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Relation between the Infinite Dilution Shifts in Pyridine with the Hammett's Rule[*1]

The influence of substituents clining on an aromatic ring has successfully been established by Hammett. There have been reported so far that over several thousands compounds were consistent with this rule. Gutowsky and his co-workers[1] were the first who studied σ value of parameter of the Hammett's rule by nuclear magnetic resonance spectroscopy. By measuring the chemical shifts of F^{19} of substituted fluorobenzenes, they proved that depends on the electronegativity of the substituent, but there was a complete difference between ρ of *meta*-substituted benzoic acids and ρ of *para*-substituted benzoic acids. It indicates that it is not parallel with the case of chemical reaction. Gutowsky and his co-workers presented the following explanation, the resonance effects of substituent groups show the greater influence on chemical shifts than the other factors that make up the over-all electrical effect in general. Cario and Dailey,[2] Bothner-By and Glick[3] have measured chemical shifts of proton of benzene substituents. In this case the relation between σ and ρ was not quite so simple.

Later on, under similar idea, various experiments have been conducted on this point by Yukawa and his co-workers,[4] Diehl[5] and Lauterbur.[6]

In the present report we have measured the chemical shifts (δ_o) of mono-substituted benzoic acids diluted infinitely with pyridine and obtained the evidence that the data have the direct relation with σ value of Hammett's rule.

It has been believed that σ value indicates the changes of dissociation free energy of benzoic acids caused by the effect of substituent, and only the polar effect of substituent is obliged to this phenomenon. Further, it has also been recognized that σ value of *meta*-position (σ_m) is not affected any change by the type of solvent used.

When derivatives of benzoic acid are diluted infinitely by pyridine, interaction between

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[*1] The Abstract at 3rd Meeting of NMR Discussion in Japan, 1963, p. 8.
1) H. S. Gutowsky, D. W. Mc Call, B. R. Mc Garvey, L. H. Meyer : J. Am. Chem. Soc., **74**, 4809 (1952).
2) P. L. Cario, B. P. Dailey : *Ibid.*, **78**, 3043 (1956).
3) A. A. Bothner-By, R. E. Glick : J. Chem. Phys., **26**, 1651 (1957).
4) Y. Yukawa, M. Sakai, K. Kabazawa : Sci. & Ind. Research Osaka Univ., **17**, 185 (1960).
5) P. Diehl : Helv. Chim. Acta, **44**, 829 (1961); *Ibid.*, **45**, 568 (1962).
6) P. C. Lauterbur : Tetrahedron Letters, No. 8, 274 (1961).

acid and pyridine could be illustrated by I, II, III, and IV. In this case, substituent will influence both inductive and resonance effects against hydroxyl proton of acid. Therefore, chemical shift of hydroxyl proton sustained in pyridine will be depended on time average of each δ of I through IV, accordingly it is possible to consider that δ of hydroxyl proton in infinite dilution has linear relationship with σ value of Hammett's rule, e.g. electronic character of substituents. In Fig. 1 the relationship σ value[*2] with δ_o is illustrated.
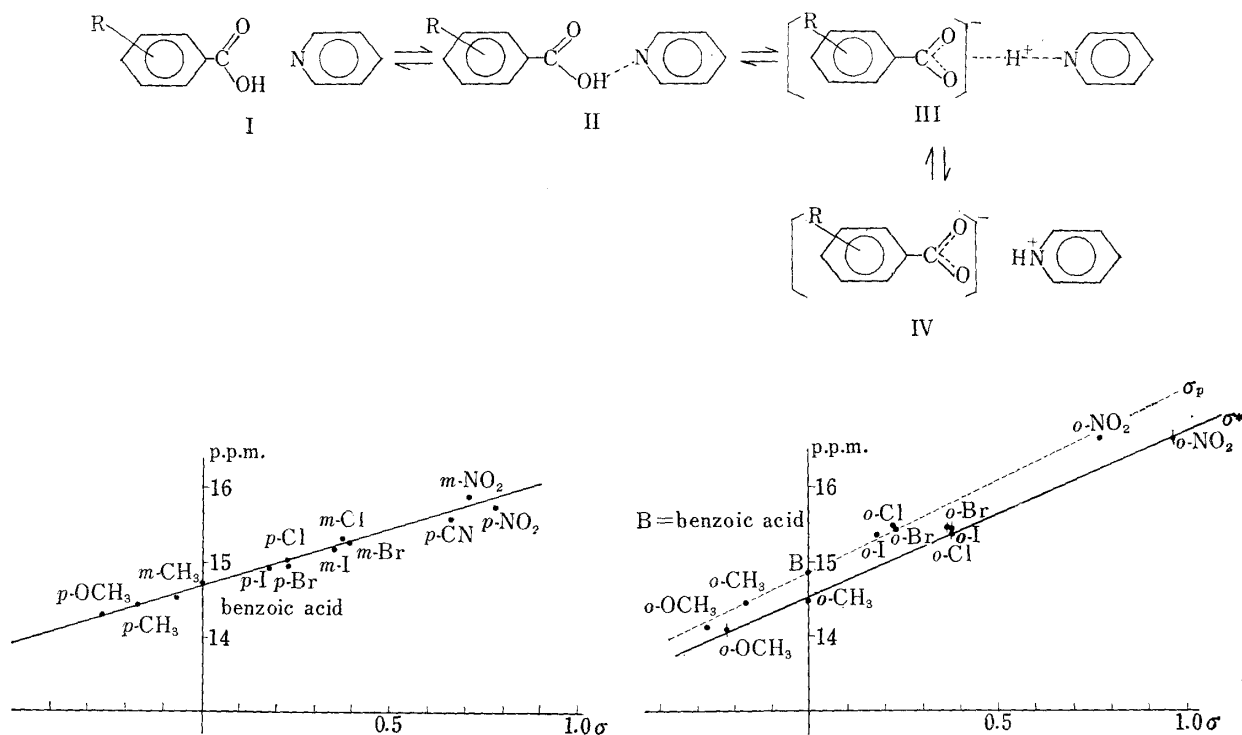

