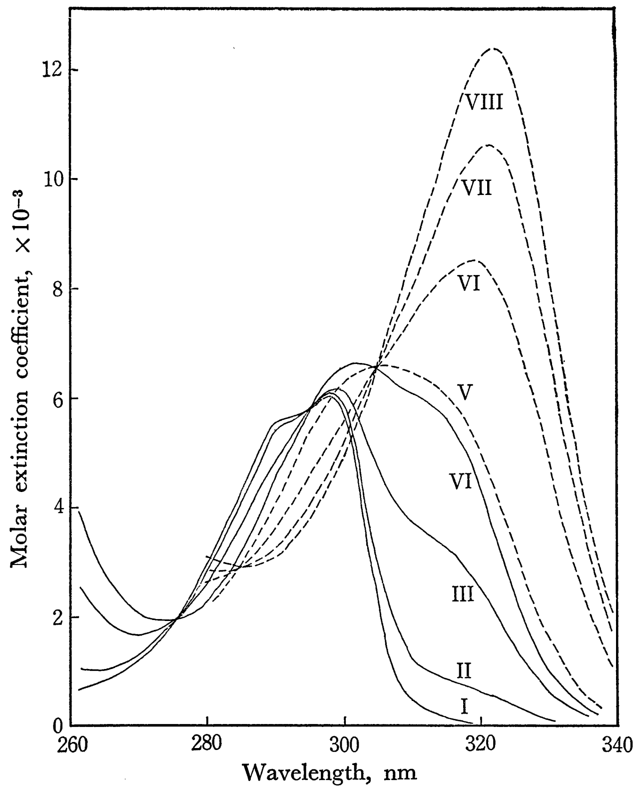


Fig. 2. Spectral change of the solution of hexachlorophene in mixed solvent of ethanol and water (1 : 1) on variation of pH.
pH; I: 3.4, II: 4.6, III: 5.4, IV: 6.7, V: 10.5, VI: 12.0, VII: 12.4, VIII: 12.9

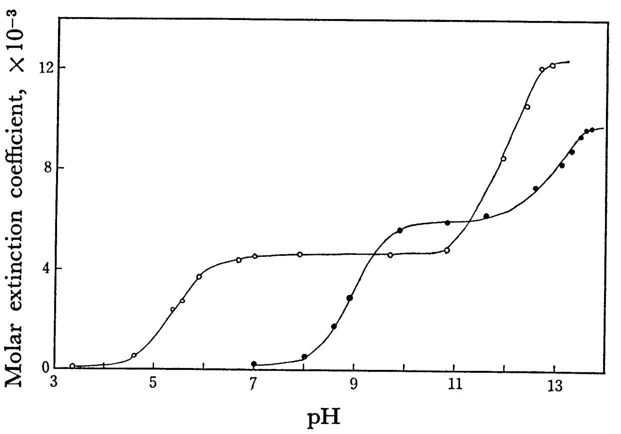


Fig. 3. Plot of absorption intensity of the new band against pH.
●: Dichlorophene, at 304 nm, ○: Hexachlorophene, at 320 nm

respective reference compounds. On the other hand, the pK_a values for the second ionizations are fairly large. These results strongly suggest that an intramolecular interaction takes place for each of the bis-phenolmethanes in the ionized species.

Next, the interaction of the bis-phenolmethanes with triethylamine in *n*-hexane was studied. It has been established that various types of interactions exist between such phenols as *p*-nitrophenol and triethylamine, including the formations of a simple hydrogen bond, a hydrogen-bonded ion pair, a solvent-separated ion pair, and dissociation into individual ions, depending upon the solvent employed.[7,8] The spectral changes on the addition of triethylamine to a *n*-hexane solution of the present bis-phenolmethanes are shown in Fig. 4. As for hexachlorophene, the first ionization into the ions, probably the ion pair, is considered to occur in *n*-hexane on the addition of triethylamine, judging from the spectra shown in Fig. 4. In the case of dichlorophene, however, the ionization does not occur; however, the hydrogen bonding with triethylamine does seem to take place, because the addition of triethylamine causes a small shift of the absorption band (from 286 nm to 293 nm) compared with the case of the ionization. By the application of the method of Rose and Drago,[9] the equilibrium constants for the first ionization of hexachlorophene in *n*-hexane and for the formation of the hydrogen bond between dichlorophene and triethylamine were determined to be 29500 and 5900 at 25 °C respectively. 2,4,5-Trichlorophenol undergoes only the hydrogen-bonding with triethylamine in *n*-hexane. That the difference in the pK_a values determined in aqueous ethanol reflects the different types of interactions for hexachlorophene and 2,4,5-trichlorophenol with triethylamine in *n*-hexane clearly indicates that the abnormally high acidity of hexachlorophene can not be attributed to the effect of the solvation of the ionized species.

