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The Effect of Alkyl Groups on 4-Nitro- and 4-Nitroso-phenols

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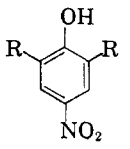
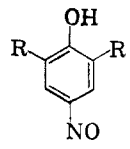
Four symmetrical 2,6-dialkyl-4-nitrophenols and the four corresponding nitrosophenols, and two symmetrical 3,5-dialkyl-4-nitrophenols and the corresponding nitrosophenols have been examined for the effect of the alkyl substituents on the infrared and ultraviolet spectra as well as the *p*Ka values of the phenols. Possible steric and polar factors are discussed in the light of the available data, and a number of apparent anomalies are considered. Most striking is the acidic character of 2,6-di-*tert*-butyl-4-nitrophenol which proves to be a stronger acid than 4-nitrophenol in 35 mole-% ethanol.

In the interests of obtaining data on the effect of size and position of alkyl groups on the properties of 4-nitro- and 4-nitrosophenols, two series of compounds were prepared: (I) the 2,6-dialkyl-4-nitrophenols, and (II) the 3,5-dialkyl-4-nitrophenols; and the corresponding 2,6-dialkyl-4-nitrosophenols (III) and 3,5-dialkyl-4-nitrosophenols (IV)



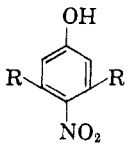
I

(a) R = CH_3
(b) R = C_2H_5
(c) R = *i*-C_3H_7
(d) R = *tert*-C_4H_9



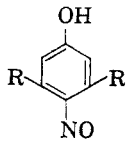
III

(a) R = CH_3
(b) R = C_2H_5
(c) R = *i*-C_3H_7
(d) R = *tert*-C_4H_9



II

(a) R = CH_3
(b) R = C_2H_5



IV

(a) R = CH_3
(b) R = C_2H_5

PHYSICAL MEASUREMENTS

The effect of size and position of alkyl groups in 4-nitro- and 4-nitroso-phenols was studied by means of two primary techniques: spectrometry, both ultraviolet and infrared; and determination of acid dissociation constants. The latter was of particular interest in view of the excellent work of Wheland, Brownell, and Mayo[2] wherein the steric inhibition of resonance in 4-nitrophenol by 3,5-dimethyl substitution was demonstrated. In the present instance an increase in size of the 3,5-substituents was desired to see to what extent such inhibition could be increased.

Spectrophotometric analysis. The spectrophotometric (infrared) results were such as to enable demonstration of the effect of the alkyl groups on the quinone-monoxime equilibrium with *p*-nitrosophenols and the extent to which hydrogen bonding is affected by increasing the size of alkyl groups flanking the phenolic and oximic hydroxyls.

The infrared spectra were obtained from Nujol mulls and from dilute solutions. Coggeshall[3] has shown that the amount of hydrogen bonding is the same in concentrated solutions as in crystalline samples, so these two procedures provide the extremes of hydrogen bonding. Since the chief interest in these spectra is in the region of the O—H stretching frequency, the wavelengths of maximum absorption in this region are given in the first four columns of Table I.

By means of ultraviolet spectroscopy the relative amount of quinoid character in the 4-nitrosophenols

(1) Abstracted in part from the Ph.D. dissertation of Gaylord Kirkwood Finch, University of Michigan, 1954.

(2) G. W. Wheland, R. M. Brownell, and E. C. Mayo, *J. Am. Chem. Soc.*, **70**, 2492 (1948).

(3) N. D. Coggeshall, *J. Am. Chem. Soc.*, 69, 1620 (1947).

TABLE I
SPECTROPHOTOMETRIC DATA

Phenol	Infrared (μ) Phenol —OH Dilute Soln.	Phenol —OH Nujol Mull	Oxime —OH Dilute Soln.	Oxime —OH Nujol Mull	Ultraviolet (mμ) λ_{max} Methanol	Log ϵ
2,6-Di-*tert*-butyl-	2.74[a]	2.75	—	—	—	—
4-Nitroso-	2.90[b]	3.15	3.06[c]	3.26	303	4.09
2-Methyl-4-nitroso-	2.90[b]	3.16	3.05[c]	3.26	305	4.26
2,6-Dimethyl-4-nitroso-	2.90[b]	3.17	3.04[c]	3.25	306	4.32
2,6-Diethyl-4-nitroso-	2.84[a] 2.90[b]	3.15	3.08[a] 3.05[b]	3.25	307	4.28
2,6-Diisopropyl-4-nitroso-	2.84[a] 2.90[b]	3.12	3.08[a] 3.05[c]	3.25	308	4.26
2,6-Di-*tert*-butyl-4-nitroso-	2.82[a] 2.89[b]	3.05	3.08[a] 3.04[c]	3.25	304	4.25
3,5-Dimethyl-4-nitroso-	2.91[a]	3.14	3.10[c]	3.29	301	4.33
3,5-Diethyl-4-nitroso-	2.91[a]	3.17	3.10[c]	3.28	299	4.16
4-Nitro-	2.80[a]	3.02			315[d]	4.05[d]
					345[d]	3.72[d]
2-Methyl-4-nitro-	2.81[a]	2.91			320	3.99
2,6-Dimethyl-4-nitro-	2.79[a]	2.89			322	4.00
2,6-Diethyl-4-nitro-	2.79[a]	2.93			322	3.96
2,6-Diisopropyl-4-nitro-	2.78[a]	2.90			323	3.95
2,6-Di-*tert*-butyl-4-nitro-	2.77[a] 2.78[b]	2.83			320	3.95
3,5-Dimethyl-4-nitro-	2.81[a] 2.84[e]	3.03			331 (min.)	3.08
3,5-Diethyl-4-nitro-	2.81[a] 2.84[e]	3.01			324 (min.)	2.88

[a] CCl_4. [b] C_6H_6. [c] CH_3CN. [d] L. Marchalewski and A. Moroz, *Bull. soc. chim.*, [4] **35**, 473 (1924). [e] CH_2Cl_2.

is demonstrable and can be related to the relative intensities of the O—H absorptions due to the phenolic and oximic hydroxyls. The ultraviolet spectra were obtained from absolute methanol solutions and the wavelengths of maximum absorption and log ϵ values are recorded in the last two columns of Table I.

Determination of pKa values. Since many of the compounds of interest were practically insoluble in water, an aqueous ethanol system was used as solvent for most of the titrations. The compounds were dissolved in absolute alcohol and titrated with aqueous sodium hydroxide. The solutions used were of approximately the same ionic strength which was low enough so that dilution with the titrating aqueous solution would have little or no effect on the activities.

Previous investigators[4,5] have shown that an approximately linear relationship exists between the *p*Ka values of acetic acid and propionic acid and the mole fraction of dioxane when aqueous dioxane is used as the solvent. However, the deviation from a strictly linear relationship may be considerable, as shown by Hammett.[6] Since the variation of *p*Ka with solvent is probably due to the decrease in the dielectric constant of the solvent, a slight decrease in the activity coefficient of the undissociated acid and an increase in the activity coefficient of the anion of the acid is expected: for example, Schwarzenbach and Rudin[7] give the *p*Ka values at 20–22° for *p*-nitrophenol as 7.68 in 49% alcohol and 9.76 in 95% alcohol. Similar variations were observed in the present study, but the change of *p*Ka values with mole fraction of ethanol proved to be strictly linear.

