solved in 5 ml. of boiling ethyl acetate. On cooling, 0.45 g. (50%) of yellow crystals was obtained. Recrystallization from ethyl acetate gave colorless needles, m.p. 226–227°.

Anal. Calcd. for $C_{25}H_{20}N_2O_2$: C, 78.92; H, 5.30; N, 7.37. Found: C, 79.11; H, 5.30; N, 7.34.

The infrared spectrum shows the presence of C=N bands at 1587 cm.$^{-1}$ and no –NH– bands.

Cyclopentadiene Adduct of 4-Chloro-*o*-quinonedibenzimide (XVIII).—From 4-chloro-*o*-quinonedibenzimide and cyclopentadiene in a similar way and after reaction for 3 days, a 99% yield of yellow-brown solid resulted. Recrystallization from ethyl acetate gave white needles, m.p. 236–237°.

Anal. Calcd. for $C_{25}H_{19}ClN_2O_2$: C, 72.37; H, 4.62; N, 6.75. Found: C, 72.32; H, 4.61; N, 6.60.

The infrared spectrum showed the presence of a C=N band at 1581 cm.$^{-1}$ and no –NH– band.

Dimer of *o*-Quinonedibenzimide (XIX).—A solution of 0.50 g. of *o*-quinonedibenzimide and 0.30 g. of maleic anhydride in 10 ml. of benzene was allowed to react at room temperature. Colorless chunky crystals began to form after 6 days. At the end of 13 days 0.24 g. of solid was removed by filtration. The pure product was obtained by recrystallization from ethyl acetate as white needles. The melting point with each crystallization varied in the range between 175–176° and 180–181°.

Anal. Calcd. for $C_{40}H_{28}N_4O_4$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.47; H, 4.21; N, 9.09.

Evaporation of the reaction mother liquors to dryness gave a red gum which was discarded.

Replacing the maleic anhydride by an equal weight of *p*-benzoquinone led to the precipitation of crystals after 2 days. At the end of 10 days, 0.35 g. of colorless prisms was removed by filtration. Recrystallization from ethyl acetate gave white needles with the same variable melting point mentioned under A.

Anal. Calcd. for $C_{40}H_{28}N_4O_4$: C, 76.42; H, 4.49; N, 8.91; mol. wt., 628. Found: C, 76.68; H, 4.48; N, 8.77; mol. wt. (Rast), 659.

The infrared spectra of the products from methods A and B were identical.

Diethyl 4(?)-(*o*-Phenylenedibenzamide)-malonate.—A solution of 0.75 g. of *o*-quinonedibenzimide in 10 ml. of dry redistilled dioxane and 0.40 g. of redistilled diethyl malonate was treated with about 50 mg. of sodium methoxide. After standing 5 hours the color had faded to a light brown. Addition of 30 ml. of water caused the separation of a brown oil which changed on standing to 1.09 g. (96%) of a tan solid. Recrystallization from benzene–cyclohexane and then methylcyclohexane served to purify the product; tiny white needles, m.p. 117.5–118.5°.

Anal. Calcd. for $C_{27}H_{26}N_2O_6$: C, 68.34; H, 5.52; N, 5.91. Found: C, 68.32; H, 5.28; N, 6.01.

Only a red amorphous solid was isolated from heating this product with 10% aqueous sodium hydroxide on the steam-bath for 3 hours, followed by acidification with 6 *N* hydrochloric acid.

4(?)-(3-Pentane-2,4-dione)-*o*-phenylenedibenzamide.—Addition of pure acetylacetone to *o*-quinonedibenzimide was carried out in the same manner as the diethyl malonate. The yield was 99% of a white solid. Recrystallization from ethyl acetate and then from ethanol gave a pure product; white prisms, m.p. 237.0–237.5°.

Anal. Calcd. for $C_{25}H_{22}N_2O_4$: C, 72.45; H, 5.35; N, 6.76. Found: C, 72.37; H, 5.49; N, 6.81.

4-Chloro-6(?)-(3-pentane-2,4-dione)-*o*-phenylenedibenzamide.—From 4-chloro-*o*-quinonedibenzimide (III) and pure acetylacetone, a 97% yield of product resulted. Recrystallization from glacial acetic acid gave white prisms, m.p. 271.0–271.5°.

Anal. Calcd. for $C_{25}H_{21}ClN_2O_4$: C, 66.89; H, 4.72; N, 6.24. Found: C, 66.69; H, 4.89; N, 6.25.

Treatment of III with diethyl malonate under the above conditions gave an oil which could not be crystallized.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE RICE INSTITUTE]

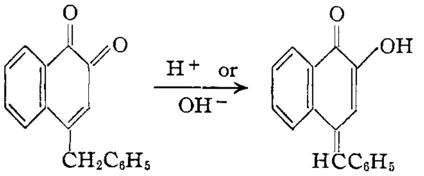
The Enolization of 9-Phenyl-2,3-benzofluorene-1,4-quinone

BY MARTIN G. ETTLINGER

RECEIVED JANUARY 25, 1954

9-Phenyl-2,3-benzofluorene-1,4-quinone (VIII) enolizes in a hydroxylic solvent to form the more stable 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone (V). The enol V is more acidic than acetic acid, whence the dissociation constant of the hydrogen on the 9-carbon atom of VIII, referred to aqueous medium, is probably at least 10^{-3}. The remarkably high acidity of VIII is caused by the five-membered ring. The enol V undergoes sulfonation; in spectra and basicity, it resembles simpler β-naphthofuchsones such as 2-diphenylmethylene-1-naphthone (XIII), a fourfold stronger base than *p*-nitrodiphenylamine.

The enolization of 1,2-quinones bearing 4-methinyl substituents, even in the absence of side chain carbonyl groups, has long been firmly established. The preparation of 2-hydroxy-4-fluorenylidene-1-naphthone[1] was succeeded by more thorough studies of 4-benzhydryl-1,2-naphthoquinone[2] and 4-benzyl-1,2-naphthoquinone[3] (I). The enolic equilibrium of 4-benzhydryl-1,2-naphthoquinone seemed to favor the quinone and was highly mobile, so that the two forms were not isolated separately. The transformation of I to the enol II by strong acid or base, in contrast, could not be reversed directly.[4] Enols of methylenedi-*p*-quinone derivatives, which are vinylogs of β-diketones, have also been prepared.[5] However, 2-methinyl-1,4-



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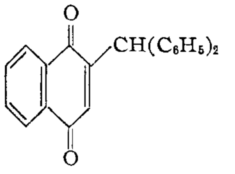
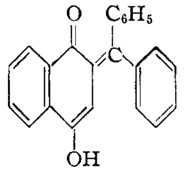


III



IV

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(1) F. Sachs and L. Oholm, *Ber.*, **47**, 955 (1914).

(2) L. F. Fieser and J. L. Hartwell, THIS JOURNAL, **57**, 1484 (1935).

