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ON THE NATURE OF THE PHENYLAZO GROUP

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Abstract—Three Hammett substituent constants for the *p*-phenylazo group were determined. The ionization of *p*-phenylazobenzoic acid in 50% ethanol gives a σ_p value of 0·26. The NBS bromination of *p*-phenylazotoluene vs toluene in benzene at 80° gives a σ^+ value of −0·15. The NBS bromination of 4-phenylazo-3-cyanotoluene vs *m*-tolunitrile in benzene at 80° give a $\sigma^\cdot$ value of 0·28. It is concluded that the phenylazo group is a −I substituent and either a +M or −M substituent depending on the reaction being studied. This makes the phenylazo group an activator in nucleophilic, electrophilic and free radical reactions.

INTRODUCTION

The azo functional group, –N=N–, is one of the most important functional groups in organic chemistry primarily because of its presence in azo dyes and in many free radical initiators. The azo dyes constitute the largest single class of dyes, making up over half of the total number of synthetic colors of known structure.[1] Over a thousand azo dyes have been used commercially,[2] and these dyes have the fullest shade range and the most diverse use.[3] The thermal or photochemical decomposition of aliphatic azo compounds provides a good source of free radicals. Three very common free radical sources are: azomethane[4]—a good source of methyl radicals; azoisobutyronitrile[5] (AIBN)—the most common azo initiator for vinyl polymerization; and phenylazotriphenylmethane[6] (PAT)—a convenient source of phenyl radicals.

The phenylazo group, Ph–N=N–, has found use as a probe to help determine the conformational structures of carbohydrates, peptides, steroids, and vinyl polymers. There has been little optical rotatory dispersion (ORD) work done on carbohydrates because of the lack of a suitable chromophore in these molecules. The phenylazo group at the 4-position of methyl glucosides allows the $n \rightarrow \pi^*$ adsorption at 400 nm to serve as the chromophore, and a positive cotton effect was observed.[7] Azopeptides have been made from L-*p*-(phenylazo)phenylalanine and γ-benzyl-L-glutamate with the phenylazo providing the probe into the nature of the asymmetric centers of the peptide chain.[8] Steroids of the cholestane series have been studied with a phenylazo group introduced into the 3-position.[9] Conformational information has also been obtained from the study of the photochemical properties of some azoaromatic derivatives of acrylic and methacrylic acid vinyl polymers.[10]

Despite the uses of azo compounds mentioned above, the phenylazo group is seldom used as a substituent to help determine reaction mechanisms. Its nature is also poorly understood regarding its electron donating or accepting properties. The value of the Hammett substituent constant given in Jaffe's review article[11] and in Hammett's book[12] ($\sigma = 0{\cdot}64$) is misleading because it is based on the reaction of *p*-phenylazophenoxide with ethylene oxide.[13] This reaction would now be classed as being a σ^- dependent reaction instead of a σ dependent reaction.

This work was designed to determine three different Hammett substituent constants for the phenylazo group: σ (effect of a substituent on benzoic acid ionization), σ^+ (direct resonance between a substituent and a positive reaction center)[14] and $\sigma^\cdot$ (direct resonance between a substituent and a free radical center).[15]

EXPERIMENTAL

Materials. *m*-Tolunitrile (K & K), N-bromosuccinimide (NBS, Aldrich), azobisisobutyronitrile (K & K) and phthalide (Aldrich) were all purified by standard methods prior to use.

Samples of *p*-phenylazotoluene and *p*-phenylazobenzoic acid were generously provided by Mr. Raymond Jones of this lab.

3-Cyano-4-phenylazotoluene was prepared from *m*-tolunitrile by a three step procedure. *m*-Tolunitrile was nitrated by the method of Macovski[16] to give 3-cyano-4-nitrotoluene in 65% yield. 3-Cyano-4-nitrotoluene was reduced to 4-amino-3-cyanotoluene with iron and AcOH in 71% yield.[17] 4-Amino-3-cyantoluene 1·3 g (0·01 mole), and 1·0 g (0·01 mole) nitrosobenzene were dissolved in 20 ml of glacial AcOH and allowed to stand for 4 days at room temp. Dilution with water, extraction with ether, evaporation of the ether, and recrystallization from hexane gave 0·5 g (22%) of an orange solid, m.p. 100–102°. The product has NMR bands (CCl_4, TMS) at δ 2·5 (s, 3H) and δ 7·3–8·2 (m, 9H); IR ($CHCl_3$) 2250 (strong, CN), 1590 (strong), 1480 cm^{-1} (strong). (Found: C, 76·21; H, 4·82; N, 19·12. Calcd. for $C_{14}H_{11}N_3$: C, 75·97; H, 5·02; N, 18·99%).