It is expected that the presence of two hydroxyl groups

Table 1. The pK_a values for the first and the second ionizations in aqueous ethanol

	pK_a(I)	pK_a(II)
Hexachlorophene	5.87(18°), 5.69(40°)	11.9(18°)
2,4,5-Trichlorophenol	8.44(18°), 8.25(38°)	
Dichlorophene	9.10(18°), 8.83(38°)	13.1(18°)
2-Methyl-4-chlorophenol	10.89(18°), 10.13(38°)	

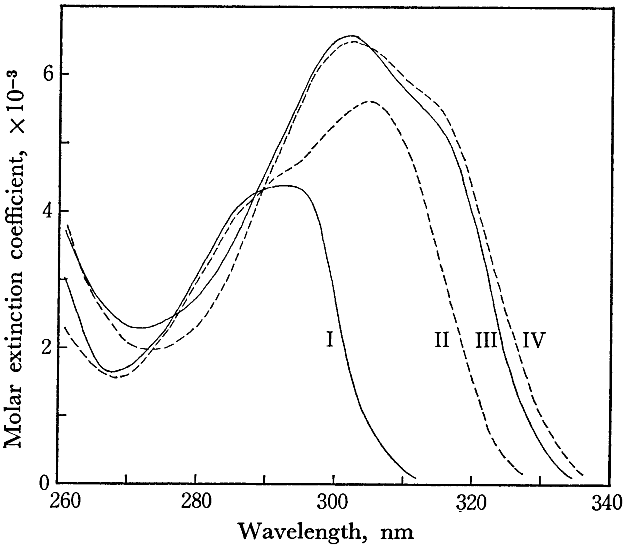


Fig. 4. Absorption spectra.
I: Dichlorophene in *n*-hexane containing triethylamine, II: Dichlorophene in aqueous ethanol, pH: 9.9, III: Hexachlorophene in *n*-hexane containing triethylamine, IV: Hexachlorophene in aqueous ethanol, pH: 6.7

in each of the bis-phenolmethanes is essentially related to the abnormal ease of the first ionizations. In fact, according to Higuchi *et al.*,[10] *o*-methylhexachlorophene has a pK_a value of 8.22 and hexachlorophene monosuccinate has a pK_a value of 8.14 for the ionization of the phenolic group. These values are very close to the pK_a value of 2,4,5-trichlorophenol. Hence, it can be considered that two hydroxyl groups of the bis-phenolmethanes take part in an intramolecular interaction. Although intramolecular hydrogen bonding has been known to be formed in bis-(2-hydroxy-3-*t*-butyl-5-methylphenyl)methane between the two hydroxyl groups judging from the fact that this compound has its infrared absorption at 3500 cm^{-1} as a broad band,[11] such intramolecular hydrogen bonding does not occur in the case of hexachlorophene. This can be deduced from the fact that the OH stretching band is sharp in shape and appears at 3525 cm^{-1}, similarly to that of 2,4,5-trichlorophenol, as is shown in Fig. 5. However, in the case of the resulting mono-anion, an intramolecular hydrogen bond may be expected to be formed between the OH and O^- groups because of the relatively strong electronegativity of the latter. From the spatial point of view, these groups are perhaps brought close together by twisting around the C(methylene)—C(ring) bond axes.