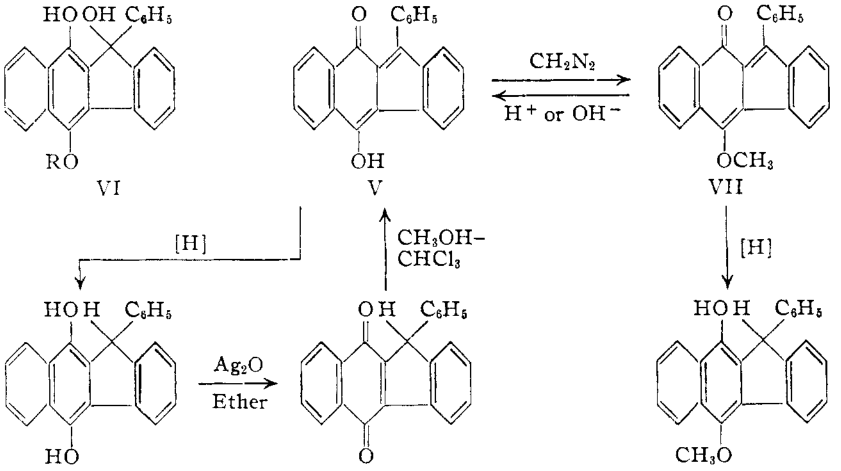
(3) L. F. Fieser and M. Fieser, *ibid.*, **61**, 596 (1939).

(4) As Dr. E. S. Lewis has remarked, the inference that II is more stable than I is probable; the instability of the enol of the 4-benzhydryl derivative can be ascribed to steric interference between the 5-hydrogen atom and the *cis*-phenyl group.

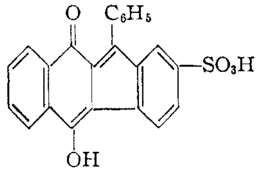
(5) L. I. Smith, H. R. Davis, Jr., and A. W. Sogn, THIS JOURNAL, **72**, 3651 (1950); E. F. Pratt and W. E. Boehme, *ibid.*, **73**, 444 (1951).

quinones containing only hydrocarbon substituents do not enolize readily: though such enols and their anions have reasonably been postulated as intermediates in reactions[3,6] and the blue colors of enolate anions containing β-alkenyl substituents have frequently been observed,[7] no free enol has previously been isolated. For example, 2-benzhydryl-1,4-naphthoquinone (III) gave no derivatives of the hypothetical enol IV.[2,8]

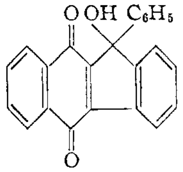
In a preceding paper,[8] the preparation of the deep red compound 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone (V) was recorded. The more important synthesis of V, by dehydration of 1,4,9-trihydroxy-9-phenyl-2,3-benzofluorene (VI, R = H), was analogous to known conversions of *o*- or *p*-hydroxytriarylcarbinols to fuchsones. The methyl ether VII of V was made similarly from VI (R = CH_3), as well as from V and diazomethane. Structure V, which can be derived formally from IV by removal of two hydrogen atoms and cyclization, may be regarded as the enol of 9-phenyl-2,3-benzofluorene-1,4-quinone (VIII), the cyclic analog of III. The preparation of VIII and its spontaneous rearrangement in solution to V could indeed be realized.



VI V VII IX VIII X



XII



XI

Upon reduction by zinc in acetic acid or by warm alkaline dithionite, V furnished nearly colorless solutions from which 1,4-dihydroxy-9-phenyl-2,3-benzofluorene (IX) was isolated as a solid which rapidly turned red in air and was not purified. More stable were the 1,4-diacetate of IX, which resembled in ultraviolet spectrum its 9-hydroxy and 9-acetoxy derivatives,[8] and the 4-methyl ether X, which was obtained by reduction of VII and evidently was easily reoxidized by air in the molten or dissolved states. If the hydroquinone IX was shaken with silver oxide in ether at room temperature, largely amorphous products resulted in solution, but when the oxidation was conducted at $-15°$, 9-phenyl-2,3-benzofluorene-1,4-quinone (VIII) precipitated and could be extracted with pure chloroform and crystallized from chloroform–ligroin. The structure of VIII was proved by means of the ultraviolet absorption spectrum (Table I), which corresponded closely to that of the 9-hydroxy derivative of VIII, XI.[8] The uncommon bathochromic shift of the spectrum of XI on passage from alcohol to chloroform solution (Table I) may indicate a hydrogen bond between the 9-hydroxyl and 1-carbonyl groups. The absorption of VIII decreased smoothly at wave lengths beyond 413 mμ (log ϵ in chloroform at 500 mμ 1.83 for VIII, 2.18 for XI) and gave no hint of the presence of V (log ϵ 3.9 at 500 mμ).

TABLE I

ULTRAVIOLET AND VISIBLE SPECTRA OF 2,3-BENZOFLUORENE-1,4-QUINONES

Compound	Absorption maxima, wave lengths in mμ (log ϵ)
VIII[a]	260 (4.46), 308 (3.92), 413 (3.50)
XI[b]	258 (4.34), 308 (3.86), 417 (3.41)
XI[a]	262 (4.35), 315 (3.87), 427 (3.47)

[a] In pure chloroform. [b] In ethanol.[8]

The quinone VIII formed yellow crystals, which were stable for at least nine months at room temperature. Solutions in dry, alcohol-free chloroform remained unchanged for hours, but addition of methanol, which could act as a base toward the 9-hydrogen atom and raise the dielectric constant, caused transformation of the quinone to V. Since the isomerization was accompanied by a shift of the visible absorption maximum by some 65 mμ to longer wave lengths, the change in color from yellow to deep orange which developed within a few minutes after a chloroform solution of VIII was mixed with an equal volume of methanol and several drops of acetic acid (to destroy traces of free alkali, which would form the blue salt) furnished striking visual evidence of the enolization. When a solution of VIII (0.263 mg.) in a mixture of 2 cc. of methanol and one drop of acetic acid diluted to 10 cc. with chloroform was allowed to stand three hours, the optical extinction differed no more than 0.05 logarithmic unit from that of the same concentration of V throughout the range 245–590 mμ, and the yield of V calculated from the maximum visible absorption was 95%. Dissolved in chloroform

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(6) R. C. Fuson, *Chem. Revs.*, **16**, 1 (1935); L. I. Smith, *et al.*, THIS JOURNAL, **59**, 662 (1937); **64**, 524 (1942); **68**, 887 (1946); K. Alder and G. Stein, *Ber.*, **62**, 2337 (1929); C. F. H. Allen and L. Gilman, THIS JOURNAL, **58**, 937 (1936).

(7) P. Karrer, *Helv. Chim. Acta*, **22**, 1146 (1939); L. F. Fieser, *et al.*, THIS JOURNAL, **61**, 2206, 3216 (1939); **62**, 153, 2861 (1940).

(8) A. R. Bader and M. G. Ettlinger, *ibid.*, **75**, 730 (1953).

containing only one-twentieth volume of methanol, VIII became half enolized in approximately an hour at 25°; the further addition of one-fourth total volume of acetic acid rendered the change slow (not more than 5% per hour).

In pure methanol, the enolization of VIII of course proceeded, but the rate of solution was slow, so that solid mixtures of V and VIII obtained in preliminary experiments were actually enriched in the quinonoid form by a methanol wash. The quinone was stable in dioxane solution and enolized rapidly in acetone. However, the addition of one-tenth volume of acetone to VIII in chloroform induced no formation of V but a slow decomposition, observed also in mixtures of chloroform and acetic acid.

