Studies on the Effect of Substituents on the Spectra of Quinoline Derivatives

By Tadashi SATO and Masaki OHTA

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For interpreting the effect of substituents on the spectra of triphenylmethyl ions and other dyes, Lewis et al.[1] took account of the orientation of the molecule in the electric field and designated the absorption bands as x-bands or y-bands on the assumption that they were associated with electric moments directed along mutually perpendicular axes in the main plane of the molecule. Later, this assumption was extended to the other types of molecules and treated theoretically by some physical chemists.

In 1949, Klevens and Platt[2], using the free electron model, classified the spectra of cata-condensed hydrocarbons and gave them a systematic nomenclature: with naphthalene, they designated its absorption bands as Lb-, La- and Bb-bands in the order of decreasing wave length. The polarization diagrams were represented in Fig. 1. They stated that the Lb-band showed a red shift with increasing chain length and was therefore longitudinally polarized along an axis of molecular

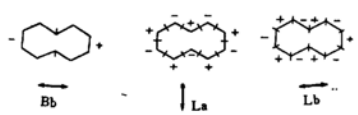
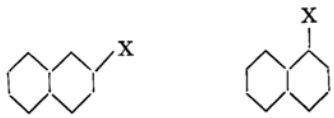


Fig. 1.

length, and that the La-band exhibited a bathochromic shift as molecular width increased. This band was, therefore, transversely polarized. A similar phenomenon was observed by Jones[3] with anthracene derivatives.

Ewing et al.[4], without referring to the above discussion, reported on the spectra of naphthols, naphthylamines, hydroxy- and aminoquinolines. These spectra showed the properties corresponding to the above discussion: in molecules of β-type, the Lb-bands were bathochromically shifted and the intensities increased, indicating the existence of three clearly distinguishable bands, whereas in α-type, the La-bands were so much bathochromically shifted that the weak Lb-bands were almost covered.

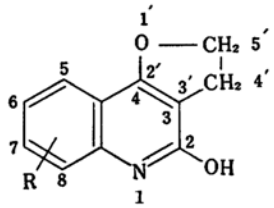
1) G. N. Lewis and M. Calvin, *Chem. Rev.*, **25**, 273 (1939); G. N. Lewis and J. Bigeleisen, *J. Am. Chem. Soc.*, **65**, 520, 2120, 2107 (1943).
2) H. B. Klevens and J. R. Platt, *J. Chem. Phys.*, **17**, 486 (1949).
3) R. N. Jones, *Chem. Rev.*, **41**, 353 (1947).
4) G. W. Ewing and E. A. Steck, *J. Am. Chem. Soc.*, **68**, 2181 (1945); **70**, 3397 (1948).



β-type* α-type

Knight et al.[5] classified the spectra of bromoquinolines along this consideration and observed the same regularity as described above. All studies so far reported have dealt with the simple monosubstituted molecules. In our synthetic study of furoquinoline alkaloid, it was necessary to determine where the nitro group would enter when methoxy-dihydrofuroquinoline derivative II was subjected to nitration. With the intention of predicting its position spectroscopically, we investigated whether the regularity existing between the displacement of bands and the position of the substituents could be observed in these rather complicated molecules.

The spectra of four compounds (I—IV) are compared in Fig. 2.** As can be noted from the comparison of the spectrum of IV



I R=H
II R=8-OCH_3
III R=7-OCH_3
IV R=6-OCH_3

with that of I, introduction of the methoxyl group in 6-position displaces the Lb-band to the red, while the La-band remains almost unchanged. In the other two cases (II and III), λ_{max} is hardly affected at all, while the intensities are much affected; as for 7-isomer, the Lb-band increases with the depression of the La-band, and with 8-isomer, the circumstance is the reverse. As noted from these data, there are two modes of exerting the effect, namely on the wave length

