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Structure of (+)-Isoolivil ((+)-Cycloolivil) and Some Lignans

Previously the *trans*-(2,3)-*trans*-(3,4) configuration was determined for lyoniresinol dimethyl ether (I), resinolide (II) and retroresinolide (III).$^{1)}$

Above conclusion was further proved by the nuclear magnetic resonance spectra of II,$^{1)}$ III$^{1)}$ and the cyclohemiacetal (IV),$^{2)}$ m.p. 173° (*Anal.* Calcd. for $C_{24}H_{30}O_8$: C, 64.56; H, 6.77. Found : C, 64.69, 64.82; H, 7.10, 7.09), minor oxidation product of I, compared with the nuclear magnetic resonance spectrum of isotaxiresinol trimethyl ether (isolariciresinol dimethyl ether) (V),*1 m.p. 174/180~181.3° (*Anal.* Calcd. for $C_{22}H_{28}O_6 \cdot H_2O$: C, 65.01; H, 7.44. Found : C, 65.00, 64.82; H, 7.13, 7.19) as a reference compound of which *trans*-(2,3)-*trans*-(3,4) configuration was proved by Schrecker and Hartwell.$^{3)}$

The signals assigned to a hydrogen atom on the carbon atom 4 were doublets, and the *trans*-(3,4) configuration was suggested by coupling constants for compounds (II, III, IV and V) (Table I).

Recently two structural formulae (VI)$^{4)}$ and (VII)$^{5)}$ were proposed for (+)-isoolivil ((+)-cycloolivil).

The presence of a hydrogen atom on the carbon atom 3 was determined as well as *trans*-(3,4) configuration for isoolivil dimethyl ether (VIII), m.p. 183.3~184° (*Anal.* Calcd. for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98. Found : C, 65.05; H, 7.02) with the nuclear magnetic resonance spectrum of this compound compared with the data tabulated on Table I.

So the structural formula of (+)-isoolivil ((+)-cycloolivil) was determined exclusively as VII.

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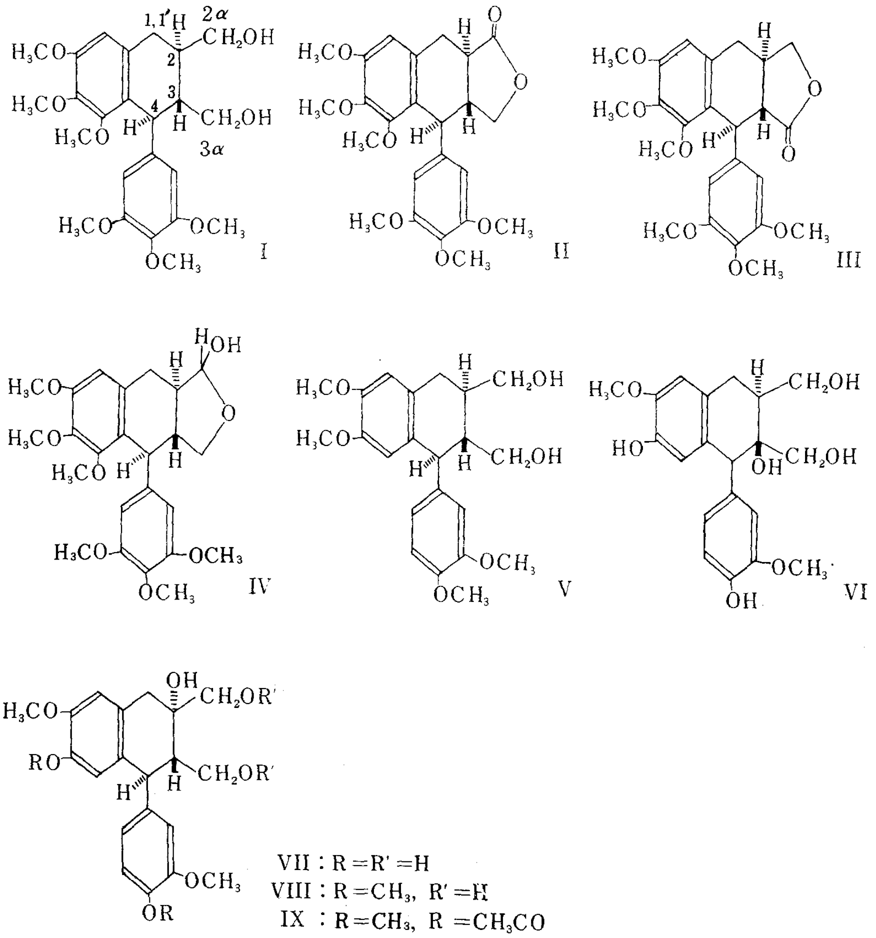
*1 Obtained by methylation of isotaxiresinol, extracted from the wood of *Taxus cuspidata* Sieb. et Zucc.$^{6)}$

1) Y. Kato : This Bulletin, **11**, 823 (1963).
2) V.P. Arya, H. Erdtman, M. Krolikowska, T. Norin : Acta Chem. Scand., **16**, 518 (1962).
3) A.W. Schrecker, J.L. Hartwell : J. Am. Chem. Soc., **77**, 432 (1955).
4) K. Freudenberg, K. Weinges : Tetrahedron Letters, **1962**, 1077.
5) M. Smith : *Ibid.*, **1963**, 991.
6) M. Hasegawa, T. Shirato, H. Nakamura : Transactions of the 62nd Meeting of the Japanese Forestry Society, 265 (1953).



VII : $R=R'=H$
VIII : $R=CH_3,\ R'=H$
IX : $R=CH_3,\ R=CH_3CO$

Chart 1.

Table I. Chemical Shifts of Protons, p.p.m. (δ)[a]

Compounds	4	3α	2α	CH_3O	1,1'	3	2	CH_3CO
IV	4.3[b] J=11.4 c.p.s.	4.32~ 4.09	5.2[b] J=3.6 c.p.s.	3.86, 3.80, 3.76, 3.74, 3.20	3.65~3.38	2.89~2.55		
V	4.44[b] J=9.4 c.p.s.	4.32~3.92		3.79, 3.76, 3.64, 3.53	3.27~3.01	2.64~2.10		
VIII	4.75[b] J=12 c.p.s.	4.53~4.08		3.75, 3.73, 3.59, 3.51	3.11[b] J=16.8 c.p.s. 3.79[b] J=16.8 c.p.s.	2.82~ 2.61		
IX	4.22~4.13			3.88, 3.86, 3.81, 3.6	2.70[b] J=17.4 c.p.s. 3.25[b] J=17.4 c.p.s.	1.72~ 1.37		2.11, 2.04

a) Spectra were determined in pyridine (V, VIII) and $CDCl_3$ (IV, IX), usingl tetramethylsilane as internal reference.
b) Doublet

The two signals assigned to the methyl hydrogens of acetyl groups of isoolivil dimethyl ether diacetate (IX), m.p. 150° (*Anal.* Calcd. for $C_{26}H_{32}O_9$: C, 63.92; H, 6.60. Found : C, 64.15; H, 6.60) indicated that this compound was just diacetate as reported previously[7] and not triacetate.[8]

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[7] G. Traverso : Gazz. chim. ital., 88, 851 (1958).

[8] M. Hasegawa, T. Shirato : J. Japan. Forestry Soc., **41**, 1 (1959).

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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_0) 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).