Conclusions

1. The 1-amino-7-naphthol was prepared in good yield and of good quality from α-naphthylamine-7-sulfonic acid by caustic soda fusion, at much higher temperatures than were given by Cassella and was isolated both as the base and as the hydrochloride.
2. The 1-amino-6-naphthol was prepared in good yield and of good quality from α-naphthylamine-6-sulfonic acid, by caustic soda fusion, and was isolated both as the base and as the hydrochloride.
3. Acetylation of the 1-amino-6-naphthol was unsuccessful.
4. The melting point of the picrate of 1-amino-6-naphthol was found to be 170°, corrected, as against 185° as given by Sachs.

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[Contribution from the Rockefeller Physical and Baker Chemical Laboratories of Cornell University]

THE ABSORPTION SPECTRA OF SOME HALOGENATED FLUORESCEINS[1]

By R. C. Gibbs and C. V. Shapiro[2]

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In previous investigations on the absorption spectra of resorcinolbenzein,[3a] fluorescein[3b] and sulfonefluorescein[3c] in various solvents, the effect of introducing acid groups, carboxyl and sulfoxyl, into the benzein was studied. It was shown that in the presence of the highly dissociated sulfonic acid group an inner salt was formed with the basic, quinoid oxygen atom. Dibromosulfonefluorescein[3c] also exhibited the inner salt configuration, but the bands in its absorption spectra were shifted toward longer wave lengths relative to those of sulfonefluorescein, as the result of the addition of two bromine atoms.

Data are now presented for di- and tetrabromofluorescein (eosin), in which the bromine atoms are attached to the phenol residues, and for tetrachlorofluorescein, in which the chlorine replaces the hydrogen atoms of the phthalic acid residue. It is known from the work of B. Cohen[4] on indicators of the sulfonephthalein class that halogen substitution in the phenolic residues results in an increase in the apparent dissociation constant of the phenolic hydrions. Although his data on the halogen derivatives give

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[1] The investigations upon which this article is based were supported by grants from the Heckscher Foundation for the Advancement of Research, established by August Heckscher at Cornell University.

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[3] (a) Orndorff, Gibbs and Shapiro, This Journal, **48**, 1327 (1926); (b) *ibid.*, **50**, 819 (1928); (c) Gibbs and Shapiro, *ibid.*, **50**, 1755 (1928).

[4] B. Cohen, *Public Health Reports*, **41**, 3053 (1926).

no indication of a similar effect on the dissociation of the acid group, carboxyl or sulfoxyl, such an effect is nevertheless to be expected, since it has been shown that the properties of the acid group, as well as the hydroxyl, are modified by alkyl[4] and hydroxyl[5] substitutions. In order that a change in the acid properties shall be recognizable from a study of absorption spectra, it is necessary in the case of fluorescein, which exists as a free acid in the quinoid state, that substitution shall either increase the acid properties to such an extent that an inner salt is formed, or decrease them to a point where the lactone becomes stable. In the first case the absorption spectra of the neutral and acid solutions will be found to be similar;[5] in the second case, the neutral solutions will show the characteristic absorption bands of the benzenoid phthaleins.[6] The results of the present investigation bring out, however, a complete similarity between the absorption spectra of fluorescein and its halogen derivatives and indicate that any changes in the acid properties are relatively slight and are negligible compared with the effects produced by the introduction of hydroxyl groups. In other words, whatever effect there may be upon the acidity, it is not sufficient to produce marked changes in the absorption spectra. The result of halogen substitution is primarily to shift the absorption bands toward longer wave lengths, with the most pronounced changes occurring for eosin and the least usually for tetrachlorofluorescein. Dibromofluorescein, which has about the same molecular weight as the tetrachloro compound but differs from it in having the bromine atoms on the phenol residues, shows shifts in its absorption bands intermediate between those of eosin and tetrachlorofluorescein. It thus appears that substitution in the phenol residues is more effective than substitution in the phthalic acid portion of the molecule in modifying the absorption of fluorescein.

The compounds used in the present investigation were all of analytical purity.[7] The sample of eosin[7b] was almost white in color but its solution in absolute ethanol did not differ from that of another pure sample which was a deep pink in the solid state. It must therefore be assumed, as with the red and yellow varieties of fluorescein,[3b] that if any differences in structure exist in the solid state they disappear when in solution, probably by giving rise to an equilibrium mixture of the lactoid and quinoid forms, in which the latter predominates.