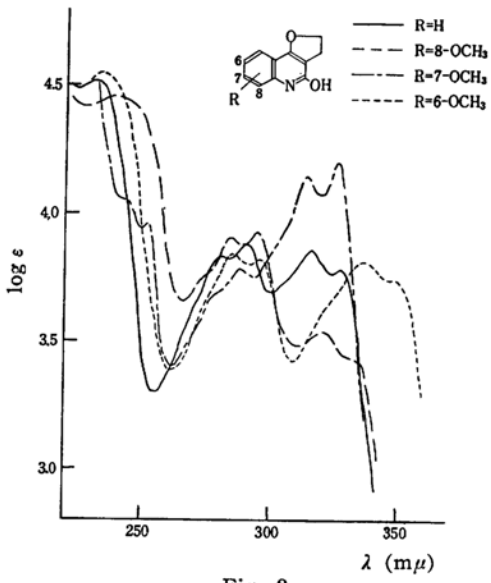


Fig. 2

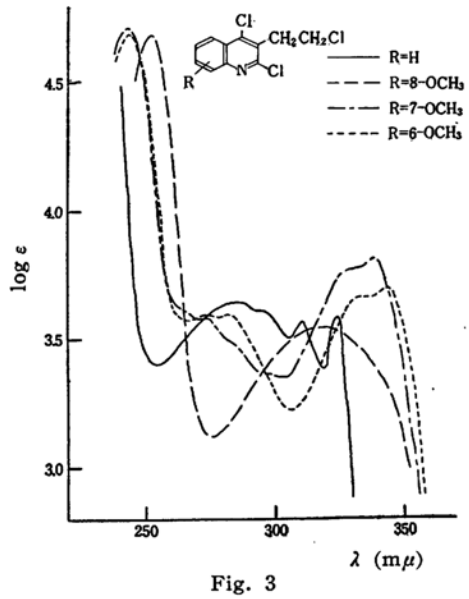


Fig. 3

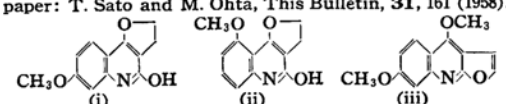
in one case, and on the intensity in the other. Though we can not find a satisfactory explanation to this difference, a generalization can be observed that the substitution which increases the molecular length (6- and 7-position) acts so as to displace the Lb-band bathochromically or to increase the intensity, while substitution perpendicular to this direction exerts the same influence on La-band.

In Fig. 3, the spectra of another series of molecules (V—VIII) are shown. Here, the spectra of 6- and 7-isomer are similar. In both cases, Lb-bands are bathochromically shifted, while La-bands are shifted

* Here, the diagram represents the naphthalene and the quinoline nucleus.

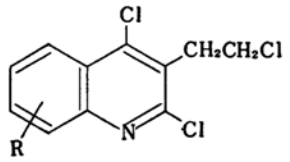
5) S. B. Knight et al., ibid., **76**, 3780 (1954).

** We prepared these compounds by the condensation of appropriate aromatic amines and diethyl β-methoxyethylmalonate[6]. As for the condensation product from *m*-anisidine, two isomers are possible (i and ii). We proved the product as to be 7-methoxy derivative (i), by converting it into evolitrine (iii). See the following paper: T. Sato and M. Ohta, This Bulletin, **31**, 161 (1958).



(i) (ii) (iii)

6) M. F. Grundon et al., *J. Chem. Soc.*, **1955**, 4284; T. Sato and M. Ohta, This Bulletin, **30**, 708 (1957).

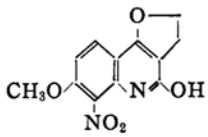


V R=H
VI R=8-OCH_3
VII R=7-OCH_3
VIII R=6-OCH_3

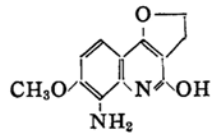
in the opposite direction. As for 8-isomer, the La-band is so much bathochromically shifted as to cover the Lb-band completely.

From these data, we can undoubtedly say that the electronic transition responsible for the Lb-band is of the type of polarization along the axis of molecular length, while that for La-band is of the type perpendicular to this axis, and that even in these rather complicated molecules, the regularity found in the simpler molecules can also be observed.

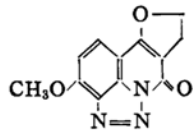
Nitration of III gave a nitro derivative IX. Reduction of the nitro derivative with stannous chloride gave the amino



IX



X



XI

derivative X, from which the triazol derivative XI was derived by the reaction with nitrous acid[7]. From this fact the position of the nitro group in IX could definitely be decided.

Comparing the spectrum of this nitro derivative IX with that of III (Fig. 4), we can see that, in accordance with the above observation, the introduction of the nitro group causes the La-band to displace bathochromically and hyperchromically. Though a little bathochromic shift is also observed with Lb-band, the extent is far smaller than that for La-band. When the spectrum of the amino derivative X is compared with that of III (Fig. 4), it is obvious that the La-band is more influenced than Lb-band.