The more water-soluble compounds were titrated by dissolving them in an excess of sodium hydroxide and back titrating with hydrochloric acid until the acid began to precipitate.

The values of *p*Ka were calculated at $^1/_4$, $^1/_2$ (Table II), and $^3/_4$ neutralization and at the end point by means of a modified neutralization equation:[8]

$$pKa = pH - \log [(salt)] - (OH^-)]/[(acid) + (OH^-)] + 2.3 \frac{RT}{F} \log \frac{p'}{p}$$

where $\Delta E \left(= 2.3 \frac{RT}{F} \log \frac{p'}{p} \right)$ has been added[9] to correct for the dielectric constant by taking into account the difference in the activity of the hydrogen ion in the mixed solvent and in pure water: p′ is

(4) H. S. Harned and B. B. Owen, *The Physical Chemistry of Electrolytic Solutions*, 2nd Ed., Reinhold Publ. Corp., New York, N. Y., 1950, p. 509.
(5) L. G. Van Uitert and C. G. Haas, *J. Am. Chem. Soc.*, **75**, 454 (1953).
(6) L. P. Hammett, *Physical Organic Chemistry*, McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 259.
(7) G. Schwarzenbach and E. Rudin, *Helv. Chim. Acta*, **22**, 364 (1939).
(8) E. J. Cohn, *J. Am. Chem. Soc.*, **49**, 173 (1927).
(9) M. Dole, *The Glass Electrode*, John Wiley and Sons, Inc., New York, 1941, p. 276.

TABLE II

*p*Ka VALUES

Phenol	Water	*p*Ka 35 mole-% ethanol (½ neutralized)	Ethanol
Phenol	9.99[a]		12.8[b]
2,6-Dimethyl-	10.59[a]		
3,5-Dimethyl-	10.14[a]		
4-Nitroso-		7.35	8.1[c]
2-Methyl-4-nitroso-		8.02	
2,6-Dimethyl-4-nitroso-		8.75	
2,6-Diethyl-4-nitroso-		8.93	
2,6-Diisopropyl-4-nitroso-		9.08	
2,6-Di-*tert*-butyl-4-nitroso-		9.63	
3,5-Dimethyl-4-nitroso-	8.04	8.43	
3,5-Diethyl-4-nitroso-	8.34	8.65	
4-Nitro-	7.24[d]	8.26	10.1[b]
2-Methyl-4-nitro-		8.54	
2,6-Dimethyl-4-nitro-	7.22[a]	8.34	
2,6-Diethyl-4-nitro-	7.73	8.55	
2,6-Diisopropyl-4-nitro-		8.54	
2,6-Di-*tert*-butyl-4-nitro-		7.96[e]	
3,5-Dimethyl-4-nitro-	8.25[a]	9.64	
3,5-Diethyl-4-nitro-		10.00	

[a] L. Canonica, *Gazz. chim. ital.*, **77**, 92 (1947). [b] Absolute ethanol, W. D. Treadwell and G. Schwarzenbach, *Helv. Chim. Acta*, **11**, 386 (1928). [c] 96% ethanol, see footnote *b*. [d] C. M. Judson and M. Kilpatrick, *J. Am. Chem. Soc.*, **71**, 3110 (1949). [e] From linear plot of *p*Ka *vs.* mole fraction of ethanol: 0.0500 *M* NaOH. See experimental.

the partial pressure of water in the mixed solvent and p is the vapor pressure of pure water. At 25°, $2.3\frac{RT}{F} = 0.05914$ and $0.05914 \log \frac{p'}{p} = 0.01$ for the concentrations used. The values of p′ are given by Foote and Scholes.[10]

The values for *p*Ka that were obtained for ½ neutralization (35 mole-% ethanol) are reported in Table II and the linear relationship between *p*Ka and mole-per cent alcohol obtains except near the end point, as expected. It is of interest that the slopes of the lines in such plots in the range of 25–55 mole-% ethyl alcohol are approximately the same for all of the compounds. However, the relative order of the compounds with respect to acid strength is not the same in water as in aqueous alcohol for the nitroso and nitro series, although it is the same within each series. This type of variation has previously been reported[11] and is to be expected, since there should be a different effect on compounds of different polarity and containing different functional groups. The extent of solvation of the —OH group and the anion is undoubtedly involved in this effect.

(10) H. W. Foote and S. R. Scholes, *J. Am. Chem. Soc.*, **33**, 1323 (1911).

(11) W. L. Bright and H. T. Briscoe, *J. Phys. Chem.*, **37**, 787 (1933).

DISCUSSION

4-Nitrosophenols

The work of Anderson and his co-workers[12] has established the tautomeric nature of the 4-nitrosophenol system and the essential lack of ionization therein, and the substitution of alkyl groups adjacent to either functional group should have a demonstrable effect on the position of equilibrium in such a system. In general terms the present data indicate that in methanol, 2,6-substitution produces more of the quinone-monoxime structure while 3,5-substitution has the opposite effect, as seen by the shift of maxima in the ultraviolet spectra (Table I, last two columns).

In the solid state two absorption bands (infrared) due to hydroxyl are observed for each member of the series. Assignment to oximic and phenolic hydroxyl may be made on the basis that in the 2,6-series one band remains at an essentially constant wavelength (oxime: no change in hydrogen bonding) while the other shifts to shorter wavelengths with increased substituent branching (phenolic). Furthermore, a band attributable to the aromatic double bonds, at ≈6.25 μ, with increased branching of the 2,6-alkyl groups clearly increases in intensity in concert with the hydroxyl band at the shorter wavelength, while the band associated with C=N bond at ≈6.15 μ decreases in intensity. Thus, the effect of 2,6-substitution in the solids is opposite to the effect observed for methanol solution; increased branching in the 2,6-positions promotes tautomerization to the phenolic form.

In the 3,5-series, on similar grounds the shorter wavelength hydroxyl band may be assigned to the phenolic hydroxyl, and 3,5-substitution and increased branching in these positions appear to favor tautomerization to the phenolic form. This, however, is expected, and it parallels to the situation which obtains in methanol solution.

