733. *Ultra-violet Absorption Spectra of Some Derivatives of Quinoline, Quinazoline, and Cinnoline.*

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The absorption spectra of 4-hydroxy-, 4-hydroxy-6-nitro-, and 4-amino-quinolines have been compared with those of related compounds of fixed structure. Similar investigations have been made on quinazoline and cinnoline derivatives. The absorption curves show that, when alternative formulations are possible, quinolone, quinazolone, and cinnolone structures are either predominant or at least important.

The absorption spectrum of α-naphthol (Ewing and Steck, *J. Amer. Chem. Soc.*, 1946, **68** 2181) is a convenient starting point for the present work. The structures (I) and (III) in resonance with (II), which involve separation of charges, contribute little to absorption in neutral solution. In alkaline solutions the corresponding quinonoid forms (IV) and (VI) contribute strongly to the resonance and account for the bathochromic effect in passing from neutral to alkaline solution. Thus, in 95% ethanol $\lambda_{max.}$ occurs at 2350 A. and 2800 A. with typical naphthalenic narrow bands in the region 3000—3250 A., whereas in 0·01N-sodium hydroxide the main peaks occur at 2480 and 3400 A.

(I.) (II.) (III.) (IV.) (V.) (VI.)

In solutions of quinoline the non-polar structures are more important than the polar structures, again because of separation of charges, but the quinolinium ion formed on acidification, with its positive charge, makes probable a number of resonance forms accounting for a bathochromic displacement. Thus, in 95% ethanol $\lambda_{max.}$ is at 2780 ($\varepsilon_{max.}$ 3500), whereas in 0·01N-hydrochloric acid $\lambda_{max.}$ occurs at 3150 A. ($\varepsilon_{max.}$ 7000). In alkaline solution there is little change as compared with neutral solution.

A similar shift occurs with *iso*quinoline and 5-hydroxy*iso*quinoline, except that alkali, too, effects a change in the spectrum of the latter.

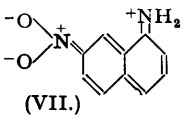
In 8-hydroxyquinoline the spectrum of the neutral solution is displaced in both 0·1N-hydrochloric acid and 0·01N-sodium hydroxide, whereas the curves for 8-methoxyquinoline agree with those of the parent substance except that there is no bathochromic effect in an alkaline

medium. There appears to be no hydrogen bridging, since the 8-hydroxy- and 8-methoxy-compounds do not differ in neutral or acid solutions.

On the other hand, 1-hydroxy*iso*quinoline (1-*iso*quinolone) shows practically the same absorption spectrum in ethanol, dilute acid, or alkali and resembles 2-methyl-1-*iso*quinolone so closely as to fix the structure (of the parent substance) as *iso*quinolone. The absence of bathochromic effects leads to the broad conclusion that " those quinoline and *iso*quinoline derivatives which have the hydroxyl substituted in the pyridine ring in the α- or γ-positions relative to the nitrogen may be written as ketonic compounds " (Ewing and Steck, *loc. cit.*).

The quinolone structure for 2-hydroxyquinoline (carbostyril) was already established by comparison of the spectra of the parent substance with those of the *O*-methyl ether and the *N*-methyl ether (Morton and Rogers, *J.*, 1925, **127**, 2698; Ault, Hirst, and Morton, *J.*, 1935, 653).

Mononitronaphthylamines, *e.g.*, 1-amino-7-nitronaphthalene (VII) (pK_a 2·93), exhibit quinonoid contributions (Hodgson and Hathway, *Trans. Faraday Soc.*, 1945, **41**, 115; 1947, **43**, 643; Bryson, *ibid.*, 1949, **45**, 257).


(VII.)

The possibility that 4-aminoquinoline may exist as the imino-form has been clearly recognized, but decisive evidence to show that it does in fact so exist under ordinary conditions has not yet been obtained (cf. Albert and Goldacre, *Nature*, 1944, **153**, 167; Irvin and Irvin, *J. Amer. Chem. Soc.*, 1947, **69**, 1091; Steck and Ewing, *ibid.*, 1948, **70**, 3397). The case of 5-aminoacridine, which might offer an analogy, is also unsettled (Albert and Ritchie, *J.*, 1943, 458; Craig and Short, *J.*, 1945, 419; Wilkinson and Finar, *J.*, 1946, 115).

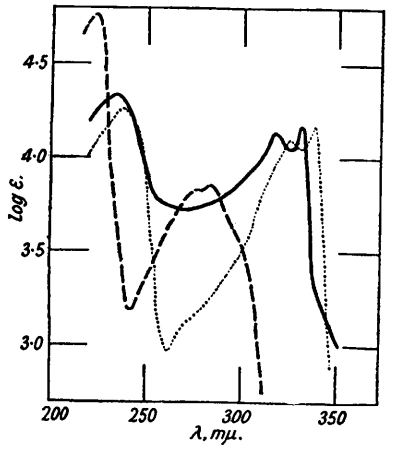
TABLE I.

Quinoline derivatives. $\lambda_{max.}$ (A.) *and* log $\varepsilon_{max.}$.

