The Synthesis and Spectral Properties of Some N-Substituted Derivatives of Phenol Blue

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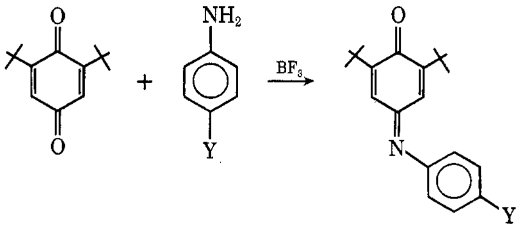
A number of 4-substituted anilines were condensed with 2,6-di-*tert*-butylbenzoquinone in the presence of BF_3 to give substituted azomethine dyes **1** in good yield. *p*-Phenylenediamine gave the corresponding dye **1**, or, in the presence of sufficient quinone, a bis dye. Studies of the effects of substituents on absorption spectra were made; as Y became more electron releasing, absorption shifted bathochromically and became more intense. Maximum electron release was obtained from dyes in which Y was anionic, as in RSO_2N^- or O^-, produced by ionization of the proton on a sulfonamide or hydroxyl group in the presence of base. The neutral sulfonamide dyes gave two-banded spectra in DMSO because of partial ionization. Anomalous shifts in absorption were observed when amido dyes were methyl-substituted on nitrogen. These shifts are the result of steric hindrance between the *N*-methyl substituent and nearby ring protons, which prevents coplanarity of the amide group and the adjacent ring. Nmr studies confirmed the nonplanar conformation of the amide group relative to the aromatic ring. Studies were made of the effects of solvents on the spectra of these dyes; increasing solvent polarity produces bathochromic shifts, but hydrogen-bonding solvents produce hypsochromic shifts in cases where Y is a substituent capable of accepting a hydrogen bond.

A previous publication describes the preparation of anils by condensation of aldehydes or ketones with anilines in chloroform, using boron trifluoride as catalyst.[1] We wish to report the extension of this synthesis to the preparation of azomethine dyes by condensation of 2,6-di-*tert*-butylquinone with para-substituted anilines. Normally, quinones undergo nuclear addition *cum* redox reactions with anilines to give complex mixtures. We have found, however, that 2,6-di-*tert*-butylbenzoquinone undergoes smooth condensation with a wide variety of anilines to give the desired azomethine dyes **1**. This behavior of 2,6-di-*tert*-butylbenzoquinone is consistent with several other reactions in which the hindered quinone shows typical carbonyl reactivity, namely, formation of a monophenylhydrazone in high yield[2] and formation of a monoxime and 2,4-DNPH.[3]



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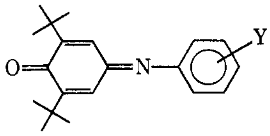
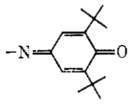
The structures and yields of the dyes prepared by this scheme are reported in Table I. We have modified the original procedure[1] by substituting tetrahydrofuran as a solvent to replace chloroform. This permits extension of the reaction to a wider variety of anilines, since insolubility of the substituted aniline in chloroform is often a limiting factor in using the procedure as originally described.

TABLE I

2,6-DI-*tert*-BUTYLQUINONE MONOIMINES 1[a]



Y^b	Mp, °C	Yield, % theory
$-NH_2$	163–165	56
$-NHCH_3$	172–172.5	62
$-N(CH_3)_2{}^c$	118–120	59
$-NHSO_2Ph$	196–197	54
$-NHSO_2C_6H_4$-*p*-OCH_3	210–212	76
$-NHSO_2C_6H_4$-*p*-NO_2	213–214	77
o-$NHSO_2C_6H_4$-*p*-CH_3	164–165, resolidified 192–193	83
$-NHSO_2CH_3$	221–222	80
$-NHCOCF_3$	174.5–175.5	85
$-NHCOCH_3$	200–201	50
$-N(Me)SO_2CH_3$	141–142	82
o-$NHSO_2CH_3$	194.5–196	28
p-NEt_2		
$-OCH_3{}^c$	72–73	67
$-H^c$	75–78	81
$-OH$	203–204	35
 (bis dye)	244–245	46

[a] Satisfactory analytical values (±0.4% for C, H, N, and, when present, s) were reported for all compounds: Ed. [b] All substituents Y are in the position para to the azomethine nitrogen atom unless otherwise noted. [c] Previously reported by A. Rieker and H. Kessler, *Tetrahedron*, **23**, 3723 (1967).