Fig. 1. δ_o Values[*3] for *meta-* and *para-* Substituted Benzoic Acid as a Function of σ Values

Fig. 2. δ_o Values[*3] for *ortho-*Substituted Benzoic Acid as Function σ^* and σ_p Values

Ortho-substituents are not considered to be inconformity with the Hammett's rule. As a matter of facts the direct experiments emplying benzoic acid derivative series has ended in failure. We used the substituent constants of *ortho*-substituted benzoic acids (σ^*) which Taft[8] had calculated and σ_p. As illustrated in Fig. 2, in all cases good conformity could be observed. From these results it is evident that, even in the case of *ortho*-substituted benzoic acids, so-called *ortho* effect does not appear and the similar substituent constants to *para*-substituted benzoic acids might possibly be employed. On the other hand, we have observed that δ_o of hydroxyl proton of *ortho*-substituted phenols in pyridine solution had shifted to higher field when compared to *meta-* and *para*-substituted phenols.[9] In fact, it is considered that steric hindrance will be effected more readily, because hydroxyl group has nearer access to nucleus in comparison with exchange proton of carboxyl group which maintained a sufficient bond length from the effect of

[*2] primary σ values.[7]

[*3] cyclohexane as standard.

7) D. H. Mc Daniel, H. C. Brown : J. Org. Chem., 23, 420 (1958).

8) M. S. Newman : " Steric Effects in Organic Chemistry " p. 591 (1956) John Wiley & Sons, Inc., New York.

9) T. Ikenoue : The Abstract at Meeting of Chemical Structure Disscussion in Japan, 1961, p. 39; T. Ikenoue, K. Kondo : The Abstract of 15th Annual Meeting of Chem. Soc. of Japan, April, 1962, Kyoto, p. 441; T. Ikenoue : The Abstract at Meeting of Molecular Structure Discussion in Japan, 1963, IV, p. 13.

steric hindrance. For the reason why the reaction constants (ρ) of Fig. 1 and Fig. 2 are not equal, we presume the influence of electric field that is possessed by *ortho*-substituted benzoic acids.

Pyridine used for this experiments had moisture content of 10^{-4} mole fraction or below, which were checked by measuring the shift of two component system of pyridine-acetic acid.[9] When pyridine contains more moisture, the larger marginal difference in δ_0 value will be resulted. Therefore, we had employed an experimental apparatus to prevent a moisture contamination while sampling; all experiments were conducted under high vacuum of $10^{-5.3}$ through $10^{-4.7}$ mm. Hg and satisfactory results were obtained in good reproducibility.

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Glycosides from the Leaves of *Euptelea polyandra* Sieb. et Zucc.[*1][*2]

In the course of our investigations[*3][1] on anti-microbial substances in buds or young leaves with more than one thousand species of plants, the authors found that the juice of the leaves of *Euptelea polyandra* Sieb. et Zucc. (Eupteleaceae) showed strong activities against some phytopathogenic fungi. Two active principles were isolated and named eupteleoside A and eupteleoside B respectively, and their chemical structures investigated.

Eupteleoside A (I), colorless needles, m.p. 269~271°, $[\alpha]_D^{22}$ +5.5° (c=1.1, pyridine), IR ν_{max}^{KBr} cm^{-1} : 3500 (OH), 1768 (lactone), (*Anal.* Calcd. for $C_{46}H_{70}O_{17} \cdot 2H_2O$: C, 59.33; H, 8.01. Found : C, 59.42; H, 7.70), is positive in the Liebermann–Burchard reaction (reddish purple), but gives negative coloration with tetranitromethane or with ferric chloride. I, on acetylation with acetic anhydride and pyridine gives eupteleoside A octaacetate (II), m.p. 179~181°, $[\alpha]_D^{22}$ +25° (c=1.10, chloroform), (*Anal.* Calcd. for $C_{62}H_{86}O_{25} \cdot H_2O$: C, 59.60; H, 7.10; $8CH_3CO$, 27.56. Found : C, 59.69; H, 7.08; CH_3CO, 27.54), and on methylation,[2]

*1 This paper forms part of the series by Sueo Tatsuoka "Studies on the Useful Components in Natural Sources."
*2 Papers partly presented at the 83rd Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, November, 1963.
*3 Partly presented at the Annual Meeting of the Pharmacognostical Society of Japan, Chiba, July, 1963.
1) M. Goto, S. Imai, H. Yamamoto, T. Murata, T. Noguchi, S. Fujioka : Annual Reports of the Takeda Research Laboratories, 22, 125 (1963).
2) R. Kuhn, L. Löwe, H. Trischmann : Chem. Ber., 88, 1492 (1955).