The enol V possessed the remarkable pK_a of 5.2 in 44% ethanol, or an acidity threefold greater than that of acetic acid in the same solvent. A dilute solution of V in neutral ethanol showed the spectrum of the anion formed by dissociation markedly beyond 530 mμ. The high acidity of V might produce hydrogen bonds in the solid and thereby the observed[8] intense color and absence of a discrete hydroxyl band near 3 μ. Another correlative is the ready hydrolysis of the methyl ether VII to V by hot dilute potassium hydroxide in aqueous dioxane. In aqueous base, VII is in equilibrium with the salt of the phenol VI ($R = CH_3$),[8] but belief that VII is the species cleaved is supported by the implausibility of alkaline hydrolysis of the naphthyl ether group in VI ($R = CH_3$) and the stability under comparable conditions of the ether X. Compound VII was also split to V by boiling acetic and hydrochloric acids, though the reverse transformation of V to VII by methanol and sulfuric acid, necessarily at lower temperature in less acidic medium, did not proceed.

The quinone VIII, since it is unstable with respect to V through the common anion, must be the stronger acid. The exact acidity of VIII and equilibrium between V and VIII are unknown. The equilibrium could be estimated,[2] were it possible to measure a reversible oxidation–reduction potential of the pair V and IX for comparison with the predicted potential of VIII, but the necessary determination could not be performed. Attempted potentiometric titrations of V and its sulfonate described below, either by catalytic hydrogenation and oxidation with ferricyanide or by reduction with titanous ion or dithionite in aqueous ethanol (pH 1–8), gave potentials that drifted, were discordant by 10 mv. or more between different gold or platinum electrodes, and varied too greatly with the fraction of oxidant. Titrations of the standard quinones lawsone and lapachol proceeded normally. The rate of reduction of V was slow: when solutions of the sulfonate of V (0.0002 M) in aqueous ethanol were treated with excess titanous chloride at pH 2 or sodium dithionite at pH 9 (reduction was even slower in respectively more acid or alkaline media), the times of decolorization were 5 to 30 minutes. The proportion of VIII at equilibrium with V and IX likely was very small, and the system, at total concentrations of 0.0002 to 0.0015 M, too poorly poised for measurement.

On treatment with concentrated sulfuric acid at room temperature, V furnished a *sulfonic acid*, crystallized from aqueous acid as dark red, hydrated needles, which lost water in high vacuum to give the hygroscopic, black, anhydrous form, perhaps the inner salt. The acid equilibrated in a humid atmosphere appeared to be the trihydrate, but material analyzed in an air-conditioned room corresponded closely to a hemipentahydrate. The homogeneity and structure of the substance were not established, but it may be plausibly represented as 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone-7-sulfonic acid (XII). The presence of the unaltered chromophore of V in the sulfonic acid was proved by comparison of absorption spectra in acid and base (Table II).

The hydroxyl group of XII with the sulfonic acid group ionized possessed the pK_a of 3.45 in aqueous solution, on the order of one unit less than that estimated for V in water.[9] The acid-strengthening effect of the sulfonate ion substituent in aromatic enols appears general: the pK_a of phenol[10] is 9.95, of the p-phenolsulfonate ion[11] 9.05, and that of 2-naphthol[12] is 9.9, of the 2-naphthol-6-sulfonate ion[13] 9.0. The introduction of an ionized sulfonate group commonly also increases the acidities of aminium ions.[14] Were V sulfonated at the 5-position, the only alternate activated by the hydroxyl group toward substitution and not directly deactivated by carbonyl, the acid-weakening electrostatic effect of the sulfonate charge, as in the exceptional 1,8-naphthalene derivatives,[13,14] would probably appear.

For comparison with V, the β-naphthofuchsones XIII[15] and XIV (the methyl ether of IV) were examined. Compound XIV was prepared from 2-benzoyl-1,4-naphthoquinone[16] (XV) by reduction and smooth partial etherification with acidic methanol[17] to 2-benzoyl-4-methoxy-1-naphthol (XVI), reaction with phenyllithium and dehydration. The

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(9) The pK_a of p-nitrophenol, perhaps as good a model for V as any available, increases from 7.2 in water[10] (corrected to 20° according to L. Michaelis and A. Gyemant, *Biochem. Z.*, **109**, 165 (1920)) to 7.7 in 42% (by weight) ethanol (G. Schwarzenbach and E. Rudin, *Helv. Chim. Acta*, **22**, 360 (1939)). The corresponding increments for phenol and p-chlorophenol are 1.3 and 1.2 units (*cf.* M. Mizutani, *Z. physik. Chem.*, **118**, 318 (1925)).

(10) C. M. Judson and M. Kilpatrick, THIS JOURNAL, **71**, 3110 (1949).

(11) R. G. Bates, G. L. Siegel and S. F. Acree, *J. Research Natl. Bur. Standards*, **31**, 205 (1943).

(12) K. Lauer, *Ber.*, **70**, 1127 (1937).

(13) H. Zollinger, *et al.*, *Helv. Chim. Acta*, **33**, 2002 (1950); **35**, 1209 (1952); R. Puetter, *Angew. Chem.*, **63**, 188 (1951).

(14) Compare the acidities of simple aromatic aminium ions (N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932)) with those of the sulfonates (A. Springer, Jr., and H. C. Jones, *Am. Chem. J.*, **48**, 411 (1912); M. Boyle, *J. Chem. Soc.*, **115**, 1505 (1919); R. O. Maclaren and D. F. Swinehart, THIS JOURNAL, **73**, 1822 (1951); F. P. Ebersbach, *Z. physik. Chem.*, **11**, 608 (1893); A. Bryson, *Trans. Faraday Soc.*, **47**, 522, 528 (1951)). However, the acidity of the cation of p-dimethylaminoazobenzene, in which the charge is distributed by resonance between two nitrogen atoms, is decreased 0.2 logarithmic unit by a p'-sulfonate group (E. Guentelberg and E. Schioedt, *Z. physik. Chem.*, **135**, 393 (1928)).

(15) H. Kauffmann and M. Egner, *Ber.*, **46**, 3779 (1913); F. Preissecker, *Monatsh.*, **35**, 889 (1914).

(16) M. G. Ettlinger, THIS JOURNAL, **72**, 3666 (1950).

(17) *Cf.* F. Russig, *J. prakt. Chem.*, [2] **62**, 30 (1900); A. H. Homeyer and V. H. Wallingford, THIS JOURNAL, **64**, 798 (1942); for a different method, by use of dimethyl sulfate, see A. C. Jain and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **35A**, 233 (1952).