As expected, the condensation failed for benzoquinones other than 2,6-di-*tert*-butylbenzoquinone; no dyes were obtained from benzoquinone or its halogenated derivatives. With respect to choice of anilines, those containing electron-releasing substituents gave good yields of dyes; we were not able to condense *p*-nitroaniline with the hindered benzoquinone. It is notable that *p*-phenylenediamine may react at one amino group only to give a good yield of the monoazomethine dye **2**. If 2 mol of benzoquinone per mole of *p*-phenylenediamine is used and the reaction is carried out for an extended period of time, a good yield of the bis dye **3** is formed. The structure of the bis dye was confirmed by its mass spectrum (parent ion peak at *m/e* 512) and its nmr spectrum. The nmr spectrum contained two intense peaks at 1.20 and 1.32 ppm corresponding to two sets of nonequivalent *tert*-butyl groups and, in the aromatic region, a single peak,

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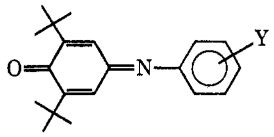
[1] M. E. Taylor and T. L. Fletcher, *J. Org. Chem.*, **26**, 940 (1960).
[2] E. Muller and K. Ley, *Chem. Ber.*, **88**, 601 (1955).
[3] S. J. Metro, *J. Amer. Chem. Soc.*, **77**, 2901 (1955).

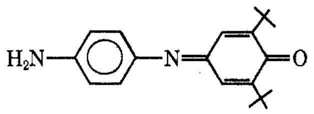
TABLE II

SPECTRAL DATA FOR AZOMETHINE DYES



No.	Y[a]	Registry no.	Cyclohexane	CCl$_4$	DMSO	DMSO + NaAc	DMSO + NaOMe	*m*-Creso
A. Wavelength Data (nm)								
A	-NH$_2$	31568-56-6	504	508	569	569	658	514
B	-NHCH$_3$	31568-57-7	527	532	583	582	682	586
C	-N(CH$_3$)$_2$	14329-32-9	542	549	585	583	584	617
D	-NHSO$_2$Ph	31568-59-9	457	456	480	612	615	440
E	-NHSO$_2$C$_6$H$_4$-*p*-OCH$_3$	31568-60-2		458	480	620	622	444
F	-NHSO$_2$C$_6$H$_4$-*p*-NO$_2$	31568-61-3		444	475	599	603	436
G	*o*-NHSO$_2$C$_6$H$_4$-*p*-CH$_3$	31568-62-4	465	467	460	625	625	453
H	-NHSO$_2$CH$_3$	31568-63-5	458	456	480	625	628	440
I	-NHCOCF$_3$	31568-64-6	452	452	470	576	576	434
J	-NHCOCH$_3$	31615-26-6	473	472	494	494	662	455
K	-N(Me)COCH$_3$	31568-65-7	446	442	454	452	*b*	418
L	-N(Me)SO$_2$Me	31568-66-8	452	449	456	454	*b*	424
M	*o*-NHSO$_2$CH$_3$ *p*-NEt$_2$	31568-67-9	573	578	605	692	694	623
N	-OCH$_3$	17119-01-6	455	477	487	486	*b*	475
O	-H	14329-20-5	443	439	445	443	*b*	420
P	-OH	31568-70-4	465	468	496	657	657	466
B. Intensity Data (Oscillator Strengths)								
A	-NH$_2$			0.214	0.312	0.311	0.584	0.218
B	-NHCH$_3$			0.242	0.315	0.326	0.486	0.303
C	-N(CH$_3$)$_2$		0.264	0.258	0.313	0.322	0.302	0.352
D	-NHSO$_2$Ph		*c*	0.111	0.154[d]	0.410	0.403	0.173
E	-NHSO$_2$C$_6$H$_4$-*p*-OCH$_3$			*c*	0.150[d]	0.418	0.422	0.183
F	-NHSO$_2$C$_6$H$_4$-*p*-NO$_2$			*c*	0.174[d]	0.399	0.412	0.220
G	*o*-NHSO$_2$C$_6$H$_4$-*p*-CH$_3$		0.133	0.138	0.090	0.088	0.126	0.129
H	-NHSO$_2$CH$_3$		*c*	*c*	0.160[d]	0.427	0.440	0.198
I	-NHCOCF$_3$		0.116	0.119	0.139	0.289	0.291	0.154
J	-NHCOCH$_3$		*c*	0.148	0.169	0.172	0.421	0.192
K	-N(Me)COCH$_3$		0.101	0.098	0.106	0.100	*b*	0.171
L	-N(Me)SO$_2$Me		0.108	0.106	0.112	0.111	*b*	0.180
M	*o*-NHSO$_2$CH$_3$ *p*-NEt$_2$		0.331	0.390	0.394	0.452	0.473	0.436
N	-OCH$_3$		0.138	0.142	0.144	0.146	*b*	0.199
O	-H		0.079	0.075	0.074	0.073	*b*	0.134
P	-OH		0.134	0.134	0.181	0.510	0.592	0.196