While most of the 4-nitrosophenols are not sufficiently soluble in non-polar solvents (*e.g.*, carbon tetrachloride, carbon disulfide, methylene chloride, etc.) to permit making spectrophotometric measurements, the 2,6-diethyl-, 2,6-diisopropyl-, and 2,6-di-*tert*-butyl-4-nitrosophenols dissolved sufficiently in carbon tetrachloride to permit obtaining infrared spectra in a 1-mm. cell. The other members of the series, as well as these, were similarly examined in benzene (for phenolic hydroxyl) and acetonitrile (for oximic hydroxyl). As in the solid state the oximic hydroxyl bond (broad) appears at a longer wavelength than the phenolic (sharp) band. In these compounds increased branching in the 2,6-substituents thus *increases* the percentage of the phenolic tautomer in dilute carbon tetrachloride solution. One might have predicted

(12) L. C. Anderson and M. B. Geiger, *J. Am. Chem. Soc.*, **54**, 3064 (1932); L. C. Anderson and R. L. Yanke, *J. Am. Chem. Soc.*, **56**, 732 (1934).

this for the 2,6-di-*tert*-butyl-4-nitrosophenol, since its ultraviolet spectrum has its peak close to that of 4-nitrosophenol, although with a smaller extinction coefficient. However, in the other compounds, whose ultraviolet absorption maxima are from 2 to 5 mμ removed from that of 4-nitrosophenol, an increase in the percentage of phenol certainly appears anomalous.

In the solid state it would appear that the optimum crystalline arrangement of the tautomers is such that approximately the same hydrogen bonding occurs at all oximic hydroxyls. The increasing intensity of the phenolic hydroxyl band with branching reflects the steric favoring of this form in the crystal state and its shift toward shorter wavelengths with increasing bulk adjacent to the phenolic group is a reflection of less efficient intermolecular hydrogen bonding as the hydroxyl encounters more hindrance to close approach to another oxygen.

Tautomerism in solutions poses different problems, since the system is now labile and subject not only to internal steric factors but to external forces associated with polar and non-polar solvents. To a certain extent the acetoacetic ester system may be considered as analogous.[13] In this compound the less polar enol form is favored in less polar (*e.g.*, hexane) solvents and the more polar keto form in more polar solvents (*e.g.*, methanol). In addition the competition of an alcoholic hydroxyl with enolic hydroxyl tends to diminish the stability of the enol form, thus favoring a shift to the keto form.

From solubility behavior it appears that the more highly branched 2,6-dialkyl-4-nitrosophenols are the less polar (greater carbon tetrachloride solubility), and since the relative intensities of phenolic and oximic absorption bands indicate an increase in phenolic form with increased branching—to a greater extent in carbon tetrachloride solution than in the solid state—one must conclude that the phenolic form in this series is the less polar. The shift toward higher oxime content in methanol solution, as indicated by the ultraviolet data, appears to support this hypothesis, since the more polar solvent should favor the more polar form. It therefore seems that the position of equilibrium in the 4-nitrosophenol-benzoquinone-monoxime tautomerism is *not* subject to purely steric influence, since, on the whole, the opposite effect is observed to that expected if there were indeed steric interference with the phenolic hydroxyl. Indeed the only detectable steric effect is simple inhibition of hydrogen bonding to the phenolic hydrogen.

In the 3,5-dialkyl-4-nitrosophenol series the situation is different. The longer wavelength hydroxyl band diminishes in intensity relative to the shorter and at the same time the azomethine band decreases relative to the aromatic double bond band in passing from 4-nitrosophenol to 3,5-diethyl-4-nitrosophenol. Also a marked shift toward shorter wavelengths is observed in the ultraviolet spectra obtained in methanol. Accordingly the crowding about the 4-position introduced by 3,5-alkylation is sufficient to repress the oxime form. Virtual insolubility of the 3,5-dialkyl-4-nitrosophenols in non-polar solvents suggests a greater polarity in this series, possibly due to the complete lack of alkyl shielding of the phenolic group, but in the absence of more than two members there is no basis for considering polar factors.

It remains to explain the existence of steric interference with the oximic hydroxyl by 3,5-dialkylation and not with the phenolic hydroxyl by 2,6-substitution. The geometry of the oxime group requires the oxygen to be coplanar with the ring; thus, in rotations of the hydroxyl about the nitrogen-oxygen bond the hydrogen will be brought into closer contact with the flanking substituents than will the hydrogen of the phenolic group in similar surroundings. Consequently, in relief of this crowding the hydrogen tends to migrate to the ketonic oxygen with concommitant bond shifts to the phenolic form. A certain amount of crowding, though considerably less, is encountered by the phenolic hydrogen in the 2,6-dialkyl series. Apparently, polar factors outweigh a minor steric factor in this series while the steric factor is enough more significant to be observed in the 3,5-series.

One anomaly in the ultraviolet spectra requires comment, the sharp decrease in λ_{max} for 2,6-di-*tert*-4-nitrosophenol. Since no reversal in oxime content seems called for, it may reasonably be attributed to complete absence of hyperconjugative contributions to the excited state(s) of the system. Such an effect has been observed previously.[14]

4-Nitrophenols

In the 4-nitrophenol series several general differences are at once apparent on comparison with the corresponding 4-nitrosophenols. First, the ultraviolet absorption maxima appear at appreciably longer wavelengths in the 2,6-dialkyl series. This is attributable to a more polar excited state involving the nitro group. Furthermore, since tautomerization is not expected (*cf.* but *one* O—H absorption band in the infrared), it is not surprising that there is no well-defined shift of maxima with change in structure. The anomalous decrease in λ_{max} for 2,6-di-*tert*-butyl-4-nitrophenol is similar to that encountered with the 4-nitroso analog and attributable to the same factors (*vide supra*).

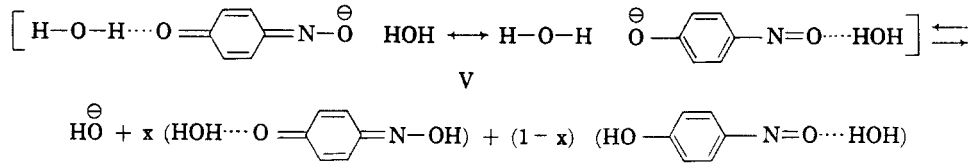
Second, there is no apparent relationship, of the type encountered in the nitroso series, between phenolic hydroxyl absorption and structure. The

(13) For discussion and leading references *cf.* Branch and Calvin, *The Theory of Organic Chemistry*, Prentice Hall, New York, N.Y., 1946, pp. 296 ff.

(14) F. A. Matsen, W. W. Robertson and R. L. Chuoke, *Chem. Revs.*, **41**, 273 (1947).

wavelengths are erratic in the solid state but, however, show about the same shift in solution toward shorter wavelengths with increased 2,6-branching, as in the nitroso series.

Finally, while there is nothing remarkable about the infrared data for the 3,5-dialkyl-4-nitrophenol series, the ultraviolet spectra are strikingly different from the 2,6-series. The 322 mμ band has disappeared entirely leaving instead a minimum at slightly longer wavelength; the inhibition of resonance of the aromatic nitro system is thus quite evident, and more pronounced for 3,5-diethyl than for 3,5-dimethyl substitution.



V

ACID STRENGTH

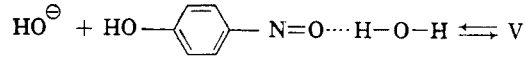
The introduction of alkyl groups characteristically may be expected to decrease the acid strength of phenol (+I effect), more significantly when the groups are close to the hydroxyl. That the size of such groups in close proximity to the hydroxyl may be significant is evident from the total lack of solubility of 2,6-di-*tert*-butylphenol in alkali of any strength. Systematic studies of this type of effect have been made[3,15-18] and need no further comment.