In order to ascertain whether or not such a hydrogen bond was present, the infrared absorption spectrum of the mono-anion of hexachlorophene was measured, using tetrachloroethylene as the solvent and triethylamine as the base.[12] The results are presented in Fig. 5. The sharp band of the OH stretching vibration at 3525 cm^{-1} diminishes on the addition of triethylamine, and a broad band appears around 2100 cm^{-1}. This spectral change is due to the first ionization, and the band at 2100 cm^{-1} can be assigned to the OH stretching vibration of the resulting mono-anion, because no other band appears on the addition of the base in the relatively higher wave number region. The very low wave number and the broadening of this band indicate that the mono-anion has an intramolecular hydrogen bond between the OH and O^- groups. Moreover, judging from the surprisingly low wave number, this hydrogen bond seems to be extraordinarily strong, and the following intramolecular proton transfer may occur in the anion.

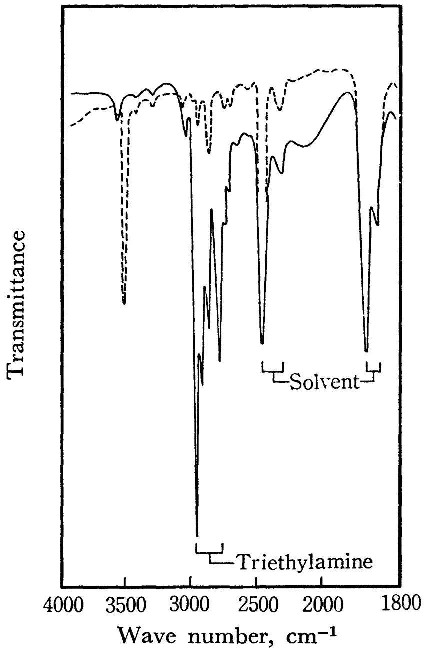
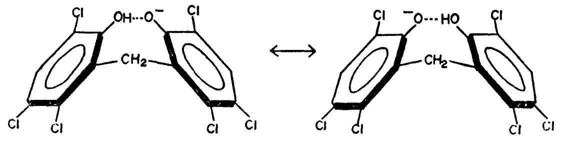


Fig 5. Infrared spectra of hexachlorophene in tetrachloroethylene.
----: Absence of triethylamine, ——: Presence of triethylamine



The formation of such an intramolecular hydrogen bond may cause an additional stabilization of the resulting mono-anion. Consequently, the difference in the pK_a values for hexachlorophene and 2,4,5-trichlorophenol may be ascribed to the presence of this intramolecular hydrogen bond in the former. This may also be the case for dichlorophene. Also, the abnormally high acidity of salicylic acid has been interpreted in terms of an intramolecular hydrogen-bonding between the hydroxyl and carboxylic groups. However, in the case of salicylic acid the hydrogen bond is formed even in the neutral species. This is in contrast with the situation with hexachlorophene.

As for hexachlorophene, its high acidity as compared with that of dichlorophene may be attributed to the additional inductive effect of the chlorine atoms at the 3- and 3′-positions.

The stabilization of the mono-anions of the bis-phenolmethanes by the intramolecular hydrogen bond should result in higher pK_a(II) values than those of the corresponding reference compounds. This is indeed the case, as is shown in Table 1. However, the high pK_a(II) values may also be attributed to some extent to the repulsion of the charge in the resulting di-anions.

Experimental

Materials. All the materials used here were obtained commercially and were purified by repeated recrystallizations from a suitable solvent for each compound.

Procedures. The values of pK_a were determined spectrophotometrically by the use of the following equations;

$$\mathrm{p}K_a(\mathrm{I}) = \mathrm{pH} + \log\frac{\dfrac{D}{A}-\varepsilon_m}{\varepsilon_n-\dfrac{D}{A}}$$

$$\mathrm{p}K_a(\mathrm{II}) = \mathrm{pH} + \log\frac{\dfrac{D}{A}-\varepsilon_d}{\varepsilon_m-\dfrac{D}{A}}$$

where A is the initial concentration of acids and where D and ε are, respectively, the absorbance and the molar extinction coefficient. The subscripts, n, m, and d, denote neutral species, the mono-anion, and the di-anion respectively. A mixture of ethanol and water (1 : 1) was used as the solvent.

The ultraviolet absorption spectra were measured with a Shimadzu Spectrophotometer QV-50, using 1 cm quartz cells. The cell box was maintained at a constant temperature by passing water from a constant-temperature bath through the cell box. The infrared absorption spectra were recorded on a Hitachi Infrared Spectrophotometer EPI-G3, using a 0.5 mm NaCl cell.

References and Notes

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