[a] All substituents Y are in the position para to the azomethine nitrogen atom unless otherwise noted. [b] Broad absorption at 400 nm with ill-defined maximum. [c] Insoluble at 10^{-4} *M*. [d] Double peaks present. Oscillator strength taken over both peaks.



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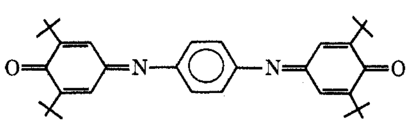

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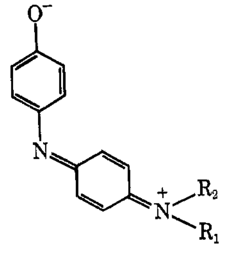
at 6.80 ppm, characteristic of the equivalent protons on the central benzenoid ring, superimposed on an AB-type pattern characteristic of the protons on the quinonoid rings.

Spectral Studies. Substituent Effects. —One of our motives in preparing the series of dyes (Table I) was to study the effects of substituents Y (1) on the visible spectra of the dyes. Results of spectral measurements are summarized in Table II, which reports the position of the absorption maxima (λ_{max}, Table II, section A) and the integrated absorption intensity (oscillator strength, Table II, section B). Spectra were obtained in several different solvents to ascertain the effects of dye structure on response of the spectra to changes in solvent polarity. Solvent effects are discussed in detail in the next section.

Introduction of an amino substituent into the benzenoid portion of dye A (Y = NH$_2$) has a large hyperchromic (intensity-enhancing) effect and shifts the dye absorption 70 nm toward the red (Table II, compare dyes A and O). This effect of the amino group can be understood in terms of charge transfer from the amino group to the chromophore, represented in valence bond terminology as an increased contribution of the dipolar structure **4** to the excited state, which is made possible by the amino group. In terms of molecular orbital language, the unshared electron pair on the terminal nitrogen atom becomes delocalized into



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the chromophore on excitation. Hückel calculations with reasonable parameter sets[4,5] confirm that the terminal nitrogen atom in the amino compound becomes more positive in the first excited state, assuming promotion of an electron from the highest filled molecular orbital to the lowest energy virtual orbital. Accordingly, structural factors which increase the electronegativity of the nitrogen substituent will result in hypsochromic shifts and, conversely, electron release at that atom will give bathochromic effects. The effects of substituents reported in Table II are readily rationalized by this picture; *e.g.*, introduction of electron-releasing methyl groups at the terminal amino group (Table II, compounds A and C) cause bathochromic shifts, while electron-attracting substituents such as sulfonyl (D, E, F, G, H), acetyl (J), and trifluoroacetyl (I) cause hypsochromic shifts. Likewise, replacement of the amino group by a hydroxyl group (P) causes a hypsochromic shift, presumably because of the higher electronegativity of the oxygen atom. The intensity variations follow the wavelength shifts; *i.e.*, a decrease in availability of electrons at the para substituent is accompanied by a decrease in the intensity of the absorption.