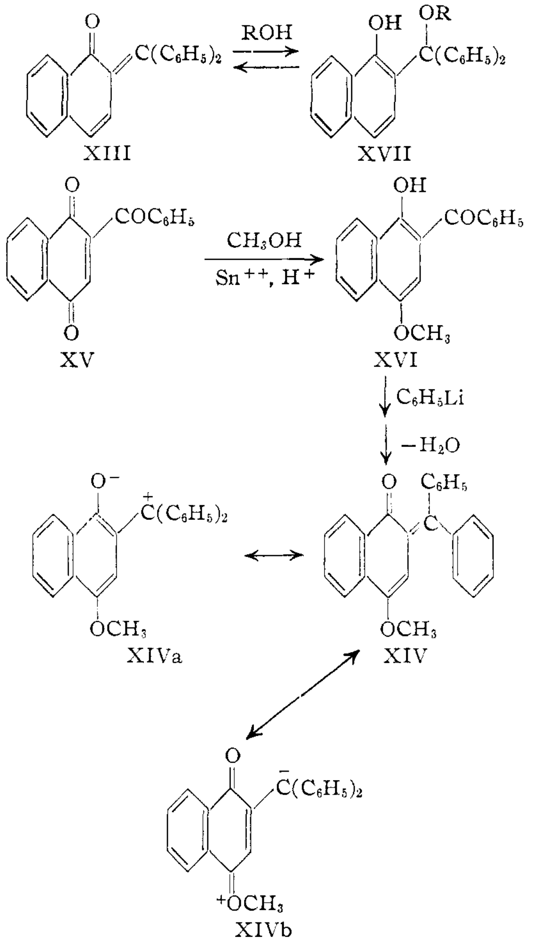

TABLE II

ULTRAVIOLET AND VISIBLE SPECTRA OF FUCHSONES AND ISOFLUORENONES

Compound	Absorption maxima, wave lengths in mμ (log ε)
	(1) Chromophore uncharged
XIII[a]	272 (4.33), 320[i] (3.97), 430 (3.79)
XIV[b]	273 (4.34), 315[i] (3.98), 452 (3.81)
VII[c]	280 (4.69), 325[i] (3.73), 450 (4.13)
V[b]	283 (4.59), 330[i] (3.77), 475 (4.01)
XII[d]	287 (4.68), 335[i] (3.76), 480 (4.07)
	(2) Chromophore negatively charged
V(XXI)[e]	.. .. , 362 (3.92), 452 (3.76), 585 (3.88)
XII[f]	278 (4.70), 363 (4.07), 445 (3.74), 567[j] (3.92)
	(3) Chromophore positively charged
XIII (XVIII)[g]	250[i] (4.22), 305 (3.88), 420[i] (4.36), 447[k] (4.43), 630[k] (3.91)
XII[h]	255[i] (4.25), 297[k] (4.75), 335 (4.33), 425 (3.92), 495[i] (4.23), 523[k] (4.47), 695[k] (3.52)

[a] In chloroform. [b] Solvent, 0.1% acetic acid in ethanol. [c] In ethanol. [d] Solvent, 0.1% hydrogen chloride in ethanol. [e] Solvent, 0.1 *N* potassium hydroxide in 50% ethanol; spectrum not measured below 320 mμ. [f] In 0.1 *N* aqueous potassium hydroxide. [g] In 80% sulfuric acid. [h] In 97% sulfuric acid. [i] Inflection. [j] In 50% ethanol this maximum lay at 575 (3.90). [k] Principal bands of cations.

unsubstituted fuchsone XIII could not be crystallized from hydroxylic solvents because of formation of addition products of type XVII. The extent of hydration or alcoholation of XIII, estimated colorimetrically after equilibration for several hours at room temperature, was 23% in 90% formic acid, 84% in 90% acetic acid and 92% in methanol (0.7 *N* in acetic acid and 0.07 *N* in acetate). However, the methoxy fuchsone XIV crystallized from methanol without apparent loss, was only slowly decolorized by hot alcoholic alkali and resembled in additive unreactivity the isofluorenones V and VII. As in a 1,2-quinone, the enlargement of the β-fuchsone system by cross-conjugation between the 2-diphenylmethylene and 4-methoxyl groups enhanced the stability, corresponding to contribution by the structural possibility XIVb besides the fuchsone resonance between XIV and XIVa. The effect of the 4-methoxyl group on the fuchsone spectrum (Table II) nevertheless was trifling: the bathochromic shift of the visible maximum was mostly illusion because of the large band width, and indeed at 500 mμ the extinctions of XIII and XIV differed by only 0.1 logarithmic unit.

1,2-Naphthoquinones and β-naphthofuchsones possess a spectral similarity, though the principal visible band of the quinones is less intense and at shorter wave length. Remarkably also, a 4-methoxyl group in a 1,2-quinone, despite the conjugation with carbonyl, hardly affects the spectrum. 1,2-Naphthoquinone[18] absorbs in ethanol at 250 mμ (log ε 4.35), 340 (3.40) and 405 (3.40) (in chloroform 405 (3.35)) and 4-methoxy-1,2-naphthoquinone[19] at 250 (4.35), 333 (3.24) and 403 (3.29).

The absorption maxima of the isofluorenones (Table II) are more intense than those of the naphthofuchsones but are not significantly translated to longer wave lengths. The hypsochromic effect in the visible of methylation of V to VII has known analogies[8] and may be partly steric[20] in origin. The visible absorption is broad and the maxima of the fuchsones are sensitive in wave length to the medium: whereas V absorbed in chloroform at 473 mμ (log ε 3.98) and in formic acid (containing 1% of sodium formate) at 475 (4.01) with negligible difference, XIV absorbed at 485 (3.79) in formic acid (contrast Table II) and XIII at 480 (3.82) in the same, 430 (3.81) in acetic acid and 425 (3.87) in dioxane. Presumably the excited state of XIII, corresponding to XIVa with the carbonium ion charge distributed, is stabilized in a solvent of high dielectric constant, but whether V differs because of greater steric compactness or lesser net polarization of the upper state is undetermined.

In strong acids, the fuchsones form cations, surely of structure XVIII (and possible resonant forms with charge on eleven other carbon atoms), and the isofluorenones are likewise converted to conjugate acids. The spectra of the protonated derivatives (Table II) extend to the short infrared (log ε 1.8–2.1 at 850 mμ). Relative to XVIII, the isofluorenone spectrum is displaced bathochromically by some 70 mμ and has a weaker band beyond 600 mμ. The fuchsones and isofluorenones generally may be distinguished by the intensity of the wide, longest wave length band of the cations also but not by its position, for in formic acid XVIII ab-

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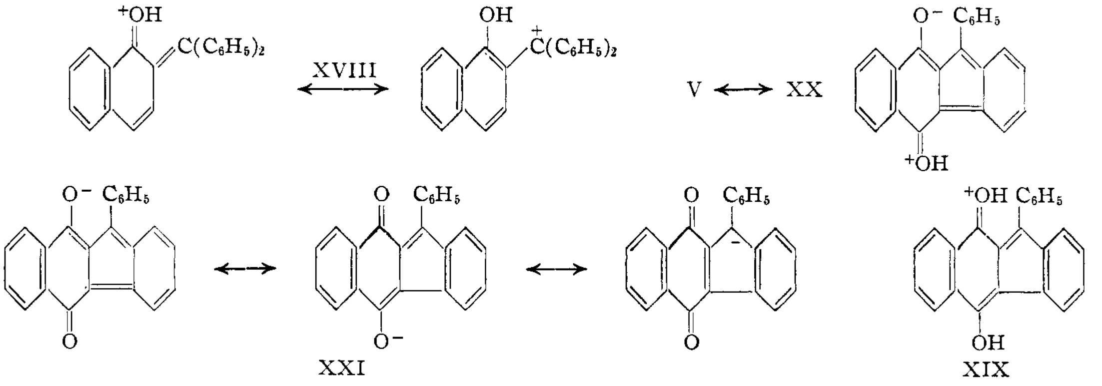
(18) S. Goldschmidt and F. Graef, *Ber.*, **61**, 1858 (1928); H. H. Hodgson and D. E. Hathway, *Trans. Faraday Soc.*, **41**, 115 (1945).

(19) A. K. Macbeth, J. R. Price and F. L. Winzor, *J. Chem. Soc.*, 325 (1935); R. G. Cooke, A. K. Macbeth and F. L. Winzor, *ibid.*, 878 (1939).