4-Hydroxyquinoline	3315 4·18	3175 4·15	2335 4·35					3260 4·06	2720 3·74		
1-Methyl-4-quinolone	3380 4·18	3250 4·11	2370 4·27					3310 4·06	2605 2·97		
4-Methoxyquinoline	~2950 3·60	2830 3·86	2755 3·83	2255 4·78				2415 3·18			
4-Hydroxy-6-nitro-quinoline	3500 3·87	~3220 3·81	2650 4·10					2900 3·4	2455 3·86		
1-Methyl-6-nitro-4-quinolone	3580 3·92	3260 3·94	2660 4·12					3445 3·89	2920 3·41	2495 3·93	
4-Methoxy-6-nitro-quinoline	3430 3·64	2990 3·90	2660 4·37					3230 3·52	2780 3·75		
6-Nitro-4-phenoxy-quinoline	3415 3·65	2960 3·94	2570 4·36					3220 3·54	2815 3·80	2330 4·12	
4-Hydroxyquinoline-3-carboxylic acid	~3215 3·95	3100 4·07	~3005 4·02	~2530 4·27	2410 4·36			2665 3·38	2355 4·34		
4-Hydroxy-6-methoxy-quinoline-3-carboxylic acid	~3450 3·63	~3260 3·86	3100 3·92	~2900 3·80	2590 4·33	2500 4·39	2380 4·38	2760 3·66	2560 4·28	2425 4·32	
4-Aminoquinoline	3200 4·01	2330 4·28						2660 2·98			
5-Aminoquinoline	3550 3·48	2520 4·42						2890 2·95			
6-Aminoquinoline	3575 3·58	2880 3·59	2460 4·56					3130 3·09	2745 3·57		
4-Acetamidoquinoline	3135 3·85	2985 3·98	2265 4·65					2585 3·40			
4-Anilinoquinoline	3360 4·16	2440 4·34						2790 3·29	2335 4·29		
4-Amino-6-nitroquinoline	3920 3·75	3240 3·65	2790 4·36					3460 3·38	3085 3·59	2450 3·85	
4-Acetamido-6-nitroquinoline	3535 3·64	3055 3·94	2640 4·27	2255 4·40				3295 3·53	2860 3·80	2400 4·05	
4-Anilino-6-nitroquinoline	3980 3·94	3355 3·73	2835 4·26	2500 4·35				3540 3·58	3135 3·63	2690 4·18	2420 4·32
4-Chloro-6-nitroquinoline	2940 3·91	2530 4·62						2740 3·78			

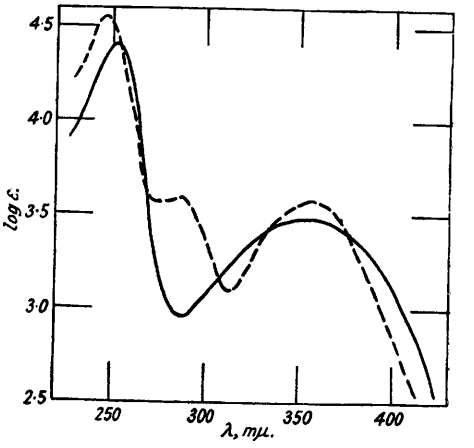
A series of investigations (Simpson *et al.*, *J.*, 1942, 353; 1943, 447; 1945, 512, 520; 1946, 480, 1035; 1947, 227, 232, 237; 1948, 354, 358, 360, 1170, 1702, 1707) has made available a range of compounds suitable for spectrophotometric study. We wish to associate with these

FIG. 1.



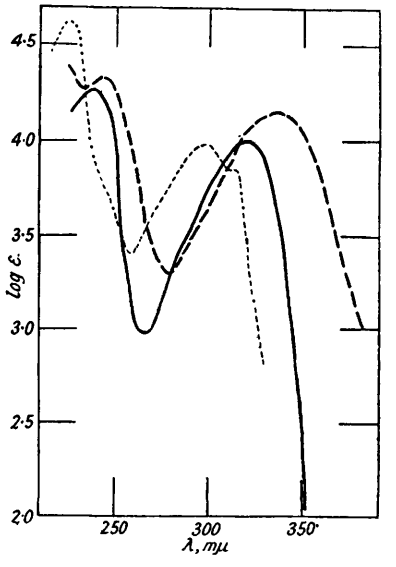
Absorption curves for: ——— 4-*hydroxyquinoline*, – – – – 4-*methoxyquinoline*, ... 1-*methyl*-4-*quinolone*.

FIG. 2.



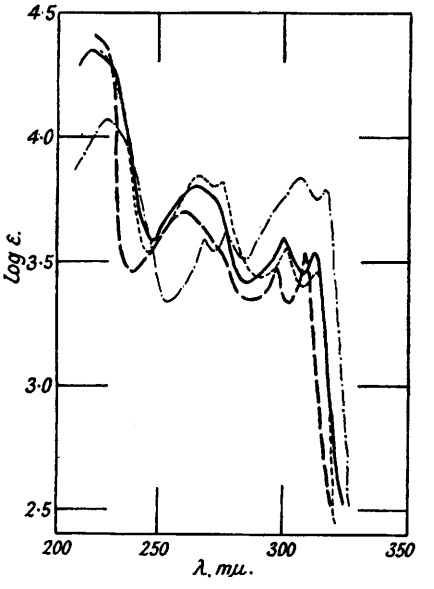
Absorption curves for: ——— 5-*aminoquinoline*, – – – – 6-*aminoquinoline*.

FIG. 3.



Absorption curves for: ——— 4-*aminoquinoline*, ——— ——— 4-*anilinoquinoline*, – – – – 4-*acetamidoquinoline*.

FIG. 4.



Absorption curves for: ——— 4-*hydroxyquinazoline*, ——— · ——— · ——— 1-*methyl*-4-*quinazolone*, – – – – 3-*methyl*-4-*quinazolone*, ——— ——— ——— 4-*methoxyquinazoline*.

studies the names of our colleagues, Drs. C. M. Atkinson, J. S. Morley, and K. Schofield, Mr. J. R. Keneford, and Mr. P. H. Wright, to whom our best thanks are due for the preparation of the majority of the samples used in this work.

Quinoline Derivatives.—Table I summarises the data for quinoline derivatives. Fig. 1 shows that the spectrum of 4-hydroxyquinoline resembles that of 1-methyl-4-quinolone very

closely and is very different from that of 4-methoxyquinoline. The relatively high absorption between 2500 and 3000 A. would, however, be consistent with some contribution from the hydroxy-form, although the quinolone structure is evidently the important one.

Similarly (see Table I) 4-hydroxy-6-nitroquinoline, with its absorption strikingly similar to that of 1-methyl-6-nitro-4-quinolone and quite dissimilar from that of 4-methoxy-6-nitro- (or 6-nitro-4-phenoxy)-quinoline, is clearly a quinolone.

Introduction of a carboxyl group to give 4-hydroxyquinoline-3-carboxylic acid results in a rather small bathochromic shift as compared with 4-methoxyquinoline, but from the spectra it seems probable that the carboxyl group in position 3 inhibits the formation of a quinolone Introduction of a methoxy-group in position 6 displaces the spectrum without apparently changing its character.