Although an *N*-methyl substituent causes a bathochromic shift when substituted on *amino* nitrogen (compare A and B, Table II), an opposite kind of shift is observed when the methyl group is substituted on *amido* nitrogen; compare compounds J and K, Table II, which show that introduction of a methyl group on the *p*-acetamido group causes a hypsochromic shift of 30 nm or more. Analogous (but smaller) effects occur with sulfonyl analogs (H and L, Table II) in carbon tetrachloride solution. These hypsochromic shifts produced by methyl substitution are also accompanied by small decreases in the intensity of the absorption. This reversal of the "normal" effect of the methyl group can be explained by steric hindrance, which prevents coplanarity of the amido group with the adjacent aromatic ring owing to interference between the *N*-methylacetamido group and the ring protons ortho to it. The possibility of such steric interference is confirmed by Courtauld models and also by observations of the nmr spectra of the methylated and unmethylated amido dyes.

The nmr spectra of the acetamido dye and of its *N*-methyl analog contain two overlapping AB-type spin-splitting patterns. One of these AB patterns corresponds to protons with chemical shifts of δ 6.70 and 6.84 ppm in the case of the *p*-acetamido compound (J, Table II) and δ 6.65 and 6.85 ppm in the case of the *N*-methylacetamido compound (K, Table II). These absorptions may be assigned to the protons on the quinonoid ring of structure **1**. This assignment is supported by the relative intensities of the absorptions (two protons) and the small value of the coupling constant, $J_{AB} = 2$ cps, expected as a result of the meta orientation of the two protons. As expected, these protons are not much affected by replacement of the proton on the remote amide group with a methyl substituent.

The other AB-type pattern corresponds to protons with chemical shifts of δ 6.70 and 7.45 ppm in the case of the *p*-acetamido compound (J, Table II) and δ 6.79 and 7.14 ppm in the case of the *N*-methylacetamido compound (K, Table II). These absorptions may be assigned to the AA′BB′ protons on the benzenoid ring in structure **1**; this is consonant with the relative intensities (four protons) and the larger coupling constant, $J_{AB} = 9$ cps, characteristic of protons situated ortho to each other. In this case, there is a relatively large *upfield shift* of about 20 cps (0.31 ppm) in the absorption of one set of protons resulting from replacement of the proton on the amide group by a methyl substituent. This is attributable to aplanarity of the *N*-methylacetamide group and the adjacent benzene ring, which exposes ortho protons to the diamagnetic portion of the field associated with the carbonyl group.[6]

Spectral Studies. Solvent Effects.—A survey of the spectral data in Table II, section A shows that all of the dyes are more or less bathochromically shifted in DMSO *vs.* carbon tetrachloride. On the other hand, there are distinct differences in responses of the dyes to *m*-cresol as solvent; while the *N*-methylamino and *N*,*N*-dimethylamino dyes (B, C, Table II) show large *bathochromic* shifts in *m*-cresol (*vs.* CCl_4), the parent amino compound (A, Table II, section A) shows a much smaller bathochromic shift and all of its amido derivatives (D–L, Table II, section A) give *hypsochromic* shifts in *m*-cresol.

In an earlier paper,[7] a mathematical model was used to measure the spectral changes produced by hydrogen bonding for a series of dyes related to **1**. In brief, the analysis depended upon fitting spectral data to an equation proposed by McRae (see ref 7) which was shown to be successful in correlating the absorption frequency ν_s of a solute in a given solvent having refractive index n and dielectric constant D, given the absence of extraneous factors such as hydrogen bonding between solvent and solute. The equation has the form (eq 1) where ν_g, A and B are parameters

$$\nu_s = \nu_g + \frac{n^2 - 1}{2n^2 + 1}A + \left(\frac{D - 1}{D + 2} - \frac{n^2 - 1}{n^2 + 2}\right)B \qquad (1)$$

evaluated by regression of observed frequencies ν_s on n and D. We showed that this equation fitted spectral data well in cases where hydrogen bonding was absent and argued that *deviations* of spectral data from this equation could be attributed to factors other than solvent polarity (measured by n and D), such as hydrogen bonding. In this way, we could separate effects of hydrogen bonding on spectra from other solvent polarity effects. In the previous work, it was concluded that the relatively small bathochromic shift shown by the amino dye (A, Table II) for the change in solvent