(20) R. N. Jones, THIS JOURNAL, **67**, 2127 (1945).

sorbed at 630 $m\mu$ (log ϵ 3.98), the cation of XIV at 710 (3.92), that of VII at 660 (3.41) (inflection) and of V (XIX) at 710 (3.44). On the other hand, cyclization of the protonated fuchsone to the isofluorenone system shifts the wave length of the strongest visible maximum (log ϵ 4.4) but not the extinction. The two effects produce a misleading visual impression, for XVIII appears green and XIX dull red.

To gain further information on the relation between the naphthofuchsones and isofluorenones, basicities were measured. The constants obtained in formic acid[21] were, for XIII, pK_a −1.9 (of XVIII); XIV, −2.9; VII, −3.5; V, −3.15. The apparent pK_a of XVIII in 50–56% sulfuric acid, calculated from the colorimetrically determined concentration of cation and known total concentration of all forms of XIII, was −3.0, which agreed with the value in formic acid on the assumption that in the aqueous solution XIII was 90–95% hydrated. The apparent constant for XII in 60% sulfuric acid was −4.5 and thus of a plausible magnitude less than that of V, but the degree of dissocation of the sulfonic acid group was unknown.[22] The fuchsone XIII, though not so remarkable as cycloheptatrienone,[23] is an unusually strong base for a molecule containing only one oxygen as heteroatom, being only one-tenth as strong as 4-chloro-2-nitroaniline.[24] The methoxy derivative XIV, in accord with its smaller additive reactivity, is less basic than XIII, for the charge in XVIII cannot move to the 4-position (alternately, the methoxyl group in XIVb does not supply electrons to the basic center). The difference in basicity of VII and V confirms the spectral indication that electron transfer from the 4-oxygen atom to the fluorene nucleus decreases on methylation.



XVIII

V ⟷ XX

XXI

XIX

The formal cyclization of a β-naphthofuchsone to an isofluorenone produces small spectral changes, for the theoretical analysis of which insufficient data exist. The effects on acidity, however, are intelligible in terms of known differences between derivatives of diphenylmethane with trivalent central carbon atom and of fluorene. The transition from XIII to V is sterically equivalent, aside from the 1-oxygen atom, to that from triphenylmethyl to 9-phenylfluorenyl, which fixes two benzene rings in a plane and thereby facilitates resonance between them and the 9-carbon atom; the increase in acid strength by at least ten thousandfold from fluorene to 9-phenylfluorene[25] suggests that the 9-phenyl group accepts part of the charge in the anion and cannot be forced far out of plane.[26] Cyclization also creates resonant structures in which the bond connecting the two aromatic rings in fluorene becomes double. The new structures, which interrupt Kekulé resonance in two rings, are comparatively of high energy and low weight, but may produce important electron redistributions.[27] A charge in a fluorenyl group on the 9-carbon can be stabilized by transfer to any other carbon atom. Finally, the five-membered ring of fluorene tends strongly to hold a negative charge. As direct evidence, 9-diphenylmethylenefluorene has a dipole moment of 1 *D* toward the fluorene moiety.[28]

In fluorene derivatives that bear a negative charge on the 9-carbon atom, the comparative

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[21] L. P. Hammett and A. J. Deyrup, THIS JOURNAL, **54**, 4239 (1932).

[22] The values of pK_a exhibited a seemingly systematic drift from −4.56 in 59% acid to −4.43 in 66% acid. The H_0 scale used applies only to protonation of a neutral base not a dipolar ion.

[23] H. J. Dauben, Jr., and H. J. Ringold, THIS JOURNAL, **73**, 876 (1951); W. v. E. Doering and F. L. Detert, *ibid.*; *cf.* azulene (P. A. Plattner, E. Heilbronner and S. Weber, *Helv. Chim. Acta*, **35**, 1036 (1952)).

[24] L. P. Hammett and M. A. Paul, THIS JOURNAL, **56**, 827 (1934).

[25] W. K. McEwen, *ibid.*, **58**, 1124 (1936).

[26] The geometric hindrance to planarity in the 9-phenylfluorenyl anion is surely less than in 9-phenylanthracene.[20]

[27] In one approximate treatment (L. Pauling and G. W. Wheland, *J. Chem. Phys.*, **1**, 362 (1933); **2**, 482 (1934)) of the 9-phenylfluorenyl radical, the "extra" structures were dismissed as combinations of Dewar or Dewar and Kekulé forms, and it was concluded that the resonance energy difference between radical and ethane was less than for triphenylmethyl. A molecular orbital calculation furnished the opposite result (G. W. Wheland, THIS JOURNAL, **63**, 2025 (1941); "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 195). Experimentally, the free energy of dissociation of 9,9′-diphenyldifluorenyl was estimated to be some 8 kcal. greater than that of hexaphenylethane (J. B. Conant, *J. Chem. Phys.*, **1**, 427 (1933)), but it has been plausibly suggested that the difference reflects part of the *steric* stability of the first ethane and the excess resonance energy of 9-phenylfluorenyl is the larger. The heat evolved on peroxidation of diphenyldifluorenyl is some 15 kcal. *less* than for hexaphenylethane (H. E. Bent and J. E. Cline, THIS JOURNAL, **58**, 1624 (1936)); one can object that the bond from oxygen to the electronegative 9-phenylfluorenyl group may be weak, but an indirect calculation of the energies of hydrogenolysis gives a similar answer. The free energy of addition of two atoms of sodium to hexaphenylethane in ether solution is approximately −41 kcal. (H. E. Bent, *ibid.*, **52**, 1498 (1930)), to diphenyldifluorenyl −62 kcal. (H. E. Bent and N. B. Keevil, *ibid.*, **58**, 1228 (1936); *cf.* N. B. Keevil, *ibid.*, **59**, 2104 (1937)), whereas the free energy of conversion of 9-phenylfluorene to the sodium derivative in ether is at least 16 kcal. more negative than for triphenylmethane.[25] Hence, the free energy of hydrogenolysis of diphenyldifluorenyl to 9-phenylfluorene roughly is at least 11 kcal. (2 × 16 + 41 − 62) more positive than the corresponding quantity for hexaphenylethane.

[28] H. Lumbroso, A. Pacault and B. Pullman, *Bull. soc. chim.*, 34 (1950); E. D. Bergmann, E. Fischer, *et al.*, *ibid.*, 709, 712 (1952).

multiplicity of charge distributions and electron attraction are both stabilizing influences, but if the charge is positive, the two factors are opposed and generally, as in the 9-phenylfluorenyl cation, stability is decreased by the dominant electronegative character of the ring. The results are most conspicuous in conversions of 9,9-disubstituted fluorenes, not containing a fulvene system or equivalents, to ions. 9-Phenyl-9-fluorenol is weakly basic,[29] and the dissociation constant of 9-chloro-9-phenylfluorene in sulfur dioxide is slightly larger than one ten-thousandth that of trityl chloride.[30] On the other hand, 9-phenylfluorene is at least 10^{12} times more acidic than triphenylmethane.[25] 9-Benzoylfluorene is appreciably enolized[31] (3% in methanol, 17% in ether) and, though it is precipitated from aqueous base by carbon dioxide,[32] is sufficiently acidic in alcoholic solution to form an ammonium salt. The enol of 9-benzoylfluorene is stabilized by electron donation from the oxygen atom to the ring, and cannot be more acidic than the unstable triphenylvinyl alcohol by nearly as much as the difference between the corresponding ketones.