In the aminoquinolines, the 5- and 6-amino-compounds, with $\lambda_{max.}$ about 3550 A. (log $\varepsilon_{max.}$ *ca.* 3·5), are very different from 4-aminoquinoline (Figs. 2 and 3). The spectrum of the latter resembles that of 4-hydroxyquinoline which, as already stated, is essentially quinolone in structure, and it therefore follows that an imino-structure must be ascribed to 4-aminoquinoline. 4-Anilinoquinoline gives a spectrum like that of 4-aminoquinoline but slightly displaced in the direction of longer wave-lengths and is probably "quinolone" in structure; 4-amino- and 4-anilino-6-nitroquinoline are very different in spectra from 4-chloro-6-nitroquinoline, the latter being clearly a quinoline in structure. On the other hand, although the argument from analogy is not infallible, it seems likely that 4-acetamido- and 4-acetamido-6-nitro-quinoline resemble in spectra 4-methoxy- and 4-methoxy-6-nitro-quinoline closely enough to exclude quinonoid structures.

TABLE II.

Quinazoline derivatives. $\lambda_{min.}$ (A.) *and* log $\varepsilon_{min.}$.

4-Hydroxyquinazoline	3130	3005	2650	2235		3080	2860	2480	
	3·54	3·60	3·81	4·36		3·45	3·41	3·59	
1-Methyl-4-quinazolone	3170	3065	2775	2690	2300	3140	2850	2725	2545
	3·79	3·84	3·63	3·60	4·08	3·76	3·52	3·55	3·34
3-Methyl-4-quinazolone	3135	3015	2760	2670	2300	3080	2910	2730	2475
	3·46	3·56	3·82	3·85	4·35	3·40	3·44	3·81	3·54
4-Methoxyquinazoline	3090	2975	2610	2250		3030	2870	2395	
	3·54	3·48	3·71	4·42		3·34	3·35	3·46	
4-Phenoxyquinazoline	3100	2980	2635			3040	2900	2430	
	3·62	3·57	3·79			3·54	3·50	3·72	
4-Hydroxy-6-nitroquinazoline	3165					2700			
	4·01					3·38			
1-Methyl-6-nitro-4-quinazolone	3220					2740			
	4·02					3·56			
3-Methyl-6-nitro-4-quinazolone	3175	2226				2710			
	4·14	4·41				3·35			
4-Methoxy-6-nitroquinazoline	~3250	2950				2545			
	3·64	3·91				3·59			
6-Nitro-4-phenoxyquinazoline	2985					2685			
	3·94					3·73			
4-Aminoquinazoline	~3290	3245	3130	2840	~2400	2990	2540		
	3·60	3·67	3·83	3·86	4·14	3·71	3·51		
4-Acetamidoquinazoline	3140	2810	2430			2970	2646	2380	
	3·86	3·82	4·15			3·63	3·73	4·10	
4-Anilinoquinazoline	3330	2940	2345			3025	2690	2285	
	4·19	3·90	4·16			3·88	3·75	4·13	
4-Amino-6-nitroquinazoline	3320	2550				2850	2430		
	3·92	4·24				3·38	4·15		
4-Acetamido-6-nitroquinazoline	3310	2520				2840	2410		
	3·92	4·17				3·61	4·06		
4-Anilino-6-nitroquinazoline	3640	2395				3025			
	4·04	4·41				3·60			

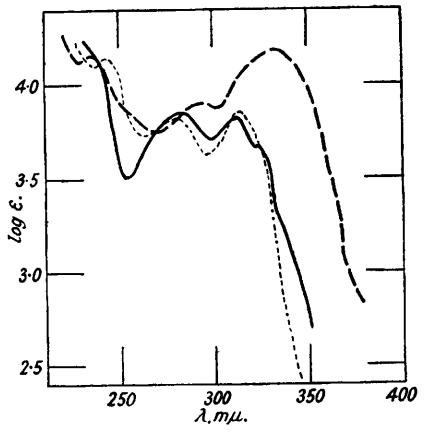
Quinazoline Derivatives.—The absorption curve for quinazoline shows maxima near 3100 (log ε 3·3) and 2700 A. (log ε 3·35) with very intense absorption (log ε 4·5) near 2200. The spectra of a number of substituted compounds are recorded in Table II. The curve for 4-methoxyquinazoline (Fig. 4) shows sharp maxima near 3090 and 2975 A. (log ε *ca.* 3·5) and

2610 A. (log ε 3·71). Now among the possible structures for 4-hydroxyquinazoline are (VIII)—(X). From the spectra of the methyl-substituted derivatives of fixed structure the following approximate molecular extinction coefficients would be expected (Fig. 4).

λ (A.):	*ca.* 3100	3000	2760	2650	2610	2300
(VIII)	3430	3000	—	—	5100	26000
(IX)	6200	6900	4200	4000	—	12000
(X)	2900	3600	6700	7000	—	22000
Observed	3460	3980	—	6460	—	22800

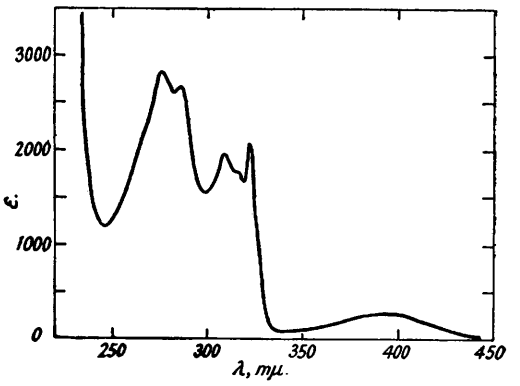
Since the observed ε value at 3000 A. is greater than that at 3100, (VIII) cannot be the exclusive structure. It is equally clear that neither (IX) nor (X) can be the sole structure. Is, therefore, (VIII) in equilibrium with (IX) or (X) or both? The ε values for (X) are clearly too low to account for the rise near 3000 A. which requires some of (IX). In the region 2600—2650 A. the evidence points, on the other hand, to (VIII) and (X) being in equilibrium. The intensities at 2300 A. would fit with a small amount of (VIII) being present, but would not

FIG. 5.