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[4] W. F. Smith, *Tetrahedron*, **20**, 671 (1964).

[5] A. J. Wohl, *ibid.*, **24**, 6889 (1968).

[6] L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," Pergamon Press, Elmsford, N. Y., 1969, p 88.

[7] J. Figueras, *J. Amer. Chem. Soc.*, **93**, 3255 (1971).

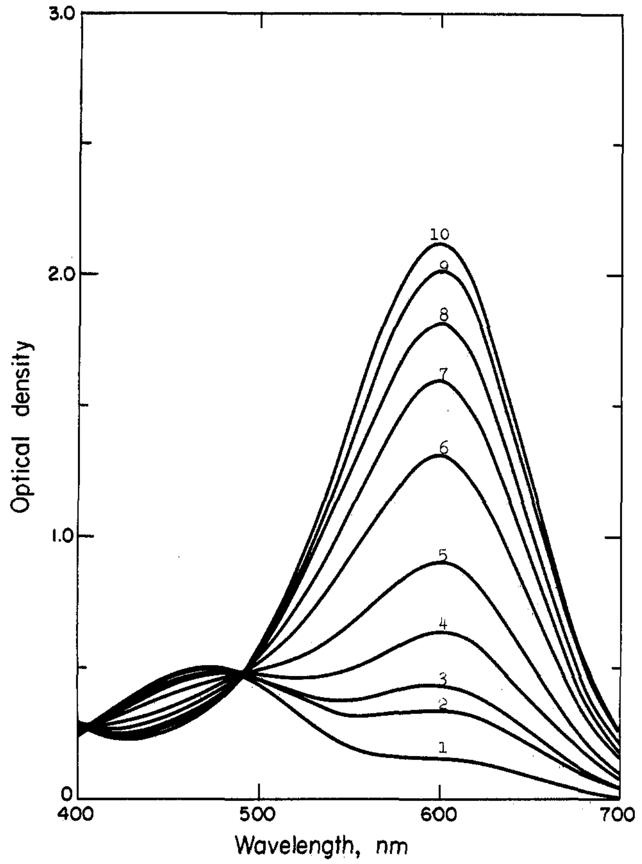
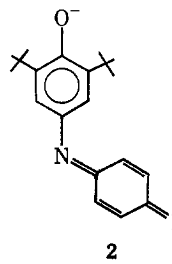


Figure 1.—Absorption spectra of *N*-[4-(4-nitrobenzenesulfonamido)phenyl]-2,6-di-*tert*-butylenenzoquinone monoimine: triethylethylamine concentrations (mol/l.), (1) 0, (2) 1 × 10^{-5}, (3) 2 × 10^{-5}, (4) 4 × 10^{-5}, (5) 8 × 10^{-5}, (6) 2 × 10^{-4}, (7) 4 × 10^{-4}, (8) 8 × 10^{-4}, (9) 2 × 10^{-3}, (10) 1 × 10^{-2}; dye concentration, 10^{-4} *M;* solvent, dimethyl sulfoxide.

from CCl_4 to *m*-cresol, as compared with the much larger shifts shown for the same solvent change by *N*-alkylated analogs (B and C, Table II) was the result of a hypsochromic component arising from stronger hydrogen bonding of the primary amino group of dye A with the O–H group of *m*-cresol. Hydrogen bonding at the terminal nitrogen atom is expected to shift dye absorption hypsochromically owing to increased localization of the unshared pair on nitrogen, which would destabilize the dipolar contributing structure 2. Extension of this argument to the amide dyes (D–L, Table II) explains the hypsochromic shift which they generally show in the more polar *m*-cresol *vs.* CCl_4 even though the "normal" effect of increasing solvent polarity appears to be bathochromic (compare spectral data in DMSO *vs.* those in CCl_4, Table II). It is not possible to discern whether bonding involves the terminal amide nitrogen as in **5**, or acyl (sulfonyl) oxygen as in **6**, although bonding at oxygen is believed to be more likely (*vide infra*). Both kinds of interaction would be expected to give hypsochromic spectral shifts.