The carbonyl group of fluorenone is less polar than that of benzophenone, and the oxygen atom may be positive or negative in structures with single carbon–oxygen bonds. Energetically, the increased conjugation slightly predominates over electron withdrawal toward the oxygen atom, for relative to the respective alcohols fluorenone is more stable than benzophenone by 0.6 kcal. (equilibrium constant factor of 2.6).[33] The addition of sodium to fluorenone to form the ketyl negative ion-radical is more favored than to benzophenone by 2.7 kcal.[34] (equilibrium factor of 100). In the present investigation the basicities of the two ketones were measured: for benzophenone, pK_a was -6.2, near the value (-6.19) for *p*-phenylbenzophenone,[24] whereas fluorenone with pK_a -6.95 was a weaker base by one-fifth. The effects are small but qualitatively as predicted. In both cation and ketyl, the oxygen atom can hold a principal part of the charge.

The reversal of stability of quinone and enol on passage from the benzhydryl quinone III to VIII is explicable. Since III is ionized only by hot alcoholic alkali,[8] the difference of acidity between III and VIII must be of similar origin and enormous magnitude to that between triphenylmethane and 9-phenylfluorene. The enol V, analogously to the enol of 9-benzoylfluorene, can be relatively little more acidic than IV, perhaps by no greater than four powers of ten, since IV might well be stronger than phenol. The complex formal structures possible for V may be summarized by the remark that in the dipolar form XX the positive charge may be left on the 4-oxygen atom and the negative charge moved to any of the nine carbon atoms of the right-hand indene ring, or the negative charge left on the 1-oxygen and the positive charge transferred to any of the seventeen carbon atoms of the benzofluorene skeleton. The electronegative character of the five-membered ring must diminish in importance the structure corresponding to XIVa and enhance the analog of XIVb and that of XIVa with reversed polarity. In the blue common anion (XXI) of V and VIII, the charge can be shared by both oxygen and nine carbon atoms of the nucleus, with the central structure most important. In the conjugate acid (XIX) of V the charge can be placed on the 4-oxygen or any carbon atom of the rings drawn. The data indicate that the interaction between the oxygen atoms does not greatly stabilize the ions with respect to V. In particular, the series of basicities shows that the five-membered ring in VII (compared to XIV) exerts approximately the small base-weakening influence of the same feature in fluorenone, which even in V outweighs the charge transfer to the 4-oxygen atom. The most distinctive property of V remains its stability.

I take pleasure to acknowledge the hospitality of Dr. E. R. Buchman, in whose laboratory at the California Institute of Technology the title substance was investigated.

Experimental

Reductions of Isofluorenones.—A suspension of 0.1 g. of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone in 5 cc. of acetic acid was warmed to 90° and treated with two 0.25-g. portions of zinc dust. The pale yellow solution was filtered, diluted with boiled water and chilled to give 0.08 g. of 1,4-dihydroxy-9-phenyl-2,3-benzofluorene as a red-brown solid, m.p. 181–183°. When a mixture of 0.1 g. of the hydroxyisofluorenone, 0.15 g. of sodium hydroxide, 2 cc. of methanol and 5 cc. of water was warmed with 0.6 g. of sodium dithionite until nearly colorless, shaken with 0.5 g. of sodium bicarbonate, filtered and the residue washed with water, there remained 0.1 g. of pink hydroquinone, m.p. 179–180°.

A mixture of 0.1 g. of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone, 0.25 g. of zinc dust, 0.2 g. of sodium acetate and 3 cc. of acetic anhydride was warmed five minutes until colorless, filtered, diluted with a little acetic acid and 5 cc. of water and chilled to furnish 0.08 g. of **1,4-diacetoxy-9-phenyl-2,3-benzofluorene**, m.p. 230–234° dec. The analytical sample, crystallized from acetic acid containing a little acetic anhydride, formed white granules, m.p. 237.5–240° (dec., bath preheated to 225°), and had ultraviolet absorption maxima in chloroform solution at 261 mμ (log ϵ 4.63), 270 (4.71), 307 (4.23), 319 (4.25) and 343 (3.06).

Anal. Calcd. for $C_{27}H_{20}O_4$: C, 79.39; H, 4.94. Found: C, 79.46; H, 5.09.

When the diacetate and methanolic alkali were boiled in air, 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone was regenerated.

Reduction of 4-methoxy-9-phenyl-2,3-benzo-1-isofluorenone by zinc dust in acetic acid afforded **1-hydroxy-4-methoxy-9-phenyl-2,3-benzofluorene**, which crystallized from ligroin (b.p. 60–90°) or 75% ethanol as yellow needles, m.p. 145.5–147° (sealed in nitrogen), and gave a yellow solution in warm aqueous alcoholic alkali. A mixture with 4-methoxy-9-phenyl-2,3-benzo-1-isofluorenone (m.p. 153°) melted at 123–129°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.08; H, 5.47.

A solution of 0.03 g. of 4-methoxy-9-phenyl-2,3-benzo-1-isofluorenone in 2 cc. of warm dioxane treated with 0.15 g.

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(29) K. Ziegler and B. Schnell, *Ann.*, **445**, 266 (1925).

(30) K. Ziegler and H. Wollschitt, *ibid.*, **479**, 90 (1930).

(31) K. H. Meyer and H. Gottlieb-Billroth, *Ber.*, **54**, 575 (1921); H. Ley and W. Manecke, *ibid.*, **56**, 777 (1923); W. Wislicenus and A. Fehrle, *ibid.*, **48**, 1320 (1915); *cf.* W. Wislicenus and P. Neber, *Ann.*, **418**, 274 (1919).

(32) The acidity and enolization of 9-benzoylfluorene perhaps are less than expected from the effects observed in 9-phenylfluorene and VIII and indicate possible steric interference with the degree of planarity required in enol and anion.

(33) R. H. Baker and H. Adkins, THIS JOURNAL, **62**, 3305 (1940).

(34) H. E. Bent and N. B. Keevil, *ibid.*, **58**, 1367 (1936); H. E. Bent and A. J. Harrison, *ibid.*, **66**, 969 (1944).

of sodium dithionite, 0.3 g. of potassium hydroxide and 5 cc. of water gave a yellow-brown solution which was boiled under reflux in nitrogen four hours to test stability. The product, precipitated by bicarbonate, separated from silica and crystallized, was 0.02 g. of 1-hydroxy-4-methoxy-9-phenyl-2,3-benzofluorene, m.p. 143.5–146.5°.

9-Phenyl-2,3-benzofluorene-1,4-quinone.—A filtered solution of 125 mg. of 1,4-dihydroxy-9-phenyl-2,3-benzofluorene in 35 cc. of absolute ether was chilled in ice and salt, let stand with 0.5 g. of silver oxide (Merck) for 1.5 hours with occasional agitation, filtered and the residue washed with 5 cc. of cold ether and dried *in vacuo*. The solid was stirred 15 minutes at 0° with 25 cc. of pure chloroform (stored over calcium chloride and distilled from phosphorus pentoxide shortly before use) and filtered on sintered glass, and the filtrate was evaporated *in vacuo* at 20°. The yellow, crystalline residue (73 mg.) was dissolved in 10 cc. of pure chloroform, diluted with 25 cc. of ligroin (b.p. 60–70°) and chilled to furnish 37 mg. of clustered, yellow prisms of **9-phenyl-2,3-benzofluorene-1,4-quinone**, which decomposed at 180° to a dark mass melting at 215–225°, and gave a light purple solution in concentrated sulfuric acid. The ultraviolet and visible spectrum was a good index of purity: in chloroform, the ratio of optical density at 380 mμ to that at 420 mμ was 0.78 and the ratio of densities at 470 and 420 mμ 0.20.