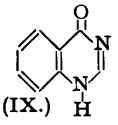
Absorption curves for: ——— 4-*aminoquinazoline*, – – – – 4-*acetamidoquinazoline*, ——— ——— ——— 4-*anilinoquinazoline*.

FIG. 6.

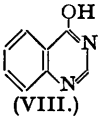


Absorption curve for cinnoline (*in* cyclo*hexane*).

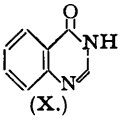
exclude both (IX) and (X) being present. So far as the argument goes all three structures are possible and indeed probable.



(IX.)



(VIII.)



(X.)

By taking the intensities of the two long-wave peaks and solving simultaneous equations, structures (VIII), (IX), and (X) appear to be present to the extent of 17·8, 14·4, and 67·8%, respectively. By taking the peaks near 2230 and 2700 A. the corresponding figures are 23, 4, and 73%. Careful inspection of the curves shows that the curve for 4-hydroxyquinazoline could be accounted for if it were (X) to the extent of 70 ± 2·5% and (IX) 10 ± 5% and (VIII) 20 ± 2·5%.

The whole argument may however be weakened by second-order effects of methylation on ε values.

The corresponding 6-nitroquinazoline derivatives quite strongly favour a structure for 4-hydroxy-6-nitroquinazoline resembling that of 3-methyl-6-nitro-4-quinazolone with very little of the quinazoline alternative. 4-Phenoxyquinazoline shows a spectrum very closely similar to that of the 4-methoxy-compound.

In the case of 4-aminoquinazoline the data indicate a quinazoline rather than a quinazolone structure. Thus, 4-acetamidoquinazoline differs little from the 4-amino-compound (Fig. 5).

4-Amino-6-nitroquinazoline shows a spectrum much closer to that of the 4-methoxy-6-nitroquinazoline than that of the two quinazolones.

Cinnoline Derivatives.—The absorption curve of cinnoline (Fig. 6) does not appear to have been obtained before. There is first a weak maximum at 3900 A. (ε 265) which may well owe its origin to the presence of the $-N{=}N-$ group in the molecule. The three maxima at 3085, 3170, and 3225 A. (ε values 1960, 1770, and 2080, respectively) seem to belong to one band system and are reminiscent of naphthalene. The two maxima at 2755 and 2860 A. are more intense (ε 2820 and 2650, respectively) and there is intense absorption below 2300 A. The curve was obtained in *cyclo*hexane.

TABLE III.

Cinnoline derivatives. $\lambda_{min.}$ (A.) *and* log $\varepsilon_{min.}$

4-Hydroxycinnoline	3520	3430	3380	2960	2845	2620	3490	3010	2905	2740	2600
	4·09	4·10	4·14	3·43	3·44	3·85	4·01	3·31	3·36	3·32	3·84
	2550	2370					2460				
	3·95	4·05					3·87				
1-Methyl-4-cinnolone	3690	3520	2515				3590	2890	2390		
	4·11	4·11	3·95				4·00	3·05	3·80		
4-Methoxycinnoline	3130	2910	2240				3040	2580			
	3·65	3·74	4·57				3·55	3·26			
4-Phenoxycinnoline (in *cyclo*hexane)	3230	~3200	3105	2925	2825	2250	3160	3040	2860	2535	
	3·69	3·66	3·64	3·82	3·80	4·68	3·59	3·56	3·79	3·33	
4-Ethoxycinnoline (in *cyclo*hexane)	3625	3215	3180	3100	2905	2800	3420	3195	3160	3025	2850
	2·67	3·57	3·42	3·43	3·79	3·79	3·55	3·40	3·40	3·37	3·77
≃3930, 3900, 3830, 3770							2810				
							3·24				
4-Hydroxy-6-nitrocinnoline	3645	3245	2670	2360			3350	2910	2560		
	4·09	3·94	3·97	4·16			3·85	3·40	3·94		
1-Methyl-6-nitro-4-cinnolone	3700	3280	2695	2410			3400	2940	2625		
	4·11	3·97	3·91	4·22			3·80	3·37	3·89		
4-Methoxy-6-nitrocinnoline	3535	3000	2905	~2550	2430		3130	2960	2820		
	3·73	3·68	3·74	4·19	4·28		3·26	3·66	3·64		
6-Nitro-4-phenoxycinnoline	3535	2895	2540				3150	2815	2495		
	3·76	3·79	4·08				3·39	3·75	4·05		
4-Hydroxy-3-methylcinnoline	3585	3475	2920	2810	2500	2375	3530	3025	2875	2730	2470
	4·03	4·06	3·52	3·52	3·97	4·08	3·97	3·09	3·40	3·31	3·93
3-Ethyl-4-hydroxycinnoline	3575	3440	2915	2825	2495	2375	3525	3015	2820	2715	2470
	4·06	4·07	3·62	3·59	4·01	4·12	4·01	3·18	3·50	3·40	3·98
4-Hydroxy-6 : 7-dimethylcinnoline	3620	3470	2895				3580	3060	2820		
	3·91	3·99	3·40				3·89	3·25	3·32		
4-Hydroxy-3-methyl-6-nitrocinnoline	3760	3255	~2700	2385			3400	2890			
	4·21	4·04	3·97	4·32			3·90	3·45			
4-Hydroxycinnoline-3-carboxylic acid	~3540	~3460	3390	2630	~2380		2850	2530			
	3·97	4·04	4·10	3·87	4·05		3·28	3·69			
4-Hydroxy-6-methoxycinnoline-3-carboxylic acid	3520	2545					2870	2420			
	4·08	4·30					3·22	4·20			
4-Hydroxy-6 : 7-methylenedioxycinnoline	3580	3485	3410	2925	2650	2565	3525	3455	2980	2810	2610
	4·19	4·10	4·16	3·43	4·22	4·25	4·08	4·07	3·42	3·36	4·13
	2450	2370					2510	2410			
	4·22	4·20					4·19	4·20			
3-Chloro-4-hydroxy-6-methylcinnoline	3515	2990	2880	2435			3090	2955	2765		
	4·07	3·66	3·63	4·16			3·28	3·52	3·44		
6-Bromo-3-chloro-4-hydroxycinnoline	3675	3510	3030	2910	2495		3595	3140	2965	2735	2260
	4·04	4·01	3·87	3·78	4·31		3·96	3·40	3·04	3·29	3·86
3 : 6-Dibromo-4-hydroxycinnoline	3690	3500	3040	2910	2530		3610	3140	2990	2730	2265
	4·05	4·01	3·94	3·82	4·31		3·97	3·42	3·70	3·30	3·89
Methyl 4 : 6 : 7-trimethoxy-3-cinnolylacetate	3640	3510	2940	2700	2620	2345	3560	3025	2880	2650	2530
	4·14	4·14	3·43	4·35	4·31	4·39	4·09	3·32	3·42	4·27	4·13
Methyl 6 : 7-dimethoxy-1-methyl-3-cinnolon-4-ylacetate	3790	3630	2810	2730	2405		3700	2965	2770	2610	
	4·18	4·14	4·15	4·16	4·58		4·08	3·26	4·13	4·00	
Tetrahydro-4 : 6-diketocinnoline 6-oxime methyl ether *N*-oxide	3990	3355	3220	~2800	2585	~2360	3440	3280	3100	2310	
	4·11	3·60	3·49	3·82	4·20	3·94	3·45	3·51	3·30	3·86	