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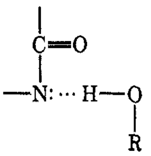
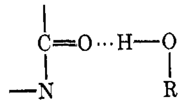


$$\overset{\overset{|}{\mathrm{C{=}O}}}{\overset{|}{-\mathrm{N}{:}}}\cdots\mathrm{H}-\underset{\mathrm{R}}{\underset{|}{\mathrm{O}}}$$

5



$$\overset{|}{\underset{-\mathrm{N}}{\underset{|}{\mathrm{C}}}}{=}\mathrm{O}\cdots\mathrm{H}-\underset{\mathrm{R}}{\underset{|}{\mathrm{O}}}$$

6

Quantitative estimates of deviations from the McRae eq 1 for solutions in *m*-cresol and trifluoroethanol (TFE) were made for four of the amido dyes,[8] namely, the acetamido dye, the *N*-methylacetamido dye, the sulfonamido dye, and the *N*-methylsulfonamido dye (J, K, H, L, respectively, Table II). Spectral data were obtained in 16 different solvents for each dye and were fitted to the McRae eq 1 using the computer program described in ref 7. The deviations from the McRae equation for the amide dyes in *m*-cresol and TFE are particularly large, and negative, compared with the large, positive deviation shown by the dimethylamino derivative. These deviations are obtained by subtracting the calculated transition energy (in kcal/mol) using the McRae equation from the observed transition energy. The results are summarized in Table III; data for the parent amino and methylamino dyes are taken from our earlier study. As noted previously, and as exemplified in Table III, the introduction of methyl groups at the terminal amino nitrogen atom reduces in large degree the hypsochromic effect resulting from interaction of the amino group with solvent O–H groups (first three lines of Table III). This is not observed, however, with the amido dyes, where N-methylation has a relatively small effect on the magnitude of the hydrogen-bond shift, a result which suggests that the interaction of the amide group with cresol solvent or TFE involves acyl oxygen rather than nitrogen (*cf.* ref 6, above). Gramstad and Fuglevik[9] found, by means of infrared spectroscopy with mixtures of N,N-disubstituted amides and phenol, that the carbonyl oxygen atom in all of the amides that they studied participated in hydrogen bonding. It is of interest that these authors observed enthalpies of hydrogen-bond formation of 4.0–5.7 kcal/mol in carbon

TABLE III

DEVIATIONS[a] FROM THE MCRAE EQUATION, KILOCALORIES/MOLE

Substituent Y	*m*-Cresol	TFE
$-NH_2$	−3.6	−6.7
-NHMe	1.1	−2.2
$-N(CH_3)_2$	3.6	−2.2
$-NHCOCH_3$	−4.0	−4.7
$-N(Me)COCH_3$	−3.5	−5.4
$-NHSO_2CH_3$	−2.6	−4.7
$-N(Me)SO_2CH_3$	−2.1	−5.0

[a] Deviation = $E - \hat{E}$ where E = observed transition energy and $\hat{E}$ = transition energy calculated from eq 1.

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(8) Listings of solvents, solvent parameters, spectral data, and results from regression analysis will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Reprint Department, ACS Publications, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to author, title of article, volume, and page numbers. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche.

(9) T. Gramstad and J. Fuglevik, *Acta Chem. Scand.*, **16**, 1369 (1962).