Anal. Calcd. for $C_{23}H_{14}O_2$: C, 85.69; H, 4.38. Found[35]: C, 85.83; H, 4.50.

The solid quinone was unaltered by a methanol wash. However, when a suspension of 30 mg. of quinone in 25 cc. of methanol was boiled 20 minutes, until solution occurred, concentrated to 3 cc. and chilled, there deposited 18 mg. of dark red 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone, m.p. 218–224° (uncor.), undepressed on mixture with an authentic sample.

A filtered solution of 0.05 g. of 1,4-dihydroxy-9-phenyl-2,3-benzofluorene in 25 cc. of ether was allowed to stand 24 hours at room temperature over 0.25 g. of silver oxide, filtered, evaporated after a day to 2 cc., diluted with 2 cc. of petroleum ether and chilled to give 0.02 g. of yellow, amorphous solid, m.p. 187–192°. The material gave an orange solution in sulfuric acid and a dark blue color in alcoholic alkali, and could be separated by reprecipitation from ether–petroleum ether into fractions ranging in m.p. from 205–210° to 170–180°. The absorptions in chloroform decreased monotonically from 245 to 500 mμ, with inflections at 305 and 340 mμ.

Hydrolyses of 4-Methoxy-9-phenyl-2,3-benzo-1-isofluorenone.—A suspension of 0.05 g. of 4-methoxy-9-phenyl-2,3-benzo-1-isofluorenone in a solution of 0.15 g. of potassium hydroxide in 2 cc. of dioxane and 3 cc. of water was boiled three hours under reflux, diluted with 5 cc. of water, filtered from silica and acidified. The product, crystallized from 6 cc. of acetic acid, was 26 mg. of dark red plates of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone, m.p. 224–230°. 1,9-Dihydroxy-4-methoxy-9-phenyl-2,3-benzofluorene[8] also yielded the hydroxyisofluorenone under identical conditions.

A suspension of 0.05 g. of 4-methoxy-9-phenyl-2,3-benzo-1-isofluorenone in 5 cc. of 6 *N* hydrochloric acid and 5 cc. of acetic acid was boiled four hours under reflux, chilled and filtered. The residue, crystallized from 4 cc. of acetic acid, furnished 17 mg. of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone, m.p. 224–231°.

After 0.1 g. of the hydroxyisofluorenone in 10 cc. of methanol and 1 cc. of sulfuric acid was boiled under reflux 48 hours, the starting material was quantitatively recovered.

Sulfonation.—A solution of 0.1 g. of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone in 5 cc. of 97% sulfuric acid was let stand at room temperature for an hour, poured into 50 cc. of water, heated to 95° with 0.2 g. of kieselguhr, filtered, treated with 10 cc. of concentrated hydrochloric acid and cooled. The fine, dark red needles of **4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenonesulfonic acid**, washed with cold 5% hydrochloric acid and dried in air, weighed 0.1 g. and darkened and decomposed above 145°. The aqueous solution was orange in acid and blue-violet in base. The hydrate lost all water when dried ten hours over phosphorus pentoxide at 0.4 mm. and 30°; both the loss and the gain in weight on re-exposure to air were measured.

Anal. Calcd. for $C_{23}H_{14}O_5S \cdot 3H_2O$: H_2O, 11.84. Found (in Houston atmosphere): H_2O, 12.17, 11.87. Calcd. for $C_{23}H_{14}O_5S \cdot 2^1/_2H_2O$: C, 61.73; H, 4.28; H_2O, 10.07. Found (in air-conditioned rooms): C, 61.86; H, 4.60; H_2O, 10.3.

β-Naphthofuchsones.—The vigorous reaction of 2-benzoyl-1-naphthol[16,36] with excess phenyllithium in ether furnished crude 1-hydroxy-2-naphthyldiphenylcarbinol, which was chromatographed on alumina (eluted by benzene) and dehydrated by fusion at 160°. 2-Diphenylmethylene-1-naphthone formed dark orange prisms from ligroin (60 cc./g.), m.p. 138–140° (lit.[15] 139°), and was rapidly decolorized by warm alcoholic alkali. The substance in 90–97% sulfuric acid gave a deep green coloration that turned red in a few minutes; the green solution in 80% acid was stable. The "carbonyl" infrared absorption band in chloroform solution lay at 6.05 μ.

A solution of 0.5 g. of 2-benzoyl-1,4-naphthoquinone and 1 g. of stannous chloride dihydrate in 10 cc. of methanol was treated with 1 cc. of sulfuric acid and boiled under reflux in nitrogen overnight. The mixture was diluted with water and filtered, and the solid was freed from tin salts by solution in 10 cc. of ether and crystallized from 15 cc. of methanol to yield 0.41 g. of **2-benzoyl-4-methoxy-1-naphthol**, m.p. 111–112°. The substance formed large, bright yellow prisms that gave a yellow solution in aqueous alkali and a red solution in sulfuric acid.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found: C, 77.64; H, 5.36.

A suspension of 0.3 g. of 2-benzoyl-4-methoxy-1-naphthol in 5 cc. of ether was treated with the phenyllithium from 0.5 cc. of bromobenzene and the pale brown solution was decomposed with 2% acetic acid, extensively diluted with ether and separated. The ether, concentrated to 3 cc. and chilled, deposited 0.2 g. of pale orange crystals of 1-hydroxy-4-methoxy-2-naphthyldiphenylcarbinol. The substance turned bright orange above 100° and melted at the same temperature as the fuchsone. A 0.15-g. sample of the carbinol was fused and the melt crystallized from 40 cc. of methanol to give 0.09 g. of orange prisms of **4-methoxy-2-diphenylmethylene-1-naphthone**, m.p. 201.5–203°. The bright green solutions in 80–97% sulfuric acid had long wave length absorption maxima at 650–680 mμ (log ε 3.8–3.85) but slowly turned pink.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 84.66; H, 5.59.

Determinations of Acidity Constants.—A 2-cc. sample of stock solution of 0.45 mg. of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone in 10 cc. of ethanol was mixed with 2 cc. of 0.2 *N* aqueous potassium hydroxide and the optical density, 0.470, at 600 mμ determined. Two buffers were prepared from acetic acid and 0.2 *N* aqueous sodium acetate and the *p*H values, 4.3 and 4.65, measured, whence the concentration ratios of acetate to acetic acid were respectively 0.45 and 1. Samples of the hydroxyisofluorenone stock were added to equal volumes of the buffers and the densities at 600 mμ, 0.265 and 0.347, determined, whence the ratios of ionized to un-ionized indicator were 1.3 and 2.8. Since in 44% ethanol the pK_a of acetic acid is 5.65,[37] the pK_a of the enol is 5.2.

The acidity of the 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenonesulfonate ion was determined spectrophotometrically in aqueous acetate buffers at the ionic strength 0.01. The scatter of three values was 0.05 logarithmic unit.

The basicity of benzophenone was determined by dilution of a stock solution in 96.5% sulfuric acid to 79.2 and 75.8% acid and spectrophotometric analysis for the cation at 340 mμ.[38] For fluorenone the acid dilutions were 82.9 and 79.2% and the wave length was 400 mμ.[38] The scatters of pK_a were 0.01 and 0.06.