TABLE III.—(*continued*).

4-Acetoxy-3-chloro-6-methylcinnoline	3515 4·05	2645 4·18	2470 4·32		3050 3·23	2590 4·12		
4-Acetoxy-3-chloro-6 : 7-dimethylcinnoline	3490 4·09	3075 3·59	2675 4·22	2460 4·34	3135 3·56	2930 3·50	2610 4·19	2300 4·00
4-Acetoxy-6-nitrocinnoline	3620 3·96	3235 4·05	2630 4·10	2360 4·20	3400 3·88	2910 3·57	2540 4·04	
4-Acetoxy-6-chlorocinnoline	3465 4·12	3000 3·55	2460 4·33		3050 3·48	2940 3·53		
4-Aminocinnoline	3450 4·06	2400 4·10			2750 2·99			
4-Acetamidocinnoline	3285 3·87	3035 3·90	~2510 3·64	2260 4·63	3135 3·80	2695 3·39		
4-Anilinocinnoline	3640 4·18	2480 4·16			2900 3·30	2360 3·99		
4-Amino-6-nitrocinnoline	4020 3·91	3265 3·72	2720 4·17	2552 4·20	3495 3·46	3010 3·43	2635 4·11	2425 4·04
4-Acetamido-6-nitrocinnoline	3620 3·86	3050 3·86	2600 4·23	2290 4·7	3245 3·48	2870 3·7	2550 4·18	
4-Anilino-6-nitrocinnoline	4180 4·07	3435 3·79	2780 4·07	2470 4·39	3610 3·60	3160 3·60	2730 4·05	

4-Ethoxycinnoline has been examined in detail in *cyclo*hexane solution (Fig. 7). There is first a region of low absorption with a maximum near 3625 A. and inflexions at 3770, 3830, 3900, and 3930 A. indicative of vibrational structure (with perhaps a frequency difference of about 450 cm.$^{-1}$). There is next a group of three maxima of moderate intensity, $\lambda_{max.}$ 3100, 3180, and 3215 A.; these bands clearly have their counterparts in the cinnoline spectrum but the ε values are appreciably raised as a result of substitution. The next group consists of two peaks at 2800 and 2905 A. which are increased in intensity about two-fold compared with the corresponding peaks in the cinnoline curve. As in cinnoline, there is a deep minimum near 2500 A. and the curve rises sharply, indicating very intense absorption beyond 2300 A. 4-Methoxy- and 4-phenoxy-cinnoline in ethanol and in *cyclo*hexane are essentially similar except that solubilities do not always allow quite so full a set of measurements. This type of substitution does not seriously affect the positions of maxima on the wave-length scale, but the probabilities of the relevant electronic transitions are all increased by the substitution.

1-Methyl-4-cinnolone (Fig. 8) shows twin maxima at 3520 and 3690 A. with a marked inflexion near 3300 A. (Δ cm.$^{-1}$ 1309). There is a very low minimum at 2890 A. and a new maximum near 2515 A.

4-Hydroxycinnoline shows maxima at 3380 (~3430) and 3520 A. (Δ cm.$^{-1}$ *ca.* 1200). These bands clearly correspond with the long-wave bands of 1-methyl-4-cinnolone. Two maxima at 2845 and 2965 A. quite clearly correspond with the 2800 and 2905 A. maxima of 4-ethoxycinnoline and the 2910 A. band of 4-methoxycinnoline. 4-Ethoxycinnoline has a minimum at 2510 A. and 1-methyl-4-cinnolone has a maximum at 2515 A. 4-Hydroxycinnoline also shows a maximum near 2550 A. of low persistence.

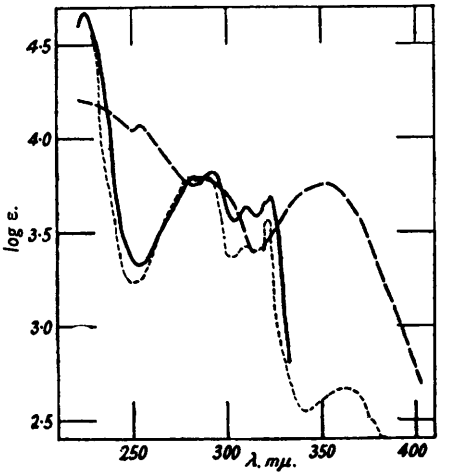
It is clear that 4-hydroxycinnoline in ethanol is in equilibrium with its tautomer, but it is not possible, from the information available, to calculate the proportions precisely. The displacement of the curve of 4-hydroxycinnoline which appears in 1-methyl-4-cinnolone (3380—3520 A.; 3520—3690 A.) is not negligible and the basis of calculating the proportions of isomerides from absorption intensities at 2900 A. is to assume that the minimum for the cinnolone tautomer of 4-hydroxycinnoline agrees in position with that of the homologous 1-methyl-4-cinnolone. However, there may well be 30% of 4-hydroxycinnoline. As judged from the regions near 3500 and 2500 A., the cinnolone tautomer obviously preponderates. The intensity of absorption of this entity would need to be greater than that of 1-methyl-4-cinnolone to make the spectra completely consistent.