Both nitroso and nitro groups are generally accepted as strongly electron withdrawing in the inductive sense, and when suitably located, (*i.e.*, *ortho* or *para* to a phenolic group), in the resonance sense as well. In general the nitro group is considered the more effective, and consequently it is somewhat surprising to find 4-nitrosophenol a stronger acid than 4-nitrophenol. Likewise, the 2-methyl compounds possess this unexpected relationship. However, in the 2,6-dialkyl compounds the expected greater acidities are found for the 4-nitro series.

In the 3,5-dialkyl series, again, the 4-nitrosophenols are the stronger acids. This might be expected in view of the similar relationship in the parent compounds, since the effect of 3,5-alkylation is chiefly steric inhibition of resonance.[2] The increase in such steric inhibition of resonance by increasing the bulk of the 3,5-dialkyl substituents is apparent from the marked decrease in acidity in both nitro and nitroso series (Table II) and is supported by the ultraviolet absorption data (Table I).

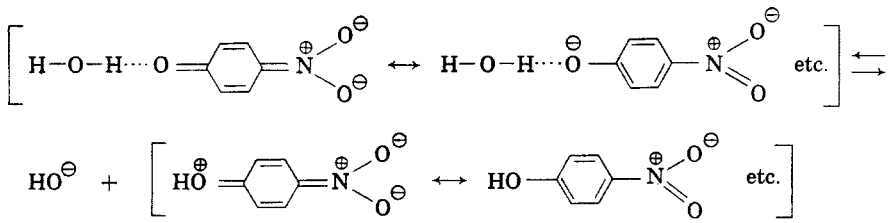
4-Nitrosophenols

In considering the acid strength of 4-nitrosophenols the following reaction is of prime significance: Any factor tending to inhibit solvation at either end of the anion will decrease its stability thus decreasing the strength of the conjugate acid. At the same time any factor tending to inhibit hydrogen bonding to either phenolic or oximic hydrogen will interfere with effective removal of the proton involved, and likewise decrease acidity. Thus either 2,6- or 3,5-disubstitution should weaken the acid, progressively as the substituent bulk increases. This is observed (Table II). The additional steric inhibition of resonance has been considered above, and from the available data appears to be the most significant factor involved in the 3,5-series. The gradual increase in *p*Ka values for the 2,6-series (from diethyl through di-*tert*-butyl) parallels the decrease in effectiveness of hydrogen bonding (solid state, Table I) through the phenolic hydrogen, and consequently one may state that in these compounds the acid strengths are governed chiefly by the ability of a base to approach the phenolic hydrogen:



4-Nitrophenols

A similar equation for this series is:



(15) W. C. Sears and L. J. Kitchen, *J. Am. Chem. Soc.*, **71**, 4110 (1949).

(16) R. A. Friedel, *J. Am. Chem. Soc.*, **73**, 2881 (1951).

(17) N. D. Coggeshall and E. L. Saier, *J. Am. Chem. Soc.*, **73**, 5415 (1941).

(18) M. Orchin and C. Golumbic, *J. Am. Chem. Soc.*, **71**, 4151 (1949).

Clearly solvation about the nitro group can be approximately the same in either the anion or its conjugate acid (2,6-substitution) and thus need not be considered, since proton transfer at this site is contraindicated by the infrared data, and the potential *aci* form can be neglected. At the same time the infrared data reveal a direct proportionality between *p*Ka values (Table II) and hydrogen bonding capacity (Table I, solid state) for the 2,6-series. Thus the stronger acids have the *lesser* hydrogen bonding capacity except for 4-nitrophenol itself. That this is indeed significant emerges from the fact that the expected continual shift toward shorter wavelengths with increasing 2,6-dialkyl bulk is not encountered. Hence, the acid strengths in this series do not appear to be a function of the ease of approach of a base to the phenolic hydrogen but rather to be a question of the intrinsic stability of the conjugate base (anion).

One might expect the stability of such anions to be governed in part by the ease of accommodating the solvating molecule on the phenolic oxygen; but this, like the approach to the phenolic hydrogen, should be governed by the extent of crowding about the 1-position. Consequently, the above equation does not appear to express the situation properly. It is evident that 2,6-di-*tert*-butylphenol has an intrinsically shorter O—H bond than 2,6-di-*tert*-butyl-4-nitrophenol (Table I, column 1: no hydrogen bonding due to extreme dilution). Consequently approach by a base to the hydrogen of the former phenol should be more difficult than to that of the latter, and at the same time the solvation of the former's anion by a polar solvent should be more difficult *via* the oxygen and ineffective at any other site. Both of the latter conditions as well as the former contribute to the striking non-acidity of 2,6-di-*tert*-butylphenol (*vide supra*). In its nitro derivative, however, the phenolic hydrogen is somewhat more accessible, and the polar character of the nitroaromatic ring, especially in the anionic form, permits considerably more facile solvation by polar solvents, thus producing a greater acidity. Why, however, should 2,6-di-*tert*-butyl-4-nitrophenol possess the *most stable* of the 2,6-dialkyl-4-nitrophenoxide ions?

The answer to this question may be found in the more effective distribution of the formal negative charge of the ion through the close associations with the surrounding hydrogens of the *tert*-butyl groups. That such carbon to oxygen bonding can effectively influence the polarity of an oxygen has been established by the investigation of Prelog[19] into the properties of macrocyclic ketones. The latter have less polar oxygen than the present phenoxide ion, which fact offsets the less effective conformation of the latter.

If this premise is correct, that stabilization of the anion occurs through effective hydrogen bonding to nearby alkyl hydrogens, it must follow that the effectiveness of such C—H—O bonding be reflected in the *p*Ka values. This appears to be true in passing from 2,6-diethyl- to 2,6-di-*tert*-butyl substitution. At the same time the same effect in the phenols themselves should make the phenolic oxygen less negative, which in turn should enhance the hydrogen bonding capacity of the phenolic proton when the effect first appears (2,6-diethyl-4-nitrosophenol); and subsequent increase in bulk will diminish the hydrogen bonding capacity while stabilizing the anion. This, too, is observed (Table I, solid state).

Another anomaly is seen in the relative values for *p*Ka and hydrogen bonding which obtain for 2,6-dimethyl- and 2,6-diethyl-4-nitrophenol; the former shows less hydrogen bonding but greater acidic character. It is, in fact surprisingly more acidic than 2-methyl-4-nitrophenol and exhibits correspondingly less hydrogen bonding. If one considers the order of hydrogen bonding capacities normal (decreasing from 4-nitrophenol to 2,6-dimethyl-4-nitrophenol, with the next member of the series showing an increase for the reasons stated above), then the inverse order for 4-nitroso- through 2,6-dimethyl-4-nitrosophenol is anomalous, but may be attributable to obscure factors arising from the nature of the tautomeric forms.

