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Absorption Spectra of Heterocyclic Compounds. V. Some Substituted 4-Quinolones[1]

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Introduction

A discussion of the influence of the position of hydroxyl groups upon the absorption spectra of quinolinols and isoquinolinols has been presented in the first paper of this series.[2] The behavior of the 4-substituted compound, which was indicated to have the quinoline structure, was sufficiently interesting to warrant an extension of the study. A considerable number of 4-quinolone derivatives were available from other work in these Laboratories.[3-5] All compounds were prepared through use of the synthetic method of Conrad and Limpach,[6] with some recent improvements.[7]

Discussion

A bifurcation in the 320–360 mμ region of the spectra of 4-quinolone and its 2- and 3-methyl homologs was observed when the studies were made in alcoholic solution.[2] This unique character of the 4-quinolones was much less noticeable or absent in the absorption spectra in acidic or basic media. It was of interest to examine the influence of substituents upon the pattern of 4-quinolone spectra. The 3-substituted types were employed not solely because of ready accessibility, but also because certain features in the molecule result in an amplification of fine structure in the spectra.

A comparison of the patterns exhibited by 4-quinolone and the 3-methyl derivative in alcoholic solution[2] shows a definite batho- and hypochromic shifting which is greater than when the alkyl group is in position 2. The bifurcation in the 320–360 mμ region is affected to a varying extent by the steric and electron-repelling effects of the alkyl rest. In the case of the parent compound and the 3-substituted one in alcohol, the second peak of the twin maxima is the greater, while the 2-methyl-4-quinolone spectrum shows a higher maximum around 320 mμ. While 4-quinolone shows a bifurcation in alcohol and *p*H 7 buffer, the spectra in acid and base fail to present this feature. This twinning is absent only with the spectrum in acid for 2-methyl-4-quinolone; however, the related 3-methyl compound exhibits it in alcohol, acid and base. The principal underlying causes of these effects, and also the shoulder around 280–300 mμ presumably resides in the influence of the substituents upon the tautomerism of the quinolinol–quinolone type. It should not be forgotten that the 2-methyl group may also complicate the pattern due to its lability and concomitant effects (Fig. 1). These are also to be observed in chemical behavior of the several types.

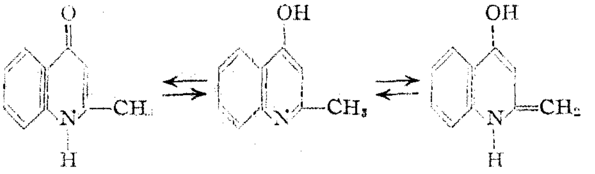

Fig. 1.

The introduction of substituents into the benzene moiety of quinolinone types and the concomitant alterations in spectral characteristics is closely akin in form to our earlier studies on aminoquinolines[8] and certain 4-aminoquinoline derivatives.[9] The comparison of the spectra of the 4-quinolone types was carried out using alcoholic solutions because the greatest amount of structural resolution was found in that solvent. The characteristic bifurcations in the short wave range (below 260 mμ) are approximately the same for the bz-methyl- and bz-chloro-3-methyl-4-quinolones (Figs. 2 and 3). The chloro-3-methyl types show a constant bathochromic shift of 6 mμ when compared with the corresponding dimethyl compounds. It should be noted that the resolution of spectral characteristics is more pronounced with the more electrophilic chloro group. This is not only true for the doublet peaks in the 320–360 mμ region, but also for the inflection which occurred around 280–300 mμ in the case of the parent 4-quinolone. While the inflection does become a true secondary maximum with the introduction of a 3-methyl group, substitution of the benzenoid ring results in marked alterations in form. The positions being considered *in toto*, we notice that the most profound change occurs when the methyl or the chloro group is introduced into position 7. The character of the alkyl substituent would be expected to result in less influence upon the tautomerism than the more electron-attracting halogen. This is indeed the case, as has been shown in Figs. 2 and 3. In all instances, the resolution of the dimethyl compounds is less marked than of the 3-methyl-bz-chloro compounds. There is not only a greater

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[2] Ewing and Steck, THIS JOURNAL, **68**, 2181 (1946).

[3] Steck, Hallock and Holland, *ibid.*, **68**, 129, 131, 380 (1946).

[4] Steck and Hallock, forthcoming publication.

[5] Surrey and Cutler, THIS JOURNAL, **68**, 2570 (1946).

[6] Conrad and Limpach, *Ber.*, **20**, 944 (1887); Limpach, *ibid.*, **64**, 969 (1931).

[7] Steck, Hallock and Holland, THIS JOURNAL, **68**, 1241 (1946).

[8] Steck and Ewing, *ibid.*, **70**, 3397 (1948).

[9] Steck, Ewing and Nachod, *ibid.*, **70**, 3410 (1948).