Substitution of methyl groups in 4-hydroxycinnoline in positions 3, 6, and 7 makes practically no difference in the spectrum which remains consistent with some 70% of cinnolone and 30% of cinnoline. The same applies to introduction of an ethyl group in position 3. The compound 4-hydroxy-6 : 7-methylenedioxycinnoline is preponderately of cinnolone type.

A specially simple spectrum is shown by 4-hydroxycinnoline-3-carboxylic acid. The 3380, 3430, and 3520 A. selective absorption of 4-hydroxycinnoline is shown practically un-

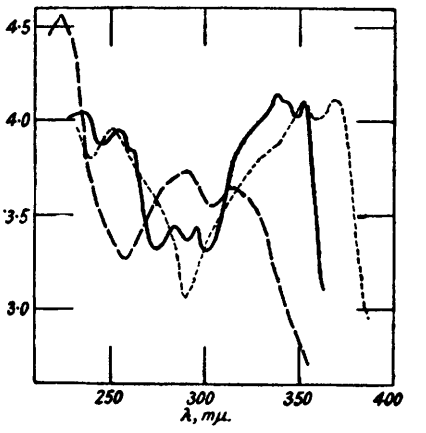
changed and there is a deep minimum near 2850 A. and a maximum near 2630 A. The carboxylic acid is unequivocally a cinnolone. The same applies to 4-hydroxy-6-methoxycinnoline-3-carboxylic acid.

FIG. 7.



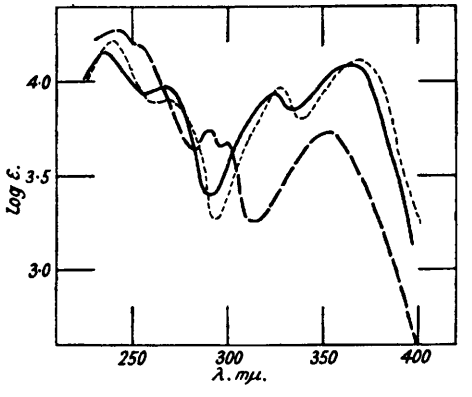
Absorption curves for: ——— 4-*phenoxycinnoline*, – – – – 4-*ethoxycinnoline*, —— —— —— 6-*nitro*-4-*phenoxycinnoline*.

FIG. 8.



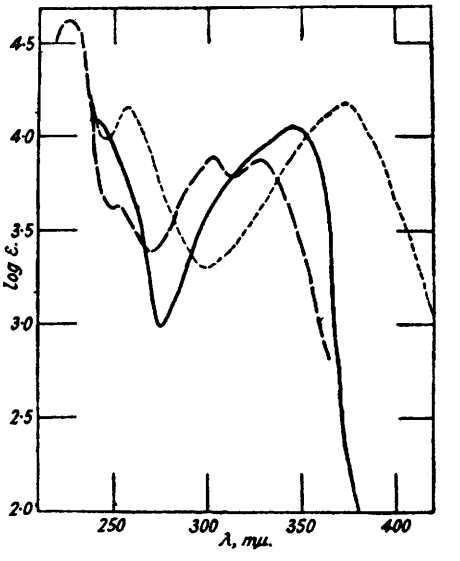
Absorption curves for: ——— 4-*hydroxycinnoline*, —— —— —— 4-*methoxycinnoline*, – – – – 1-*methyl*-4-*cinnolone*.

FIG. 9.



Absorption curves for: ——— 4-*hydroxy*-6-*nitrocinnoline*, —— —— —— 4-*methoxy*-6-*nitrocinnoline*, – – – – 1-*methyl*-6-*nitro*-4-*cinnolone*.

FIG. 10.



Absorption curves for: ——— 4-*aminocinnoline*, —— —— 4-*acetamidocinnoline*, – – – – 4-*anilinocinnoline*.

Inspection of the curves of the halogen-substituted cinnolines 3-chloro-4-hydroxy-6-methylcinnoline, 6-bromo-3-chloro-4-hydroxycinnoline, and 3 : 6-dibromo-4-hydroxycinnoline suggests the co-existence of cinnolines and cinnolones in equilibrium. The minimum near 2900 A. has disappeared and the two strong bands of the cinnoline structure are clearly seen.

An interesting extension of the argument is seen in the spectra of the 6-nitro-derivatives (Fig. 9).

1-Methyl-6-nitro-4-cinnolone agrees very closely with 4-hydroxy-6-nitrocinnoline, which must therefore be a cinnolone. The *N*-methyl compound shows only a small bathochromic

shift. The 2900 A. minimum persists. Introduction of a nitro-group displaces the part of the absorption curve on the long-wave side of about 3400 A.

Similarly, the spectrum of 4-methoxy-6-nitrocinnoline closely resembles that of 4-methoxycinnoline except that the nitro-group brings about a bathochromic shift which is least for the middle section of the curve from 2750 to 3000 A. and greatest for the region near 3500 A.

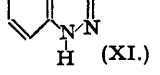
4-Hydroxy-3-methyl-6-nitrocinnoline is evidently also a cinnolone.

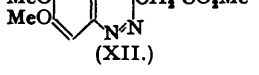
4-Aminocinnolines.—4-Ethoxycinnoline being accepted as a compound of fixed structure, the cinnolines should have absorption in the region 3100—3300 A., with selective absorption at 2800—2900 A. and very intense absorption near 2260 A. The cinnolone structure shows a peak near 3500 A., a deep minimum near 2900 A., and a maximum near 2500—2550 A.