As we could thus extend this consideration to somewhat complicated molecule, it

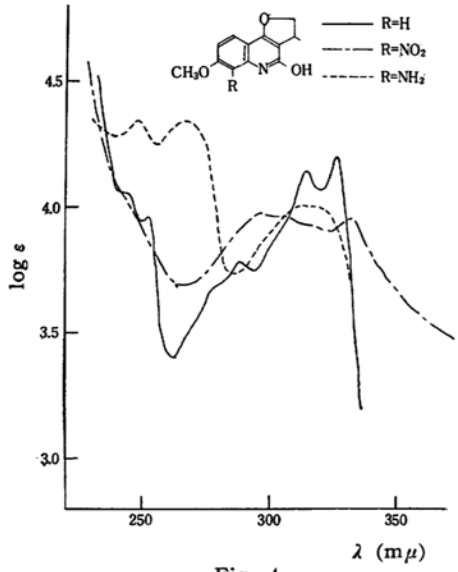


Fig. 4

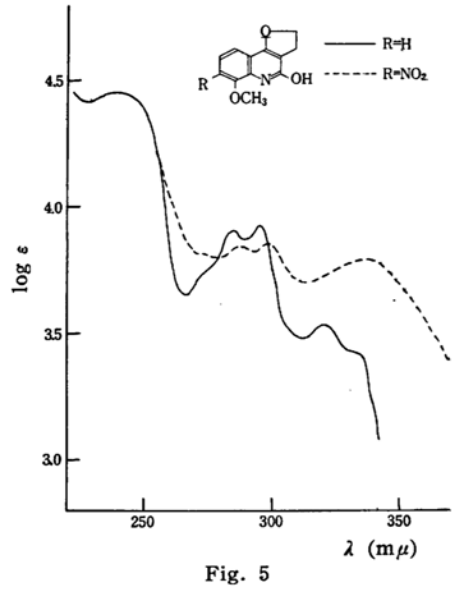
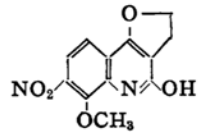
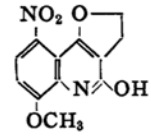


Fig. 5

is now possible to determine which of the two possible products XII and XIII was produced by the nitration of II. The fact that the spectrum of this nitro derivative suffers much bathochromic and hyperchromic shift on the Lb-band when compared with that of II, as shown in Fig. 5, seems to show that it would probably be 7-isomer XII.



XII



XIII

7) S. E. Krahler and A. Burger, *J. Am. Chem. Soc.*, **64**, 2417 (1942).

Experimental

Absorption Spectra — All spectra were measured in methanol with Beckman Quartz Spectrophotometer, Model DU.

2-Hydroxy-4′, 5′-dihydrofuro (3′ : 2′—3 : 4) quinoline (I),* 2-hydroxy-8-methoxy-4′, 5′-dihydrofuro (3′ : 2′—3 : 4) quinoline (II), 2, 4-dichloro-3-(β-chloroethyl) quinoline (V), and 2, 4-dichloro-3-(β-chloroethyl)-8-methoxyquinoline (VI).**—These compounds were prepared according to the methods reported by Grundon and by us[6] All were identified by their melting points and nitrogen analyses.

2-Hydroxy-7-methoxy-4′, 5′-dihydrofuro (3′ : 2′—3 : 4) quinoline (III) — A solution of *m*-anisidine (12 g.) and diethyl β-methoxyethylmalonate (25 g.) in diphenyl ether (35 cc.) was heated under reflux for 3 hours. After cooling, the product was recrystallized from nitrobenzene. m. p. 250°. A pure sample resulting from the recrystullization from dilute acetic acid. m. p. 252°.

Anal. Found: C, 66.15; H, 5.55; N, 6.69. Calcd. for $C_{12}H_{11}O_3N$: C, 66.35; H, 5.10; N, 6.45%.

Addition of petroleum ether to the diphenyl ether mother liquor gave a solid from which a small amount of unidentified crystals was obtained, in addition to III, by repeated recrystallization from acetic acid. m. p. 334°.

2-Hydroxy-6-methoxy-4′, 5′-dihydrofuro (3′ : 2′—3 : 4) quinoline (IV)—This was prepared from *p*-anisidine in a manner similar to that used for 7-isomer (III). A pure sample was recrystallized from ethyl "Cellosolve". m. p. 277°.

Anal. Found: N, 6.31. Calcd. for $C_{12}H_{11}O_3N$: N, 6.45%.

2, 4-Dichloro-3-(β-chloroethyl)-7-methoxyquinoline (VII)—A mixture of III (0.5 g.) and phosphorus oxychloride (5 cc.) was heated under reflux for 1.5 hours. Decomposition of the excessive phosphorus oxychloride with ice gave a solid which was recrystallized from dilute methanol. m. p. 121°.

Anal. Found: N, 4.79. Calcd. for $C_{12}H_{10}ONCl_3$: N, 4.82%.