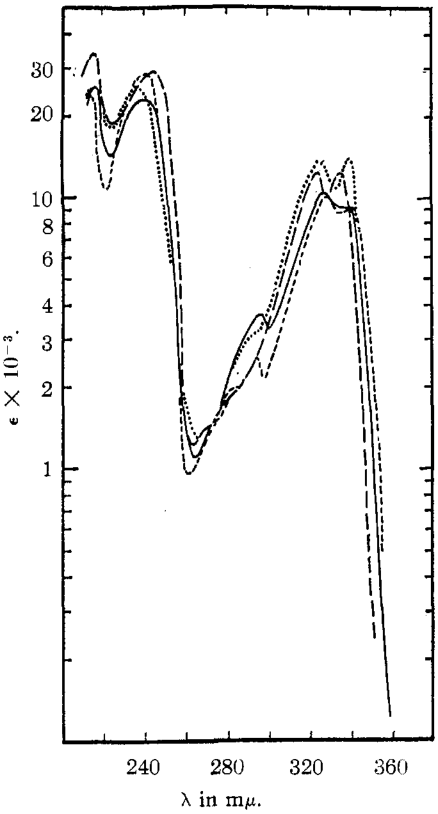

Fig. 2.—Absorption spectra of: —, 3,5-dimethyl-4-quinolone; - - - -, 3,6-dimethyl-4-quinolone; — —, 3,7-dimethyl-4-quinolone; ......, 3,8-dimethyl-4-quinolone; in 95% ethanol.

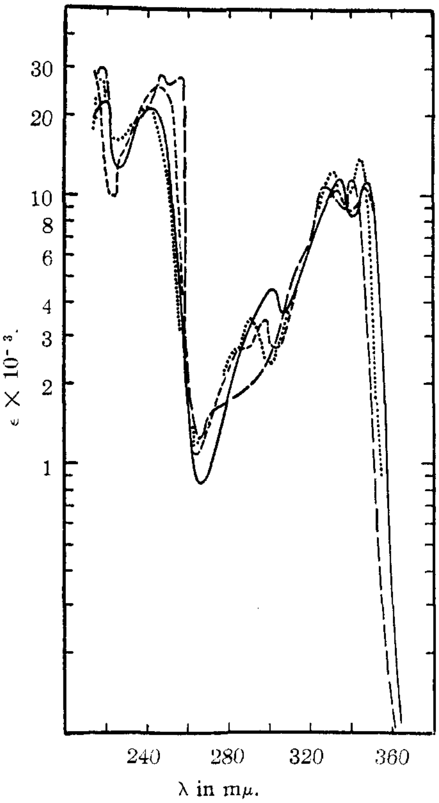

Fig. 3.—Absorption spectra of: —, 5-chloro-3-methyl-4-quinolone; - - - -, 6-chloro-3-methyl-4-quinolone; — —, 7-chloro-3-methyl-4-quinolone; ....., 8-chloro-3-methyl-4-quinolone; in 95% ethanol.

retention of the secondary maximum in the 280–300 mμ region throughout, but also the 7-chloro-3-methyl-4-quinolone exhibits an additional feature of structure in the twinning of the peak in the 240–260 mμ region. The importance of the position of a nucleophilic grouping is apparently less marked than an electrophilic rest. The substituent in the benzene ring influences the state in a molecule through resonance effects, and also the dipoles which are associated with its location (Fig. 4). It is in position 7 of the 4-quinolones that the grouping might well prove to be of greater importance than in positions 5, 6 or 8. An analogous effect has been indicated for derivatives of 4-aminoquinoline.[9,10] The combination of these influences appear to be responsible factors in the poorly developed character in the 3,8-dimethyl-4-quinolone spectrum.

The extent of the influence of a halo substituent is brought into focus when a comparison is made of the spectra of 3-methyl, 3,5-dimethyl, and 3,5-dichloro-4-quinolones, all in alcoholic solution (Fig. 5). While the additional alkyl group in position 5 does cause a slight batho- and hyperchromic shifting, the 3,5-dimethyl compound shows a decrease in the second peak of the bifurcation in the 320–360 mμ region. This may well be due to steric effects. The 3,5-dichloro-4-quinolone exhibits the expected characteristics resulting from the electrophilic halogen substituents. The entire spectrum is bathochromically shifted, and, for the most part, also a displacement is noted. Of particular interest is the batho- and hyperchromic shifting of the secondary maxima in the 290 mμ region with increase in nucleophilic substitution.

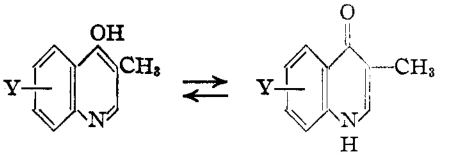

Fig. 4.