Finally the 3,5-dialkyl-4-nitrophenols deserve comment. They are the weakest acids in the entire group of compounds. There is, however, nothing unexpected about their positions in the group or the relative size of the two *p*Ka values. As expected, diethyl substitution should more effectively inhibit the resonance of the nitroaromatic system than does dimethyl. The wavelengths of their O—H bonds suggest that the weaker acid has less hydrogen bonding capacity, contrary to the comparable 4-nitrosophenols. But in the latter compounds such an anomaly may be attributable to the nature of the tautomeric system.

PREPARATIONS

The 2,6-dialkyl-4-nitrophenols were made by the method of Hill[20] as modified by Jones and Kenner[21] wherein sodionitromalonaldehyde is condensed with the necessary symmetrical ketones.

The diethyl and di-*n*-propyl ketones reacted fairly rapidly, but it was necessary to allow at least 17 days for the diisobutyl ketone to obtain a 49% yield. Runs made by keeping the solution at 50° for one to two days gave the desired 2,6-diisopropyl-4-nitrophenol (Ic) but in low yield and very impure.

The 2,6-diisopropyl-4-nitrophenol (Ic) appar-

(19) V. Prelog, *J. Chem. Soc.*, 420 (1950).

(20) H. B. Hill, C. A. Soch, and G. Oenslager, *Amer. Chem. J.*, **24**, 1 (1900).

(21) E. C. S. Jones and J. Kenner, *J. Chem. Soc.*, 1842 (1931).

ently can exist in two crystal forms, for a sample placed in the melting point bath at 112° melted immediately, while a sample in the bath at 100° and heated with a 2° temperature rise per minute melted at 119.0–119.6°.

The preparation of 3,5-dimethyl-4-nitrophenol (IIa) involved the direct nitration of 3,5-dimethylphenol with nitric acid. The ratio of *ortho* to *para* nitration with respect to the hydroxyl group was 8.3/1 (reported[22a] as 1.4/1). The two isomers were separated by steam-distillation of the *ortho*-nitrophenol and extraction of the *para* isomer from the remaining mixture. The difference in *ortho/para* ratios may be due to an indeterminate quantity of oxides of nitrogen in our reaction, which would give rise to $NO^{\oplus}$ ion, which is known to catalyze nitration of phenols *via* the nitrosophenol. Such a mechanism would surely give rise to more *para* isomer.[22b]

The direct nitration of 3,5-diethylphenol then was investigated. The diethylphenol was prepared by a high temperature Friedel-Crafts reaction using diethyl ether and a large excess of anhydrous aluminum chloride, following the procedure of Jannasch and Rathjen.[23] The diethylphenol was nitrated under the same conditions used for nitration of 3,5-dimethylphenol, giving a ratio of *ortho* to *para* nitration of 7.3/1. The *ortho* isomer again was removed by steam-distillation. The desired *para* isomer was obtained as a very viscous oil which could be frozen to a solid but not satisfactorily recrystallized. However, a sample of the oil crystallized after standing for two years and was used to seed the later runs.

The 2,6-dialkyl-4-nitrosophenols (III) were made in several ways. The dimethyl (IIIa) compound was made by direct nitrosation of 2,6-dimethylphenol, and by oximation of 2,6-dimethylbenzoquinone. The quinone was prepared in two different ways. In the first method 3,5-dimethyl-4-nitrosophenol (IVa) was reduced to the aminophenol with sodium hydrosulfite, and the aminophenol was oxidized to the quinone with ferric chloride. In the second method the nitrosophenol (IVa) was subjected to conditions used to hydrolyze the oxime form of the nitrosophenol. The general procedure of Summerford and Dalton[24] was followed, using cuprous oxide, acetone, and dilute hydrochloric acid in Methyl Cellosolve as a solvent. In both methods the quinone was separated from the reaction mixture by steam-distillation. The quinone then was treated with an excess of hydroxylamine hydrodrochloride to give 2,6-dimethyl-4-nitrosophenol (IIa). Good yields of pure dialkylnitrosophenols were obtained when sodium acetate was used; however, when no base was used a mixture was obtained that was not separated by repeated recrystallizations. Due to the steric hindrance of the methyl groups *ortho* to the one carbonyl, only the unhindered carbonyl reacted with the hydroxylamine; thus, methods are available that can be used to convert 3,5-dialkyl-4-nitrosophenols and 2,6-dialkyl-4-nitrophenols to 2,6-dialkyl-4-nitrosophenols by way of the 2,6-dialkylquinones.

The 2,6-diethylquinone[25] was made by oxidation of 2,6-diethyl-4-nitrophenol (Ib) with lead tetraacetate or sodium dichromate-sulfuric acid, and by hydrolysis of the 3,5-diethyl-4-nitrosophenol (IVb) by the method described above for the dimethylquinone. The quinone was converted to the 2,6-diethyl-4-nitrosophenol (IIb) by reaction with hydroxylamine hydrochloride and sodium acetate.

The 2,6-diisopropyl-4-nitrosophenol (IIIc) was made from 2,6-diisopropyl-4-nitrophenol (IIIc) *via* the quinone which then was oximated in the usual manner to give the desired nitrosophenol.

A slightly different procedure was necessary for the 2,6-di-*tert*-butyl-4-nitrosophenol (IIId) since the intermediates were not available for this compound. The first method investigated was the oxidation of 2,6-di-*tert*-butyl-*para*-cresol (Shell Ionol) to the corresponding aldehyde by the procedure of Smith and Wilson.[26] However, all attempts at oxidation of the aldehyde to the acid (which was to be decarboxylated) failed, giving either no reaction or a yellow-orange oil that was subsequently identified as 2,6-di-*tert*-butylquinone. Then it was discovered that the quinone could be obtained directly by oxidation of the di-*tert*-butyl-*para*-cresol. Using potassium permanganate in acetic acid a yield of 50–60% of a mixture of the desired quinone and 3,3′,-5,5′-tetra-*tert*-butyldiphenoquinone was obtained. The di-*tert*-butylquinone corresponds in properties with those subsequently reported.[27] When chromic anhydride in acetic acid was used, a complex with chromium was apparently obtained, which was decomposed with sulfuric acid; and the two previously mentioned quinones were separated by dis-

(22a) R. Adams and H. W. Stewart, *J. Am. Chem. Soc.*, **63**, 2861 (1941).

(22b) For a discussion of this type of nitration see C. K. Ingold, *Structure and Mechanism in Organic Chemistry*. Cornell University Press, Ithaca, N. Y., 1953, pp. 285–288.

(23) P. Jannasch and A. Rathjen, *Ber.*, **32**, 2392 (1899).

(24) W. T. Summerford and D. N. Dalton, *J. Am. Chem. Soc.*, **66**, 1330 (1944).