Method. Due to the insolubility of *p*-phenylazobenzoic acid in water, its ionization constant was determined in aqueous EtOH using the procedure of Szmand and Suld.[18] Distilled water and EtOH were boiled to remove CO_2. Equal volumes of alcohol and water were mixed to give the 50% EtOH solvent used in this procedure. One ml of a saturated soln of NaOH was diluted to 100 ml with the 50% EtOH solvent. A $1{\cdot}09 \times 10^{-3}$ M soln of *p*-phenylazobenzoic acid was then prepared in the 50% EtOH solvent. A 100 ml sample of the acid soln was titrated with the NaOH soln. The titrations were followed potentiometrically using a Beckman Research pH meter. The titrations were carried out at 25°. The pK_a was determined at 1/4, 1/2 and 3/4 neutralization. Triplicate titrations were performed with the pK_a values agreeing within 2%. The same titration was repeated with benzoic acid. By this method, the pK_a of *p*-phenylazobenzoic acid was found to be $5{\cdot}46 \pm 0{\cdot}01$ and the pK_a of benzoic acid to be $5{\cdot}84 \pm 0{\cdot}01$. The reactions constant for benzoic acid ionization in 50% EtOH is 1·46.[18] This gives a σ_p for the phenylazo group of 0·26, when the above data are substituted in the Hammett equation.

The σ^+ value for the phenylazo group was determined using the competetive N-bromosuccinimide bromination of *p*-phenylazotoluene and toluene in benzene at 80° by the method of Pearson and Martin.[19] A mixture of 109·3 mg of toluene, 272·9 mg of *p*-phenylazotoluene, 105·1 mg of NBS and a catalytic amount of AIBN were diluted to 10·0 ml with benzene. The mixture was degassed 3 times using a freeze–thaw procedure and dry ice–acetone cooling. The tube containing the degassed mixture was sealed and placed in a bath thermostated at 80° for 3 hr. A UV lamp was placed about 20 cm from the tube to insure efficient

initiation. The cooled mixture was evaporated to 2 ml and then analyzed by NMR using added phthalide as an internal standard to determine the yield of the reaction. The relative amounts of the benzyl bromide products were determined by integration of the benzyl H's at δ 4·4 with an average of 5 integrals taken for each determination. Duplicate determinations agreed within 5%. *p*-Phenylazotoluene was found to brominate 1·62 ± 0·08 times as fast as toluene. Using the known ρ value for this reaction ($\rho = -1{\cdot}46$),[19] a value of −0·15 was obtained for σ_p^+ for the phenylazo group.

The $\sigma^\cdot$ value for the phenylazo group was determined using the same reaction conditions just described for σ^+, but using different substrates. The NBS bromination of 3-cyano-4-phenylazotoluene was found to 3·19 ± 0·06 times as fast as *m*-tolunitrile. This relative rate value converts to a $\sigma^\cdot$ of 0·28 from the equation $\sigma^\cdot = \log 3{\cdot}19 - (-1{\cdot}46)(-0{\cdot}15)$.

RESULTS AND DISCUSSION

The effect of the phenylazo group on aromatic substitution of the electrophilic, nucleophilic and free radical types should give a good qualitative look at the nature of the phenylazo group. Electrophilic substitution of azobenzene goes *ortho*, *para*, but with little or no activation. Sulfonation[20] and halogenation[21,22] in acetic acid have been studied with only the latter reporting kinetic data. Robertson[21] found that azobenzene is brominated 4·6 times as fast as benzene, but on further study[22] he discovered that the reaction is HBr catalyzed. When an inhibitor was added to trap the HBr by-product, no reaction occurred at 35° after 16 hr. This result was explained as an initial addition of HBr to give a bromohydrazobenzene which is then ring brominated. Robertson concluded that there is very little if any resonance possible between the phenylazo group and the ring because of the geometry change needed for it. The evidence on nucleophilic aromatic substitution is more straightforward. The phenylazo group is found to increase the rate in all cases studied including the reaction of: 2-nitro-4-phenylazochlorobenzene with methoxide,[23] *p*-phenylazobromobenzene with piperdine,[24] and *p*-phenylazotoluene with benzaldehyde in base[25] (not a S_NAr reaction). In the free radical phenylation of azobenzene using N-nitrosoacetanilide as the phenylating agent, Miller[26] found the phenylazo group to be the most activating group yet found to phenylation, even better than nitro. Table 1 is a summary of the rate studies alluded to above showing two electron donating and two electron withdrawing groups for comparison.