In Fig. 6, the spectra of five bz-alkoxy-3-methyl-4-quinolones are compared. The differences in effect of the methoxy and ethoxy groupings are but slight, as is to be seen in the figure. The 7-ethoxy-3-methyl-4-quinolone is unique in the lack of a secondary maximum in the 260–320 mμ region. Actually there are two secondary maxima in the case of both the 6-methoxy and 6-ethoxy compounds, whereas the 8-methoxy shows an inflection and the 8-ethoxy-

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(10) Irvin and Irvin, THIS JOURNAL, **69**, 1091 (1947).

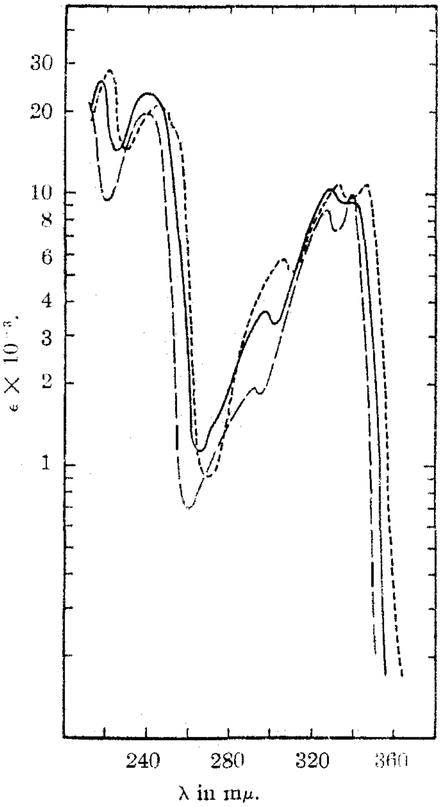

Fig. 5.—Absorption spectra of: — —, 3-methyl-4-quinolone; —, 3,5-dimethyl-4-quinolone; ....., 3,5-dichloro-4-quinolone; in 95% ethanol.

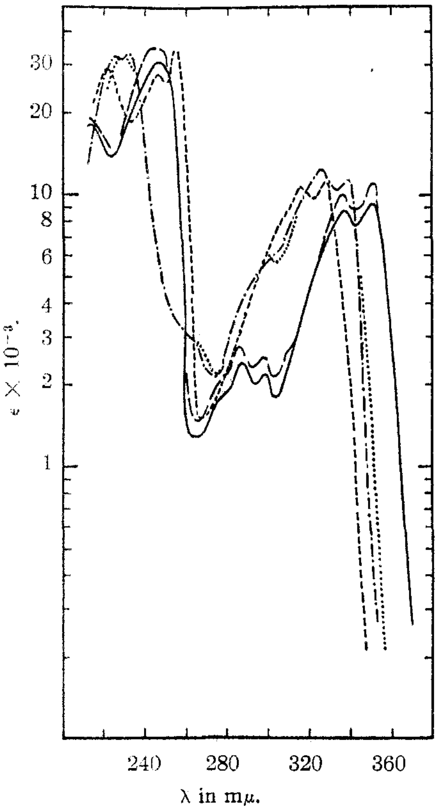

Fig. 6.—Absorption spectra of: —, 6-methoxy-3-methyl-4-quinolone; — —, 6-ethoxy-3-methyl-4-quinolone; - - -, 7-ethoxy-3-methyl-4-quinolone; —·—, 8-methoxy-3-methyl-4-quinolone; ....., 8-ethoxy-3-methyl-4-quinolone; in 95% ethanol.

3-methyl-4-quinolone a slight singular inflection apart from the related methoxy analog. All of the alkoxy compounds show the characteristic bifurcations in the 300–360 mμ region. The 6- and 8-alkoxy-substituted 3-methyl-quinolones are bathochromically shifted with respect to the 7-ethoxy derivative. While there is little difference in the patterns presented by the methoxy and ethoxy compounds when the substituent is in position 8, the influence of the additional methylene group in the alkoxy substituent is made apparent when that rest is in position 6. The passage from 6-methoxy-3-methyl-4-quinolone to the 6-ethoxy analog results in a definite hyperchromic intensification of all maxima.

The evidence presented concerning the spectra of the disubstituted 4-quinolones indicates that the 7-position of the molecule is exceptional in its influences. This is in agreement with our earlier observations.[9]

Experimental

I. **4-Quinolones.**—The preparation of the requisite compounds has been described in detail in contributions relating to 4-substituted quinoline types.[3–5]

II. **Absorption Spectra.**—All spectra were determined with a Beckman Quartz Spectrophotometer, Model DU, Serial No. D-377. The method has been indicated in the first paper of this series.[2]

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Summary

The absorption spectra of fourteen disubstituted 4-quinolones have been determined and the effects of substitution discussed critically.

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