(25) Attempts at reduction of the 3,5-diethyl-4-nitrophenol (IIb) to the amino compound followed by oxidation to 2,6-diethylquinone were not successful. The reducing agents used were alkaline sodium hydrosulfite, and acidic stannous chloride. Ferric chloride was used as the oxidizing agent. A slight amount of a yellow oil with a quinone odor steam-distilled over in each case. The oil partially solidified at room temperature and was solid at 0° indicating that it might be the desired 2,6-diethylquinone. Oxidation of this small quantity of oil usually resulted in an oily solid that could not be purified by recrystallization. It is possible that this small quantity, separated by chromatography and by reduction and oxidation, is the 2-nitro isomer. This would indicate that the hindered nitro group is very resistant to reduction.

(26) W. M. Smith and C. J. Wilson, U. S. Patent, Reissue 22,909 (1947).

(27) S. J. Metro, *J. Am. Chem. Soc.*, **77**, 2901 (1955).

tillation, giving a 20% yield of 2,6-di-*tert*-butylquinone. The quinone then was oximated in the usual manner to give a 90% yield of 2,6-di-*tert*-butyl-4-nitrosophenol whose properties correspond with those recently reported.[27]

The 2,6-di-*tert*-butylphenol was made by a reported method[28] in which *para*-bromophenol was alkylated with isobutylene to give 4-bromo-2,6-di-*tert*-butylphenol. This then was treated in liquid ammonia with potassium to give 2,6-di-*tert*-butylphenol. All attempts at simple mono nitration of this phenol were unsuccessful. Subsequent to the original synthetic attempts, however, a sample of the desired 4-nitro derivative (Id) was kindly supplied by the Ethyl Corporation, Detroit Laboratories.

3,5-Dimethyl-4-nitrosophenol (IVa) and 3,5-diethyl-4-nitrosophenol (IVb) were readily available by the nitrosation of the corresponding phenols. 3,5-Dimethyl-4-nitrosophenol was also obtained from the attempted nitration of 3,5-dimethylphenol in the presence of an excess of nitrous acid, and by treatment of 4-acetoxymercuri-3,5-dimethylphenol with ethyl nitrite.

EXPERIMENTAL[29,30]

Data are summarized in Tables III–VI, and special details follow the tables.

2,6-Diisopropyl-4-nitrophenol. To a solution of 3.72 ml. (0.0218 mole) of diisobutyl ketone and 2.00 g. (0.050 mole) of sodium hydroxide in 40 ml. of ethyl alcohol and 25 ml. of water was added 4.40 g. (0.0317 mole) of sodionitromalonaldehyde[37,38] some of which failed to dissolve. After standing 23 days at room temperature with occasional shaking, the dark red solution still contained some finely divided solid. The solution was concentrated and the solid product was worked up as in the procedure for 2,6-dimethyl-4-nitrophenol[20,21] to give 2.40 g. (49.3%) of a light tan solid, m.p. 95–105°. The products from several runs were combined

TABLE III
PHENOLS

Compound	Source or Procedure	M.p., °C.	Reported m.p., °C.	Ref.
Phenol	EKC			
o-Cresol	EKC			
m-Xylenol	EKC			
3,5-Diethylphenol	Ref. 23	75.5–77.5[a]	77	23
2,6-Di-*tert*-butylphenol	Ref. 28	38–39	38–39 37–38	28 31

[a] Recrystallized from 60–75° petroleum ether.

TABLE IV
BENZOQUINONES

Compound	Source or Procedure	M.p., °C.	Reported m.p., °C.	Ref.
2,6-Dimethyl-	(a) Ref. 24	67-71	73	24
	(b) See text			
2,6-Diethyl-	(a) See text		39	32
	(b) See text	32–36	35	21
2,6-Diisopropyl-	See text	Oil		
2,6-Di-*tert*-butyl-	See text	68–69[a]	65–66	27

[a] Recrystallized from 60–70% aqueous ethanol.

(5.40 g.) and recrystallized from 60–75° petroleum ether (200 ml.) to give fine silvery needles (5.05 g.): m.p. 110.5–111.3°. Four more recrystallizations from 60–75° petroleum ether gave fine silvery needles which melted immediately when put in an oil-bath at 112°. However, a sample put in the bath at 100° and heated at 2° per minute softened at 118.5° and melted at 119.0–119.6°.

Anal. Calc'd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.79; H, 7.42; N, 5.87.

3,5-Diethyl-4-nitrophenol. The procedure of Adams and Stewart[22c] for 3,5-dimethyl-4-nitrophenol was followed, with the modification of adding a few crystals of sodium nitrite to initiate the reaction. The red oil obtained by ether extraction of the steam-distillate weighed 11.2 g. The residue from the steam-distillation contained a heavy black oil which was extracted with ether. The thick black oil obtained upon evaporation of the ether was extracted with *n*-hexane and the *n*-hexane was evaporated to leave a brown oil that immediately crystallized when seeded with 3,5-diethyl-4-nitrophenol.[39] The crude product (1.6 g.) was recrystallized three times from 10 ml. of *n*-hexane to give bright yellow crystals, m.p. 46.0–49.0°.

Anal. Calc'd for $C_{10}H_{13}NO_3$: C, 61.52; H, 6.71; N, 7.19. Found: C, 61.30; H, 6.44; N, 7.45.

3,5-Dimethyl-4-aminophenol, and hydrochloride. To a dark green solution of 6.65 g. (0.0440 mole) of 3,5-dimethyl-4-nitrosophenol in 40 ml. of 5% sodium hydroxide was added slowly, at 45–60°, 18.6 g. (0.096 mole) of sodium hydrosulfite (90% minimum assay). The solution gradually became colorless while a cream-colored solid precipitated. The mixture was warmed to 70° to coagulate the fine precipitate, diluted with an equal volume of water, and cooled to 25° and filtered; 1.0 g. (17% yield), m.p. 181.8–183.0° dec.: reported[40] m.p. 180.5–181.5°; mixture melting point with 3,5-dimethyl-4-nitrosophenol, 140–146°.

The filtrate was acidified with 8 ml. of concentrated hydrochloric acid to give a pink gel that sharply turned cream-colored as the last of the acid was added; 5.5 g. (76% yield), m.p., 276–278° dec. After one recrystallization from water the melting point was raised to 281–282° dec.: reported 270–280° dec.[40]

(28) G. H. Stillson and D. W. Sawyer, U. S. Patent 2,459,597 (1949).

(29) All melting points are uncorrected unless otherwise noted.

(30) The microanalyses were performed by Clark Microanalytical Laboratory, Urbana, Illinois, and by the Research Analytical Laboratories of Tennessee Eastman Company.

(31) H. Hart and F. A. Cassis, Jr., *J. Am. Chem. Soc.*, **73**, 3179 (1951).

(32) P. Karrer and R. Schläpfer, *Helv. Chim. Acta*, **24**, 298 (1941).

(33) D. A. Shirley, *Preparation of Organic Intermediates*, John Wiley and Sons, Inc., New York, 1951, p. 203.

(34) K. V. Auwers and T. Markovits, *Ber.*, **41**, 2335 (1908).

(35) K. v. Auwers and E. Borsche, *Ber.*, **48**, 1715 (1915).