One of the most common ways to get quantitative data on substituent effects is to use linear free energy relationships[27] of which the Hammett equation[28] finds most use. The number of different types of Hammett substituent constants now exceeds twenty,[29] which is obviously too many for an empirical relationship.

Attempts toward simplification have come from Wepster,[30] Yukawa,[31] and Swain.[29] Wepster proposed σ^n to designate the normal, unexalted substituent constants which are to be used to calculate ρ. Substituents that involve resonance must then be related to this basic substituent constant σ^n. Yukawa proposed to represent the substituent effects as a linear combination of two terms—one representing σ and the other representing a variable resonance effect. Swain has proposed that all substituent effects be represented as a combination of two effects—a field (F) and a resonance (R) component.

Two major uses of the Hammett equation, one practical and one theoretical, seem to unify the above diversity. The first use is involved with reactions in which a substituent can have direct resonance between the substituent and a charged species in either the transition state or in an intermediate. Three substituent constants (σ^+, σ^- and $\sigma^\cdot$)[14,33,15] provide a measure of this direct resonance interaction. The second major use of the Hammett equation is for the separation of substituent effects into independent steric, inductive, and resonance effects. Taft[33] originated this approach and did much to solve it. The simplification attempts mentioned above also concentrate in this area. The steric substituent constant,[33] E_s, can be measured from the acid hydrolysis of esters or from *o*-substituted benzenes. The inductive substituent constant (σ_I) has taken many forms including σ_m, σ' and F with the most elegant system (σ') coming from reactions of 4-substitutedbicyclo[2.2.2]octane-1-carboxylic acids.[34] The resonance substituent constant (σ_R) is usually calculated by substracting the inductive effect from σ_p which includes both effects.

If these seven substituent constants (σ, σ^+, σ^-, $\sigma^\cdot$, σ_R, σ_I and Es) are known, then a good idea of the nature of the substituent is obtained in both a theoretical and practical manner. Table 2 contains the values for six of these substituent constants for the phenylazo group and

Table 1. The effect of *p*-Ph–N=N– on relative rates of aromatic substitution

p-Substituent	Br_2, HOAc[a]	CH_3–$O^\oplus$, CH_3–OH[b]	Ph[c]
–O–CH_3	1. × 10^9		1.7
–CH_3	3.4 × 10^2		1.7
–N=N–Ph	4.6	1.1 × 10^3	10.
–CN	2. × 10^{-5}	3.8 × 10^4	3.7
–NO_2	1.8 × 10^{-6}	6.7 × 10^5	5.0

a) Ref. 21. b) Ref. 23. c) Ref. 26.

Table 2. Hammett substituent constants for *p*-Ph–N=N–

Substt. Constants	Value[a]	Reference	Reaction studied
1. σ	0.66	11-13	Ar–$O^\ominus$ + CH_2–CH_2 +
	0.35	35	Ar–CO_2H, MCS[b] +
	0.26	c	Ar–CO_2H, 50% EtOH +
2. σ^-	0.82	24	Ar–Br + piperidine +
	0.66	23	Ar–Cl + $MeO^\ominus$, MeOH +
	0.70	35	Ar–NH_2 + base +
	0.61	35	Ar–OH + base +
3. σ^+	−0.15	c	Ar–CH_3 + NBS +
4. $\sigma^\cdot$	0.28	c	CN–Ar–CH_3 + NBS +
τ	0.9[d]	26	Ph–X + Ar$^\cdot$ +
5. $\sigma_I = \sigma_m$	0.30	e	Ar–CO_2H, MCS +
6. $\sigma_R = \sigma_p - \sigma_m$	0.05	e	combination

a) All substituent constants have been rounded off to two significant figures. b) MCS = Methylcellosolve/water 4:1. c) This work. d) $\sigma^\cdot$ and τ are different substituent constants but measure a similar effect. e) Calculated using data of reference 35.

shows the reactions from which each substituent constant is obtained.