TABLE IV

EFFECTS OF STRUCTURAL CHANGE ON ABSORPTION SPECTRA IN DMSO

	Substituents, Y (para)									
	H	$NHSO_2CH_3$	$NHCOCH_3$	NH_2	NHMe	NMe_2	$^-NSO_2Me$	$^-NHCOCH_3$	^-NH	^-NMe
λ_{max}	445	480	494	569	583	585	628	662	658	682
f	0.074	0.160	0.169	0.312	0.315	0.313	0.440	0.421	0.584	0.486

tetrachloride solution, which is of the same order of magnitude as the hypsochromic spectral shifts which we have attributed to hydrogen bonding (Table III).

Substantial positive deviations from the McRae equation were obtained for spectra in DMSO and DMF. The source of these deviations is not known. Similar deviations for highly polar solvents were noted in the earlier study.[7] The deviations may not be related to hydrogen bonding, since the *N*-methyl dyes, which have no labile protons, show deviations in DMSO which are as large as those given by their parent amides.

Spectral Studies. Ionization.—In DMSO, the sulfonamido dyes D, E, F, and H (Table II, section A) give two absorption peaks: a principal band in the 480-nm region (reported in Table II, section A) and a much weaker band at ~620 nm. The long wavelength band does not appear in the spectra of the *N*-acetyl dyes, nor in those cases in which the N–H proton is replaced by methyl, nor does it appear in nonpolar media. This band is assigned to absorption of the anion resulting from ionization of the N–H proton. Addition of sodium methoxide to DMSO solutions of the sulfonamido dyes converts them completely to anions, with a large shift in the absorption peak of the dye to longer wavelengths and a large increase in absorption intensity. In fact, sodium methoxide is a sufficiently strong base in DMSO to convert all of the dyes having terminal N–H groups into their corresponding anions, as shown in the seventh columns of Table II, sections A and B. With a weaker base, sodium acetate in DMSO, only the sulfonamido dyes (D–H, Table II, section A, B) and the trifluoroacetyl dye (I, Table II, section A, B) are sufficiently acidic to be converted to anions. Analogous spectral shifts on addition of base are observed with the terminal hydroxy dye (Y = OH, dye P, Table II, section A, B). Figure 1 illustrates the changes in spectra of the 4-nitrobenzenesulfonamido dye (1, Y = $-NHSO_2C_6H_4$-*p*-NO_2) in a concentration series of triethylamine; a well-defined isosbestic point is obtained.

The anions absorb at very much longer wavelengths than do the parent dyes and with almost twice the intensity. This behavior agrees with the trend previously noted that an electron-releasing substituent on the terminal amino group causes bathochromic and hyperchromic shifts; such electron release will be greatest for anion formation at the terminal nitrogen atom. In Table IV are summarized the effects of structural change at terminal nitrogen, including anion formation. The substituents, Y, at the head of Table IV are arranged from left to right in order of increasing electron density expected at terminal nitrogen from consideration of resonance and inductive effects. Particularly striking is the large variation of nearly 240 nm in λ_{max} produced by changes in a single substituent.

Experimental Section

Dye Preparation.—2,6-Di-*tert*-butylbenzoquinone (2.20 g, 0.01 mol), an equivalent amount of the desired substituted aniline, and 6 drops of boron trifluoride etherate were dissolved in 25 ml of dry tetrahydrofuran. The mixture was heated at the boiling point for 2–3 hr. The solvent was stripped off, and the residue was taken up in chloroform and chromatographed on a 6-cm × 24-in. column packed with Florisil. The main band was eluted with chloroform and the recovered product was recrystallized from methanol–water.

In cases where the aniline hydrochloride only was available, an equivalent amount of sodium acetate or sodium methoxide was added to free the amine from its salt. The anilines were commercial materials, used without purification, or were prepared by straightforward methods. *p*-Phenylenediamine was prepared by hydrogenation of *p*-nitroaniline in THF and used directly without isolation; commercially available material gave poor results.

Spectral Measurements.—These were made at room temperature with a Hardy model spectrophotometer manufactured by the General Electric Co. Solvents were Eastman Spectro-Grade or White Label materials and were dried and stored over Linde 4A Molecular Sieves. *m*-Cresol was Practical Grade material, distilled before use. The nmr spectra were determined by means of a Varian A-60 machine.

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