Figure 1 presents the absorption curves for absolute ethanol solutions of dibromo-, Curve A,A′, tetrabromo-, Curve B,B′ and tetrachlorofluorescein, Curve C,C′. The absorption curve for fluorescein, Curve D,D′, is repeated from our previous paper,[3b] where data on the concentrations em-

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[5] Gibbs and Shapiro, This Journal, **51**, 1755 (1929).

[6] Gibbs and Shapiro, *Proc. Nat. Acad. Sci.*, **14**, 251 (1928).

[7] (a) Orndorff and Hitch, This Journal, **36**, 680 (1914); (b) Orndorff and Hemmer, *ibid.*, **49**, 1272 (1927).

ployed will be found. The positional effect of the halogen atoms is most marked in the visual and near ultraviolet regions, where the absorption of eosin is nearly eight times as intense as that of tetrachlorofluorescein or of fluorescein itself and its bands are shifted to the greatest extent. In the ultraviolet region eosin again exhibits the greatest intensity, but tetrachlorofluorescein now lies intermediate between it and dibromofluorescein.

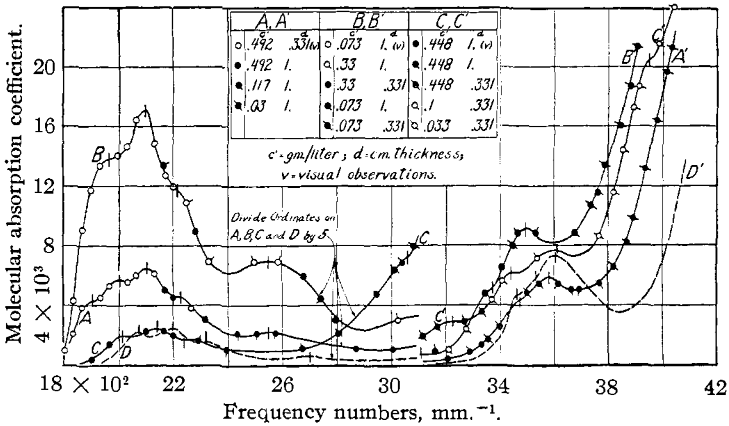

Fig. 1.—Neutral ethanol solutions: A,A', dibromofluorescein; B,B', tetrabromofluorescein–eosin; C,C', tetrachlorofluorescein; D,D', fluorescein.

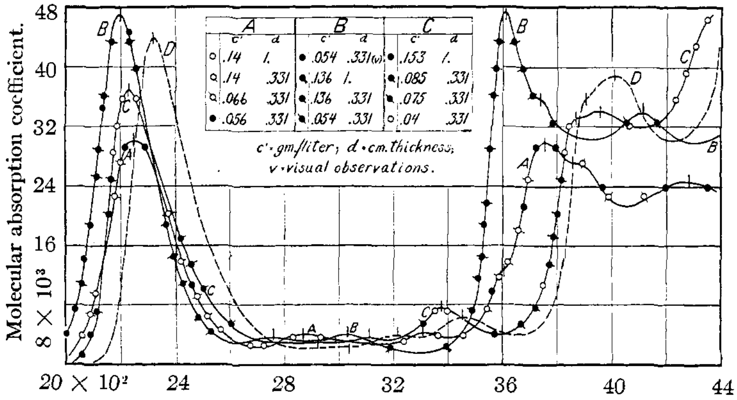

Fig. 2.—Concd. sulfuric acid solutions: A, dibromofluorescein; B, tetrabromofluorescein–eosin; C, tetrachlorofluorescein; D, fluorescein.

The mass effect of halogens is brought out in the extreme ultraviolet range by the fact that the rapid increase of absorption occurs at relatively longer wave lengths for Curves A' and B' as compared with Curve D'.

The absorption curves of the sulfuric acid solutions are given in Fig. 2.