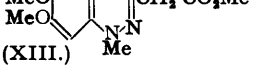
4-Aminocinnoline shows $\lambda_{max.}$ 3450 A. with an inflexion near 3250 A.; there is a deep minimum near 2750 A. and a further maximum near 2400 A.; it is thus clearly a " cinnolone," *i.e.*, the imino-compound (Fig. 10). In 4-anilinocinnoline the situation is not wholly clear. Provisionally, it may be taken as possessing the same " cinnolone " structure as 4-aminocinnoline.

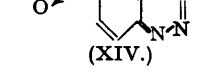
4-Acetamidocinnoline, with peaks at 3285 and 3035 A. and a very intense band at 2260 A., clearly resembles 4-alkoxycinnolines and does not possess the cinnolone structure.

4-Acetamido-6-nitro- and 4-acetamido-3-methyl-6-nitro-cinnoline show the 3285 band displaced to 3620 A., and a second peak near 3000 A. corresponds with the 3035 A. maximum. 4-Diacetylamino-3-methyl-6-nitrocinnoline is of fixed structure and with $\lambda_{max.}$ 3500, 2830, and 2220 A.; it compares well with 4-methoxy-6-nitrocinnoline. On the other hand, 4-amino-6-nitro- and 4-amino-3-methyl-6-nitro-cinnoline, with $\lambda_{max.}$ 4000 and 4085 A., respectively, and maxima near 3250, 2750, 2550, and 2270 A., show a clear resemblance to 1-methyl-6-nitro-4-cinnolone. It therefore seems legitimate to conclude that 4-aminocinnoline possesses the structure (XI) but that substitution in the amino-group results in the cinnoline type of structure.


(XI.)


(XII.)


(XIII.)


(XIV.)

Methyl 4 : 6 : 7-trimethoxy-3-cinnolylacetate (XII) and methyl 6 : 7-dimethoxy-1-methyl-(4-cinnolon-3-yl)acetate (XIII) afford a clear illustration of the bathochromic shift in the region of wave-lengths between 3500 and 4000 A. without much change in ε values when the cinnoline and cinnolone structures are compared. The structures shown would seem to be confirmed.

Tetrahydro-4 : 6-diketocinnoline 6-(oxime methyl ether *N*-oxide) (XIV) raises questions quite outside the scope of our present discussion because its structure is substantially different and its spectrum puzzling.

Acetylcinnolines. Although the spectroscopic evidence is not absolutely conclusive, the acetyl compounds are probably *O*-Ac rather than *N*-Ac derivatives. Acetyl derivatives are easily obtained from most 4-hydroxycinnolines except those substituted at $C_{(8)}$ (Keneford *et al.*, *loc. cit.*, 1950). These compounds have been regarded as *O*-acetyl derivatives on account of their ease of formation and hydrolysis, but no conclusive evidence of their structure has been available. The spectrographic data for the compound from 4-hydroxy-6-nitrocinnoline, however, clearly indicate that it is the *N*-acetyl derivative, and the possibility cannot be excluded that other compounds of this group should be similarly formulated.

TABLE IV. $\lambda_{max.}$ (A.) *and* $\varepsilon_{max.}$.

Quinoline	λ 3140	3000	2780	[2350]		
	ε 3000	2600	3500	35000		
*iso*Quinoline	λ 3200	3080	2600, 2670, 2708			
	ε 2700	2500	3700			
Quinazoline		λ 3080	2700	2200		
				4·6		
		ε 3000	3200	*ca.* 40000		
Cinnoline	λ 3900	3225	3170	3085	2860	2760
	ε 265	2080	1770	1960	2650	2820

Comparisons of Spectra of Analogous Compounds of Different Heterocyclic Series.—Table IV shows that the spectra of quinoline, *iso*quinoline, quinazoline, and cinnoline, in ethanol, are fundamentally similar in that substitution of N for CH does not completely change the character

of the curves. In cinnoline, however, there is some contribution from the ·N=N· grouping, giving rise to low-intensity long-wave-length selective absorption. Table V compares quinolone, quinazolone, and cinnolone derivatives, and Table VI gives relevant information on quinoline, *iso*quinoline, and 5- and 8-quinolinols (Ewing and Steck, *J. Amer. Chem. Soc.*, 1946, **68**, 2181).

TABLE V. $\lambda_{max.}$ (A.) *and* $\varepsilon_{max.}$.

1-Methylquinolone	λ 3380	3250	2370			
	ε 15200	12800	18700			
1-Methyl-4-quinazolone	λ 3170	3065	2775	2690	2300	
	ε 6220	6890	4220	3940	12100	
3-Methyl-4-quinazolone	λ 3135	3015	2764	2670	2300	
	ε 2880	3620	6680	7030	22400	
1-Methyl-4-cinnolone	λ 3690	3520	2515			
	ε 12900	12700	8900			

TABLE VI. $\lambda_{max.}$ (A.) *and* $\varepsilon_{max.}$.

Quinoline : in 95% EtOH	λ 3140 sharp		3000	2780	2250	
	ε 3000		2600	3500	35000	
in 0·01N-HCl	λ 3150			2350		
	ε 7000			35000		
*iso*Quinoline : in 95% EtOH	λ 3200	3080	2600	2670	2780	
	ε 2700	2500		3700		
in 0·01N-NaOH	similar to spectrum in 95% EtOH					
in 0·01N-HCl	λ 3350	2670	2730	2300		
	ε 4000		*ca.* 2000	40000		
5-Quinolinol : in 95% EtOH	λ 3280		2400			
	ε 3000		37300			
in 0·1N-HCl	λ 3700	3150	3050	2520		
	ε 2500	1700		40000		
in 0·1N-NaOH	λ 3670	3306		2540		
	ε 3500	2800		30000		
8-Quinolinol : in 95% EtOH	λ 3100			2400		
	ε 3200			50000		
in 0·01N-HCl	λ 3580	3200—3080		2500		
	ε 1950	1800		48000		
in 0·01N-NaOH	λ 3500			2550		
	ε 3000			32000		

8-Quinolinyl methyl ether curves agree very closely except that there is no shift in alkali.

TABLE VII. $\lambda_{max.}$ (A.) *and* $\varepsilon_{max.}$.