The σ value for the phenylazo group originally reported (0·64) should obviously be called σ^- by current terminology. This fits the other values of σ^- listed in Table 2 and shows that the phenylazo group is efficient at stabilizing a negative charge, thus qualifying it as an $-I-M$ group in the terminology of Ingold. The σ value that accurately represents substituted benzoic acid ionization in nonaqueous solvents in about half that originally reported, but is still in the electron withdrawing category.

There is some doubt expressed in the literature[22] about the ability of the phenylazo group to stabilize a positive charge. Two reasons for this doubt are the HBr catalyzed bromination of azobenzene mentioned earlier, and the nature of the electron pair[36] on the double bond of the azo group would require a linear bond between the phenyl ring and the azo group for use of the electron pair by resonance. Miller[23] supports the $-I+M$ nature of the phenylazo group in electrophilic aromatic substitution. The σ^+ value found here of $-0{\cdot}15$ gives support to Miller's assignment of $-I+M$.

The close approximation of the values for σ_m and σ_p for the phenylazo group illustrates the $-I$ nature of the substituent and shows that resonance is not important in the benzoic acid series. Resonance was however shown above to be important when a positive or negative charge could resonate directly with the substituent.

A special word needs to be said about the ability of the phenylazo group to stabilize a free radical. The effects of substituents on free radical reactions are not nearly as well understood[37] as the effects on charged species. Much of the confusion arises because of the fact that in many free radical reactions polar influences predominate.[38] One early attempt to correlate substituent effects on free radical reactions was the Qe scheme of Alfrey and Price.[39] The reaction studied was the copolymerization of vinyl monomers. Several more recent attempts have been made to relate free radical substituent studies to the Hammett equation. Simamura[40] has suggested a τ value to measure the free radical stabilizing effect of substituents to phenylation. Sakuri[41] has studied the effects of the addition of $\cdot CCl_3$ to substituted styrenes and suggested an E_D value related to the Q of Alfrey and Price. Yamamoto and Otsu[42] have studied the H abstraction of the tertiary cumyl hydrogen by polystyryl radicals and have reported E_R values to measure the substituent effects. Fisher and Meierhoefer[15] have studied the NBS bromination of 4-substituted-3-cyanotoluenes vs *m*-tolunitrile in benzene at 80° and have used the symbol $\sigma^{\cdot}$ to represent the stabilization of the free radical found. The free radical substituent constant $\sigma^{\cdot}$ was defined for the bromination reaction just mentioned as $\sigma^{\cdot} = \log k/k_0 - \rho\sigma^+$. The $\sigma^{\cdot}$ value found for the phenylazo group of 0·28 makes the phenylazo group nearly as good as nitro (0·34) and cyano (0·38) in stabilizing a free radical. As mentioned earlier Miller[26] recently has found the phenylazo group to be the most activating group yet found to phenylation (Table 1) and estimates a Simamura τ value of 0·9 for it.

In summary, the phenylazo group has been found to have the unusual ability to stabilize a positive charge, a negative charge and a free radical, thus making it an activator in all three types of reactions. Very few, if any, other substituents are this ubiquitous in their stabilizing influences.