(36) G. G. Henderson and R. Boyd, *J. Chem. Soc.*, **97**, 1664 (1910).

(37) H. B. Hill and J. Torrey, Jr., *Amer. Chem. J.*, **22**, 89 (1899).

(38) *Org. Syntheses*, **32**, 95 (1952).

(39) The first run made gave a very viscous sludge that could not be crystallized. On standing for two years a brownish-yellow solid was obtained which was used to seed the next run.

(40) K. v. Auwers and E. Borsche, *Ber.*, **48**, 1698 (1915).

TABLE V

4-NITROPHENOLS

Compound	Source or Procedure	m.p., °C.	Reported m.p., °C.	Ref.
4-Nitrophenol	Paragon Laboratories	112.0–113.5[a]		
2-Methyl-4-nitrophenol	Ref. 33	94.0–95.0[b]	91	33
2,6-Dimethyl-4-nitrophenol	Ref. 20, 21	168.5–168.8[b]	169–170	34
			171	21
2,6-Diethyl-4-nitrophenol	Ref. 20, 21	132.3–133.3 (corr)[b]	130–131	21
2,6-Diisopropyl-4-nitrophenol	See text	119.0–119.6[c,d]	New compound	
2,6-Di-*tert*-butyl-4-nitrophenol	Ethyl Corporation	153–154	Not reported	
3,5-Dimethyl-4-nitrophenol	Ref. 22a	107.9–108.9[b]	108.5 (corr.)	22
3,5-Diethyl-4-nitrophenol	See text	46.0–49.0[e]	New compound	

[a] Recrystallized from water. [b] Recrystallized from carbon tetrachloride. [c] In bath at 100° with 2°/min. rise. [d] Recrystallized from 60–75° petroleum ether. [e] Recrystallized from *n*-hexane.

TABLE VI

4-NITROSOPHENOLS

Compound	Source or Procedure	m.p., °C.	Reported m.p., °C.	Ref.
4-Nitrosophenol	Ref. 33	133 (dec.)[a]		
		124–126 (dec.)[b]		
2-Methyl-4-nitrosophenol	Ref. 33	130.5–131.0[c]	136	33
2,6-Dimethyl-4-nitrosophenol	See text	171.6–172.0[d]	170–171	34
	Ref. 32	172–173 (corr.)[d]		
2,6-Diethyl-4-nitrosophenol	See text	145.6–147.1[e]	New compound	
2,6-Diisopropyl-4-nitroso-phenol	See text	158.4–159.1[f]	New compound	
2,6-Di-*tert*-butyl-4-nitroso-phenol	See text	211.0–211.2[d]	219–220	27
3,5-Dimethyl-4-nitrosophenol	Ref. 32	177.4–178.0 (dec.)[g,h]	182–183	35
3,5-Diethyl-4-nitrosophenol	Ref. 32	129.8–130.0 (dec.)[h]	132	32
			136	36

[a] Slowly precipitated from water. [b] Rapidly precipitated from water. [c] Recrystallized from water. [d] Recrystallized from carbon tetrachloride. [e] Recrystallized from 30% aqueous ethanol. [f] Recrystallized from 60–75° petroleum ether. [g] Sealed tube. [h] Recrystallized from absolute ethyl acetate.

2,6-Dimethylbenzoquinone. Oxidation of 3,5-dimethyl-4-aminophenol. To 6.6 g. (0.038 mole) of the relatively water-insoluble hydrochloride of 3,5-dimethyl-4-aminophenol was added 350 ml. of water. A solution of 55 g. of ferric chloride hexahydrate in 20 ml. of concentrated hydrochloric acid and 30 ml. of water was added; and, after vigorous shaking, the mixture was steam-distilled and the distillate was extracted with ether to give approximately 3 g. (58%) of orange solid, m.p. 67–71°.

2,6-Dimethyl-4-nitrosophenol: Oximation of 2,6-dimethylbenzoquinone. To 1.8 g. (0.013 mole) of 2,6-dimethylbenzoquinone dissolved in 40 ml. of ethyl alcohol and 25 ml. of water was added 2.7 g. (0.039 mole) of hydroxylamine hydrochloride and 3.0 g. (0.022 mole) of sodium acetate. The red solution was refluxed for two hours, 70 ml. of water was added, and the solution was cooled in ice-water to give a slight amount of solid. The mixture then was evaporated on a hot plate until solid appeared in the hot solution. The mixture was cooled in ice-water and 1.4 g. (72%) of tan crystals were filtered off, m.p. 144–158°. The product was recrystallized from a 40% mixture of benzene and 60–75° petroleum ether to give fine needles, m.p. 166–169° dec. These were alternately recrystallized from the benzene-petroleum ether mixture and carbon tetrachloride until the melting point became constant at 171.6–172.0°: reported 170–171°.[34]

2,6-Diethylbenzoquinone. (*A*) *Oxidation of 2,6-diethyl-4-nitrophenol with lead tetraacetate.* To a solution of 1.95 g. (0.010 mole) of 2,6-diethyl-4-nitrophenol in 15 ml. of glacia acetic acid was added 2.22 g. (0.005 mole) of lead tetraacetate to give a red solution which was neutralized with 10% sodium hydroxide. The neutral solution was extracted with ether and the ether was evaporated to give 0.64 g. (39%) of red crystals melting at about 35°: reported 39°;[32] 35°.[21]

(*B*) *Oxidation of 2,6-diethyl-4-nitrophenol with dichromate.* A mixture of 3.7 g. (0.019 mole) of 2,6-diethyl-4-nitrophenol, 2.9 g. (0.0098 mole) of sodium dichromate, and 75 ml. of 4% sulfuric acid was steam-distilled and the distillate was extracted with ether. The ether was evaporated to give 2.2 g. (70%) of yellow needles, m.p. 32–36°.

(*C*) *Hydrolysis of 3,5-diethyl-4-nitrosophenol.* The general procedure of Summerford and Dalton[24] for dimethylbenzoquinone was followed to give yellow needles, m.p. 34–37°.

2,6-Diethyl-4-nitrosophenol. A solution of 1.8 g. (0.011 mole) of 2,6-diethylbenzoquinone, 1.52 g. (0.002 mole) of hydroxylamine hydrochloride, 0.90 g. (0.011 mole) of anhydrous sodium acetate, 70 ml. of ethyl alcohol, and 15 ml. of water was refluxed for two hours, then 40 ml. of water was added and the hot solution was evaporated to 80 ml. and cooled in ice-water. Yellow needles, 1.7 g. (86%), were filtered off, m.p. 134–144°. These were recrystallized alternately from *n*-hexane (130 ml.) and 30% ethyl alcohol (aq.) (220 ml.) until the melting point was constant, m.p. 145.6–147.1°.

Anal. Calc'd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.28; H, 7.33; N, 8.15.