4-Hydroxyquinoline	λ 3315	3175			2335		
	ε 15200	14100			22300		
4-Hydroxyquinazoline	λ 3130	3005	2650		2235		
	ε 3460	3980	6460		22800		
4-Hydroxycinnoline	λ 3520	3380	2960	2845	2620	2550	2570
	ε 12200	13800	2700	2770	7050	8910	11200

All the above compounds exist in solution in equilibrium with ketonic forms.

4-Methoxyquinoline	λ ~3100	~2950	2830	~2755	2255	
	ε 4000	3980	7280	7760	60000	
4-Methoxyquinazoline	λ 3090	2975		2610	2250	
	ε 3430	3000		5110	26000	
4-Methoxycinnoline	λ 3130	2910			2240	
	ε 4500	5500			37500	

The spectrum of 3-methyl-4-quinazolone shows a notable resemblance to those of quinoline and *iso*quinoline, whilst 1-methyl-4-quinazolone has a spectrum similar to that of quinoline in 0·01N-acid. In 1-methylquinolone there is a decided wave-length shift and the ε values are much increased. The shift is still greater in 1-methylcinnolone but the twin bands persist. All the 4-methoxy-derivatives (Table VII) illustrate the relatively small changes in band intensities resulting from substitution which leaves the respective rings practically unchanged.

Introduction of nitro-groups (Table VIII) displaces all the spectra in the direction of longer wave-lengths but in no case is there evidence of fundamental molecular rearrangement as a result. The 4-amino-derivatives of quinoline (-one), quinazoline (-ine), and cinnoline (-one) (Table IX) maintain the broad similarity seen throughout the series, but the intensity of absorption for the quinazoline is lower than that of the quinolone and the cinnolone.

TABLE VIII. $\lambda_{max.}$ (A.) *and* $\varepsilon_{max.}$.

4-Methoxy-6-nitroquinoline	λ	3430	2990	2660	
	ε	4390	7960	23600	
4-Methoxy-6-nitroquinazoline	λ	3250	2950		
	ε	4390	8180		
4-Methoxy-6-nitrocinnoline	λ	3530	3000	2905	2430
	ε	5370	4790	5520	19100

Introduction of the nitro-groups displaces the spectra in the direction of longer wave-lengths but exerts no fundamentally new effect.

1-Methyl-6-nitro-4-quinolone	λ	3580	3260	2660	
	ε	8360	8710	13200	
1-Methyl-6-nitro-4-quinazolone	λ	3220	2740		
	ε	10500	3650		
3-Methyl-6-nitro-4-quinazolone	λ	3175		2220	
	ε	13800		25400	
1-Methyl-6-nitro-4-cinnolone	λ	3700	3280	2695	2410
	ε	12900	9330	8040	16700

The effect of the nitro-group is here variable both on values and on positions of maxima.

TABLE IX. $\lambda_{max.}$ (A.) *and* $\varepsilon_{max.}$.

4-Aminoquinoline (-one)	λ	3200		2330	
	ε	10200		19000	
4-Aminoquinazoline (-ine)	λ	3245	3130	2846	~2400
	ε	4700	6730	7180	13700
4-Aminocinnoline (-one)	λ	3450	~3250	2400	
	ε	11500	*c.* 9000	12606	

Correlations between Chemical and Spectrographic Properties.—Although the chemical and spectrographic properties of a compound reflect different activated states, yet a number of interesting correlations are discernible for the compounds under discussion between the spectral data given above and some of their known chemical properties (Keneford, Morley, Simpson, and Wright, *J.*, 1949, 1356; 1950, 1104).

(i) There is significant agreement between the fine structures of 4-hydroxy-compounds of each type, as deduced from spectral evidence, and the constitutions of the methylated derivatives which these compounds yield on treatment with methyl sulphate and alkali. Thus 4-hydroxycinnoline, -quinazoline, and -quinoline are all mainly keto-dihydro in structure, and each gives rise to an *N*-methyl derivative. Furthermore, spectrographic data show that the mobile hydrogen in 4-hydroxy- and 4-hydroxy-6-nitro-quinazoline is attached mainly to $N_{(3)}$, and each compound gives the 3-methyl derivative as the sole product isolated.

(ii) Chemical evidence indicates that 4-hydroxycinnolines contain a more mobile replaceable hydrogen atom than do their quinazoline or quinoline counterparts (Keneford *et al.*, *loc. cit.*, 1950). This greater chemical reactivity may be connected with the fact that the " hydroxy-aromatic " form makes a larger contribution in the hydroxy-cinnolines than in the other two series; for whereas the " keto-dihydro " form is present almost exclusively in 4-hydroxyquinoline, yet the quinazoline analogue contains about 20%, and most 4-hydroxycinnolines about 30%, of the " hydroxy-aromatic " tautomer.

(iii) Of the various simple compounds in each series that have been examined both spectrographically and chemically, the hydroxy- and amino-compounds are the only ones for which two or more fine structures differing tautomerically are possible. For the hydroxy-compounds and other 4-substituted derivatives it has been shown that the quinoline compound is more basic than the quinazoline analogue, which in turn is more basic than the corresponding cinnoline derivative; for 4-amino-compounds, however, the order of basic strength is quinoline > cinnoline > quinazoline (Keneford *et al.*, *loc. cit.*, 1949). Although no fundamental explanation of the deviation here seen in the amino-series could be advanced, the results suggested that

either 4-aminocinnoline or 4-aminoquinazoline (but not both) differed significantly in fine structure from the other two amino-analogues. The spectrographic evidence now obtained shows quite clearly that this is indeed the case, because it requires the ascription of imino-structures to 4-aminoquinoline and 4-aminocinnoline, and an amino-structure to 4-amino-quinazoline.

It is of interest that, among the three types of 4-amino-compound, only the amino-quinazolines are hydrolysed in acid solution (Keneford *et al.*, *loc. cit.*, 1950); but, as the participating entity is here the ion and not the free base, the reaction cannot be correlated directly with the spectrographic data.

(iv) Quinazoline shows a greater spectrographic resemblance to 3-methyl-4-quinazolone than it does to the 1-methyl isomer. This may be held to correspond with the observed quaternisation of quinazoline at $N_{(3)}$ (Gabriel and Colman, 1904).

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