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REFERENCES

[1] C. R. Noller, *Chemistry of Organic Compounds* (3rd Edition) p. 743. Saunders, Philadelphia (1965).
[2] K. Venkataraman, *The Chemistry of Synthetic Dyes*, p. 409. Academic Press, New York (1952).
[3] H. A. Lubs, *The Chemistry of Synthetic Dyes and Pigments* p. 96. Reinhold, New York (1955).
[4] L. Herk and M. Szwarc, *J. Am. Chem. Soc.* **82**, 3558 (1960).
[5] J. P. Van Hook and A. V. Tobolsky, *Ibid.* **80**, 779 (1958); J. C. Bevington, *Trans. Faraday Soc.* **51**, 1392 (1955).
[6] R. F. Bridger and G. A. Russell, *J. Am. Chem. Soc.* **85**, 3754 (1963).
[7] E. O. Bishop, G. J. F. Chittenden, R. D. Guthrie, A. F. Johnson and J. F. McCarthy, *Chem. Commun.* 93 (1965).
[8] M. Goodman and A. Kossoy, *J. Am. Chem. Soc.* **88**, 5010 (1966).
[9] J. Buckingham and R. D. Guthrie, *Chem. Commun.* 781 (1966); J. Buckingham and R. D. Guthrie, *Ibid.* 1241 (1967).
[10] R. Lovrien and J. C. B. Waddington, *J. Am. Chem. Soc.* **86**, 2315 (1964).
[11] H. H. Jaffe, *Chem. Revs.* **53**, 191 (1953).
[12] L. P. Hammett, *Physical Organic Chemistry*, Chap. 7. McGraw-Hill, New York (1940).
[13] D. R. Boyd and E. R. Marle, *J. Chem. Soc.* **105**, 2117 (1914).
[14] H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.* **80**, 4979 (1958).
[15] A. W. Meierhoefer, Ph.D. Thesis, Mississipti State University, Mississippi State, Miss (1970).
[16] E. Macovski and J. Georgescu, *Bull. Sect. Sci. Acad. Roumaine* **28**, 354 (1948); *Chem. Abstr.* **43**, 3805e (1949).
[17] V. Findeklee, *Ber. Ges. Dtsch. Chem.* **38**, 3543 (1905).
[18] H. H. Szmant and G. Suld, *J. Am. Chem. Soc.* **78**, 3400 (1956).
[19] R. E. Pearson and J. C. Martin, *Ibid.* **85**, 3142 (1963).
[20] A. Chrzaszczewska and C. Dobrowolski, *Roczniki Chem.* **17**, 411 (1937); *Chem. Abstr.* **32**, 1674 (1938).
[21] P. W. Robertson, P. B. de la Mare and B. E. Swedlund, *J. Chem. Soc.* 782 (1953).
[22] P. W. Robertson, T. R. Hitchings and G. M. Will, *Ibid.* 808 (1950).
[23] J. Miller, *Aust. J. Chem.* **9**, 61 (1956); J. Miller and A. J. Parker, *Ibid.* **11**, 302 (1958).
[24] F. Kalberer, *Bull. Soc. Friboug. Sci. Nat.* **44**, 225 (1954); *Chem. Abstr.* **50**, 16718 (1956).
[25] L. Chardonnens and P. Heinrich, *Helv. Chim. Acta.* **23**, 1399 (1940).
[26] J. Miller, D. B. Paul, L. Y. Wong and A. G. Kelso, *J. Chem. Soc.* B, 62 (1970).
[27] P. R. Wells, *Chem. Rev.* **63**, 171 (1963).
[28] J. Shorter, *Chem. Brit.* **5**, 269 (1969).
[29] C. G. Swain and E. C. Lupton, *J. Am. Chem. Soc.* **90**, 4328 (1968).
[30] H. Van Bekkum, P. E. Verkade and B. M. Wepster, *Rec. Trav. Chem. Pays-Bas*, **78**, 815 (1959).
[31] Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Japan* **32**, 965, 971 (1959).
[32] Ref. 12, p. 193.
[33] R. W. Taft, *Steric Effects in Organic Chemistry*, (Edited by M. S. Newman) Chap. 13. Wiley, New York, N.Y. (1956).
[34] J. D. Roberts and W. T. Moreland, *J. Am. Chem. Soc.* **75**, 2167 (1953).
[35] M. Syz and H. Zollinger, *Helv. Chim. Acta* **48**, 383 (1965).
[36] H. Rau, *Angew Chem.* Internat. Ed. **12**, 224 (1973).
[37] A. A. Zavitsas and J. A. Pinto, *J. Am. Chem. Soc.* **94**, 7390 (1972).
[38] P. D. Bartlett and C. Rüchardt, *Ibid.* **82**, 1756 (1960); J. A. Howard and K. U. Ingold, *Can. J. Chem.* **41**, 1744 (1963); G. A. Russell, *J. Org. Chem.* **23**, 1407 (1958).
[39] T. Alfrey and C. C. Price, *J. Polymer Sci.* **2**, 101 (1947).
[40] R. Ito, T. Migita, N. Morikawa and O. Simamura, *Tetrahedron* **21**, 955 (1965).
[41] H. Sakurai, S. Hayaski and A. Hosomi, *Bull. Chem. Soc. Japan* **44**, 1945 (1971).
[42] T. Yamamoto and T. Otsu, *Chem. & Ind.* 787 (1967).