2,6-Diisopropyl-4-aminophenol hydrochloride. To a red solution of 3.00 g. (0.0143 mole) of 2,6-diisopropyl-4-nitrophenol in 20 ml. of concentrated ammonium hydroxide and 20 ml. of water was slowly added with stirring 8.0 g. (0.046 mole) of sodium hydrosulfite to give an almost colorless solution and a red oily solid. Trituration of the oily solid with dilute ammonium hydroxide-sodium sulfite solution gave a pale yellow solid that became faintly purple on standing in the air. The solid was dissolved in 2200 ml. of hot 0.01 *N* hydrochloric acid and cooled to give fine slightly pink needles, m.p. 255–258°, which were assumed to be the hydrochloride of 2,6-diisopropyl-4-aminophenol; observed neutral equivalent, 230; calculated, 240.

2,6-Diisopropylbenzoquinone. The needles described above were returned to the mother liquor and 8.0 g. of ferric chloride hexahydrate and 3 ml. of concentrated hydrochloric acid were added and the mixture was steam-distilled to give a yellow-orange oil in the distillate. The distillate was extracted with ether and the ether was evaporated to leave a reddish-orange oil, 2.2 g. (80%), with a quinone odor and an infrared spectrum characteristic of quinones.

2,6-Diisopropyl-4-nitrosophenol. The orange oil, 2.2 g. (0.11 mole), obtained in the preceding experiment was dissolved in 75 ml. of 95% ethyl alcohol and 25 ml. of water, and 1.3 g. (0.019 mole) of hydroxylamine hydrochloride was added. The solution was refluxed for 2½ hours, evaporated to 70 ml. and cooled and 1.7 g. (72%) of yellow solid filtered off, m.p. 156–158°. The filtrate then was diluted to 150 ml. with water, cooled, and 0.3 g. (13%) more of yellow solid was obtained, m.p. 155.0–157.8°. The two solids were mixed and recrystallized six times from 400 ml. of 60–75° petroleum ether to give bright yellow leaflets, m.p. 158.4–159.1°.

Anal. Calc'd for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.71; H, 8.46; N, 6.93.

2,6-Di-tert-butylbenzoquinone. To a solution of 66 g. (0.30 mole) of 2,6-di-*tert*-butyl-*para*-cresol (Shell Ionol) in 500 ml. of acetic acid was added over 2½ hours at 55° a solution of 105 g. (1.05 mole) of chromic anhydride in 70 ml. of water and 70 ml. of acetic acid. A faster addition of chromic anhydride gave considerable break-down to isobutylene. The solution was cooled to room temperature and poured into 2700 ml. of cold water to give an opalescent blue solution. After the addition of 120 ml. of concentrated sulfuric acid the solution was allowed to stand overnight at room temperature whereupon a very viscous orange oil separated at the surface. The oil was extracted with ether, washed with water, and then with 5% sodium hydroxide and finally with water until the wash water was neutral. The ether layer then was dried over sodium sulfate and distilled through a ½″ × 6″ unpacked column. Two fractions were obtained at 89–95°/0.20 mm. and 95–121°/0.23 mm., the first cut solidifying to give 13.3 g. (20%) of orange solid, m.p. 64–69°. After three recrystallizations from 60–70% ethyl alcohol the yellowish-orange crystals melted at 68–69°; reported 65–66°.[27]

Anal. Calc'd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.77; H, 8.98.

2,6-Di-tert-butyl-4-nitrosophenol. A solution of 8.0 g. (0.036 mole) of 2,6-di-*tert*-butylquinone, 4.8 g. (0.070 mole) of hydroxylamine hydrochloride, 5.4 g. of sodium acetate, 122 ml. of ethyl alcohol, and 56 ml. of water was refluxed for 3½ hours. Hot water (20 ml.) was added to the refluxing solution until solid appeared, the solution was cooled in ice-water and a bright yellow solid was filtered off, 7.7 g. (90%), m.p. 208–210° dec. The yellow leaflets were recrystallized three times from 350 ml. of carbon tetrachloride and dried, m.p. 211.0–211.2° dec.: reported[27] 219–220°.

Anal. Calc'd for $C_{14}H_{21}NO_2$: C, 71.45; H, 9.00; N, 5.95. Found: C, 71.02; H, 8.99; N, 5.91.

Absorption spectra. The infrared absorption spectra were obtained with a Baird Double Beam Infrared Recording Spectrophotometer, and subsequently were checked on a Perkin-Elmer Double Beam Recording Spectrophotometer.

The ultraviolet spectra were obtained in part by a Beckman Model DK Direct Transmittance Recording Spectrophotometer and in part by a Cary Double Beam Recording Spectrophotometer.

pH measurements. The *p*H measurements were made using a Beckman Model G *p*H meter using a Beckman general purpose glass electrode and a calomel fiber type reference electrode. The apparatus consisted of a 100-ml. tall form beaker containing the two electrodes, a small stirrer, a glass capillary which was used to keep a nitrogen atmosphere over the beaker, and a 25-ml. burette calibrated to 0.05 ml. The titration cell was in a constant temperature bath containing a stirrer, thermometer, and heating and cooling coils; and was maintained at 25.0° ± 0.1°. Carbonate free 0.03140 *N* sodium hydroxide was used, along with absolute ethyl alcohol, refluxed to remove all carbon dioxide. The procedure was to dissolve 0.70–0.73 millimole of the solid phenol in 20.0 ml. of absolute ethyl alcohol and titrate the solution with the aqueous sodium hydroxide. A complete titration curve was plotted to eliminate any individual errors in readings, and the *p*H was determined to the nearest 0.01 unit at one-quarter, one-half, and three-quarters neutralized, and at the end point. Duplicate titrations were run, and unless the *p*H values agreed to 0.02 unit additional titrations were made. The *p*H meter was checked against a *p*H 7.0 buffer solution before the titration of each compound, and the electrodes were allowed to stand in a *p*H 7.0 buffer solution for at least 0.5 hour between curves. The compounds were titrated in random order to eliminate any possible human or instrumental trends. The sodium hydroxide solution was standardized with National Bureau of Standards potassium acid phthalate at least twice a week, and was kept in a bottle protected from carbon dioxide and moisture. A correction for sodium ion error was necessary only for *p*H values above 10.0; and according to Beckman Monograph 225-N the correction was a maximum of 0.02 *p*H units for readings above 10.7.

Five of the more water-soluble compounds were titrated by dissolving the compound in the theoretical amount of dilute sodium hydroxide and titrating the solution with hydrochloric acid. Due to the limited water solubility of the compounds they could be back titrated only a few per cent before the free acid began to precipitate.

For the 2,6-di-*tert*-butyl-4-nitrophenol it was found that use of the approximately 0.03 *M* base, added to an absolute alcohol solution of the acid, resulted in precipitation of the acid and a consequent drift in apparent *p*H values after each addition. Calculation of *p*Ka at half-neutralization gave values close to 7.85. By using approximately 0.05 *M* base, precipitation was avoided and a straight line was obtained by plotting *p*Ka at ¼, ½, and ¾ neutralization *vs.* mole fraction of ethanol. From this line the value of 7.96 was obtained at 35 mole-per cent ethanol, which is the medium in which the rest of the *p*Ka values were obtained at half-neutralization.

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