The lack of any resemblance of these curves to those obtained for the neutral solutions, Fig. 1, is evidence for the non-existence of an inner salt structure for the halogenated fluoresceins. This is confirmed by the finding that fluorescein and dibromofluorescein form hydrochlorides; eosin also adds on dry hydrogen chloride but less readily than the above compounds.[7b] According to Orndorff and Hitch,[7a] tetrachlorofluorescein does not form a hydrochloride under any circumstances, but in this respect it is probably similar to phenolphthalein, whose hydrochloride is stable only at −30°.[8] Orndorff and Hitch ascribe the failure to obtain a hydrochloride to the weakly basic properties of the quinoid oxygen atom but it is evident by analogy with fluorescein that a sulfate is formed in concd. sulfuric acid. The visual band for the halogenated compounds is shifted markedly toward the red from that of fluorescein in the following order: tetrabromo > tetrachloro > dibromo. The order of these shifts, as well as their magnitude, agrees closely with the results obtained by Holmes[9] for the same compounds in weakly alkaline solutions. In the ultraviolet, however, tetrachlorofluorescein is relatively close to fluorescein, while the two dibromo derivatives exhibit a large shift toward the red. Another striking difference between these two groups is in the relative intensities of the two components of the complex ultraviolet band. For the first pair of compounds the short wave-length component is slightly the more intense, while for the second pair the long wave-length component is very much more intense. This complex band has been found to be characteristic of the sulfuric acid solutions of almost all phthaleins containing the pyrone ring and in the majority of cases its contour is of the second type. In the following list, Col. A represents those compounds for which the short wave-length component is the stronger and Col. B those for which it is the weaker.

A	B	
Fluorescein	Dibromofluorescein	Tetrabromofluorescein
Tetrachlorofluorescein	Sulfonefluorescein[3c]	Sulfonegallein[5]
Hydroxyhydroquinolphthalein[5]	Dibromosulfonefluorescein[3c]	Gallein[5]
Hydroxyhydroquinolsulfonephthalein[5]	Resorcinolbenzein[5]	Pyrogallolbenzein[5]

In ethanol solutions of these fluorescein compounds involving complex equilibrium conditions between several forms, it is not possible to isolate completely the effect of halogen substitution, whereas in concd. sulfuric acid solution we may safely assume the existence of these several compounds in analogous states and may therefore ascribe the differences in their absorption more definitely to halogen substitution. Halogenation of the phenolic groups thus appears to bring two opposing forces into action: (1) a tendency to decrease the intensity which can be ascribed to the intrinsic nature of the halogen; (2) a tendency to increase the intensity,

[8] Meyer and Hantzsch, *Ber.*, **40**, 3479 (1907).

[9] Holmes, THIS JOURNAL, **46**, 2770 (1924).

which may be ascribed to the mass action of the halogen. It should be possible to judge the relative importance of these two factors by a study of derivatives of fluorescein in which bromine is replaced by chlorine or iodine.

The positions of the absorption bands for the neutral and acid solutions of fluorescein and its halogenated derivatives are listed in Table I.

TABLE I

FREQUENCY NUMBERS OF BANDS FOR NEUTRAL AND ACID SOLUTIONS OF HALOGENATED FLUORESCEINS

Fluoresceins				Fluoresceins			
Fluorescein	Dibromo-	Tetrabromo- (eosin)	Tetrachloro-	Fluorescein	Dibromo-	Tetrabromo- (eosin)	Tetrachloro-
Absolute Ethanol as Solvent				Concd. Sulfuric Acid as Solvent			
	1905						
2075	2005	1968	2013	2317	2250	2201	2228
2198	2106	2100	2141	3039	2868	2759	2922
2319	2227	2215	2239	3215	2987	3032	3111
2700	2548	2548	3060	3451	3307		3377
3460		3107	3224		3605		
3533	3472	3371	3441	3906	3755	3605	3868
3604	3580	3492	3610	4005	3857	3738	3957
			3949		4287	4115	

Summary

1. The effects of halogen substitution on the absorption spectra and chemical properties of fluorescein are discussed. Absorption curves and data are presented for dibromo-, tetrabromo- and tetrachlorofluorescein.

ITHACA, NEW YORK

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ALBERTA]

ETHYL- AND HEXYLFLUORESCEIN. THEIR DIBROMO AND MONOMERCURY DERIVATIVES

BY REUBEN B. SANDIN AND JOHN W. SUTHERLAND

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A great number of mercury derivatives of phenolphthalein and related compounds has been prepared. Many of these have been reported in the patent literature.[1] White[2] has prepared mercury derivatives of phenolphthalein, *o*-cresolphthalein, fluorescein, dibromofluorescein and phenolsulfonephthalein, containing from one to four atoms of the metal. Very recently Harden[3] has reported salicylsulfonephthalein, its tetrabromo and monomercury derivatives. The latter compound shows marked germicidal power.

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[1] Pauly and Traumann, German Patent 201,903 (1909); Fahlberg, List and Co., German Patent, 308,335 (1918); White, U. S. Patent 1,535,003 (1925); 1,549,942 (1925).

[2] White, THIS JOURNAL, **42**, 2355 (1920).

[3] Harden, *ibid.*, **49**, 3139 (1927).