Basicities in commercial 99% formic acid were determined by spectrophotometric comparisons of the ratios of proto-

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[35] By Dr. A. Elek, 4763 W. Adams Blvd., Los Angeles, Calif.; other analyses by Mr. S. M. Nagy and staff, Massachusetts Institute of Technology.

[36] An attempted condensation of benzoic acid and 1-naphthol by boron trifluoride etherate according to a general preparation of 2-acyl-1-naphthols (L. F. Fieser and G. Fawaz, THIS JOURNAL, **72**, 996 (1950)) did not proceed favorably.

[37] Interpolated from E. Grunwald and B. J. Berkowitz, *ibid.*, **73**, 4939 (1951).

[38] Absorption spectra in sulfuric acid: L. C. Anderson and C. M. Gooding, *ibid.*, **57**, 999 (1935).

nated to unprotonated base for the fuchsones and isofluorenones in mixtures of concentrated sulfuric and formic acids with ratios for standard indicators in the same solvents. The indicators were *p*-nitrodiphenylamine, pK_a −2.5,[21,24] used as reference for 2-diphenylmethylene-1-naphthone, and 2,4-dichloro-6-nitroaniline, pK_a −3.3, used for the other unknowns. 2,4-Dichloro-6-nitroaniline, generously supplied by Dr. E. S. Lewis, absorbed maximally in 90% formic acid containing 1% of sodium formate at 417 mμ (log ε 3.67) (lit.[39] in acetic acid 408 (3.66)). *p*-Nitrodiphenylamine was prepared by reaction[40] of *p*-nitroacetanilide, boiling bromobenzene, potassium carbonate, potassium iodide and copper, followed by acid hydrolysis, and was advantageously crystallized from 80% acetic acid or as the solvate[41] from carbon tetrachloride. The puzzlingly wide apparent fusion range was interpreted by a polymorphic transition: the final sample melted at 133.5–134.5°, solidified at 134° and remelted at 136.5–137°. The visible absorption peak in formic acid containing 1% of sodium formate lay at 405 mμ (log ε 4.24) (lit.[42] in ethanol 390 (4.33)). The nitrodiphenylamine decomposed[43] rapidly in 97% sulfuric acid (contrary to a previous report[41]) with appearance of a deep purple color, but was stable in 70% acid.

For preparation of stock solutions, 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone (5 mg.) was dissolved in formic acid by heat (100°, 20 minutes), and the methoxyisofluorenone and fuchsones (5–15 mg.) were each dissolved in 2 cc. of chloroform and diluted with formic acid to 50 cc.; identical solvents were used for the indicators (2–8 mg.). The absorptions of the free nitroanilines were measured in 5- to 10-cc. aliquots diluted to 25 cc. and made up to 1% in sodium formate, of the protonated fuchsones and isofluorenones in aliquots made up to approximately 17% in sulfuric acid, equivalent to H_0 −5.0 (determined roughly with 2,4-dichloro-6-nitroaniline; the anilinium ion was examined in 75% aqueous sulfuric acid). The ionization ratios were determined from optical densities at apposite wave lengths of samples diluted with stock solutions of sulfuric acid in formic acid. Solutions of *p*-nitrodiphenylamine in pure formic acid or more acidic media faded (about 4% per hour in pure acid), perhaps from acylation, and the densities were extrapolated backward in time. Correction similarly was made for decomposition of 4-methoxy-2-diphenylmethylene-1-naphthone. Two determinations of pK_a of the methoxy fuchsone cation agreed to 0.01; for the other compounds, the maximum scatter of three values at different acidities was 0.04.

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[39] H. Lemaire and H. J. Lucas, THIS JOURNAL, **73**, 5198 (1951).

[40] I. Goldberg, *Ber.*, **40**, 4541 (1907); T. L. Davis and A. A. Ashdown, THIS JOURNAL, **46**, 1051 (1924).

[41] H. Ryan and T. Glover, *Proc. Roy. Irish Acad.*, **34B**, 97 (1918).

[42] W. A. Schroeder, *et al.*, *Ind. Eng. Chem.*, **41**, 2818 (1949).

[43] L. P. Hammett and A. J. Deyrup, THIS JOURNAL, **54**, 2721 (1932).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF DELAWARE]

2,2-Dialkyl-3,5-thiamorpholinediones

BY GLENN S. SKINNER AND JOHN B. BICKING

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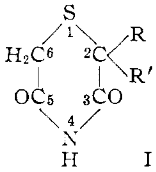
A series of 2,2-dialkyl-3,5-thiamorpholinediones has been synthesized and subjected to pharmacological screening. All except the 2,2-diphenyl derivative have significant hypnotic activity in mice.

The synthesis of 2,2-dialkyl-3,5-thiamorpholinediones (I) was undertaken for evaluation as potentially useful hypnotics, sedatives and anticonvulsants. These compounds are isosteric with the 5,5-dialkylbarbituric acids (II) in that S replaces >C=O at position 6 (or 4) and =CH_2 replaces =NH at position 1 (or 3).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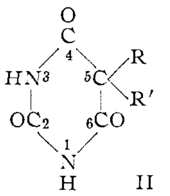
II

Thiamorpholinedione[1] was prepared by Schulze in 1866. Various alkyl derivatives[2] also are described in the literature. These alkyl derivatives are reported to be devoid of anticonvulsant activity. Derivatives corresponding to the precise pattern of two alkyls at position 2 and an unsubstituted methylene at position 6 have not been reported.

The desired thiamorpholinediones were obtained by heating the ammonium salts or amides of the α,α-dialkylthiodiacetic acids. These compounds were prepared through the action of ethyl mercaptoacetate on the ethyl bromodialkylacetate (Fig. 1), or through the action of bromoacetic acid or chloroacetamide upon the appropriate dialkylmercaptoacetic acid or amide (Fig. 2). Diphenylmercaptoacetic acid (Fig. 3) was prepared[3] from benzilic acid with the aid of its reaction on phenyl isothiocyanate. The other dialkylmercaptoacetic acids and amides were made by alkaline hydrolysis of the 5,5-dialkyl-2-imino-4-thiazolidones.

The α-bromodialkylacetyl bromides were prepared by the successive treatment of the dialkylacetic acids with thionyl chloride and bromine.[4] In the first method (Fig. 1) the α-bromodialkylacetyl bromides were converted to the esters which reacted with the sodium salt of ethyl mercaptoacetate in alcohol to give the diethyl α,α-dialkylthiodiacetates (III) whose analyses indicated the presence of impurities. These impurities could not be removed by fractional distillation but the products could be hydrolyzed to give the pure crystalline α,α-dialkylthiodiacetic acids (IV). The diethyl α,α-dimethylthiodiacetate by the action of ammonia in alcohol gave an excellent yield of the diamide VIII but the diamides of VI and VII could not be obtained in this manner. Because of the poor yields of the acids (VI and VII) only three of the 2,2-dialkyl-3,5-thiamorpholinediones (IX, X and XI) were made by this route.

In the second method (Fig. 2) the 5,5-dialkyl-2-imino-4-thiazolidones (XII) were suitably prepared by the action of the bromodialkylacetyl bromides

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[1] *Beilstein*, [4] **27**, 249 (1937).

[2] P. R. Rasenen and G. L. Jenkins, *J. Am. Pharm. Assoc.*, **38**, 599 (1949).

[3] H. Becker and H. Bistrzycki, *Ber.*, **47**, 3151 (1914).

[4] E. Fourneau and V. Nicolitch, *Bull. soc. chim.*, **43**, 1238 (1928).