2, 4-Dichloro-3-(β-chloroethyl)-6-methoxyquinoline (VIII) — This was prepared in the same way as described for 7-isomer (VII). Recrystallization from dilute methanol gave a pure sample. m. p. 118°.

Anal. Found: N, 4.95. Calcd. for $C_{12}H_{10}ONCl_3$: N, 4.82%.

2-Hydroxy-7-methoxy-8-nitro-4′,5′-dihydrofuro (3′ : 2′—3 : 4) quinoline (IX)—To a solution of methoxy-dihydrofuroquinoline derivative III (0.4 g.) in concentrated sulfuric acid (3 cc.) was added powdered potassium nitrate (0.2 g.) in portions with occational cooling. After being kept at 100° for 30 min., the solution was poured into crushed ice. The precipitates were recrystallized from dilute acetic acid. The nitro derivative contained one mole of acetic acid of crystallization. m. p. 256—60° (decomp.).

Anal. Found: C, 51.45; H, 4.47; N, 8.94. Calcd. for $C_{14}H_{14}O_7N_2$: C, 52.17; H, 4.38; N, 8.69%.

The solvent-free sample was obtained by drying over phosphorus pentoxide in vacuo at 100° for 3 hours. m. p. 260° (decomp.).

Anal. Found: C, 54.51; H, 3.76; N, 10.87. Calcd. for $C_{12}H_{10}O_5N_2$: C, 54.96; H, 3.84; N, 10.68%.

2-Hydroxy-7-methoxy-8-amino-4′, 5′-dihydrofuro (3′ : 2′—3 : 4) quinoline (X)—To a solution of dihydrated stannous chloride (1.2 g.) in concentrated hydrochloric acid (4 cc.) was slowly added powdered nitro derivative IX (0.3g.) with occational cooling. The mixture was kept at 50—60° for 20 min., and then bolied gently for 30 min. The solution was made alkaline with 10% sodium hydroxide and the solid was recrystallized from ethyl "Cellosolve". m. p. 312° (decomp.).

Anal. Found: C, 61.80; H, 5.40; N, 11.85. Calcd. for $C_{12}H_{12}O_3N_2$: C, 62.06; H, 5.21; N, 12.06%.

2-Oxo-1, 2, 4′, 5′-tetrahydrofuro (3′ : 2′—3 : 4) quinoline-1, 8-diazoimide (XI)—To a solution of the amino derivative X (0.3 g) in 20% sulfuric acid (6 cc.) was added water (4 cc.), and then 7.5% aqueous solution of sodium nitrite (2 cc.) with constant stirring and cooling with ice-water. The mixture was kept at room temperature for 30 min., and the yellow product was recrystallized from "Cellosolve ethyl." m. p. 226—8° (decomp.). This was a monohydrate.

Anal. Found: N, 16.31. Calcd. for $C_{12}H_{11}O_4N_3$: N, 16.08%.

The anhydrate was obtained by drying over phosphorus pentoxide in vacuo at 100° for 2 hours. m. p. 228° (decomp.).

Anal. Found: N, 17.26. Calcd. for $C_{12}H_9O_3N_3$: N, 17.28%.

2-Hydroxy-7-nitro-8-methoxy-4′,5′-dihydrofuro (3′ : 2′—3 : 4) quinoline (XII) — To a suspension of methoxy-dihydrofuroquinoline derivative II (1 g.) in acetic anhydride (40 cc.) was added a mixture of 60% nitric acid (1 cc.) and glacial acetic acid (4 cc.) under external cooling. The solid went into solution immediately, but soon after, new crystals began to deposit. After 2 hours' standing at room temperature, they were recrystallized from acetic acid. m. p. 260° (decomp.). The sample contained one mole of acetic acid of crystallization.

Anal. Found: C, 52.22; H, 4.51; N, 9.02. Calcd. for $C_{14}H_{14}O_7N_2$: C, 52.17; H, 4.38; N, 8.69%.

The solvent-free sample was obtained by drying over phosphorus pentoxide in vacuo at 100° for 3 hours. m. p. 260° (decomp.).

Anal. Found: C, 54.47; H, 3.92; N, 10.62. Calcd. for $C_{12}H_{10}O_5N_2$: C, 54.96; H, 3.84; N, 10.68%.

The authors are indebted to Mr. A. Kondo for the microanalyses.

Laboratory of Organic Chemistry
Tokyo Institute of Technology
Meguro-ku, Tokyo

*** The furoquinoline derivatives were named as indicated in order to make the numbering accord with that for quinoline derivatives.