A STUDY ON HYPERCONJUGATIVE AND INDUCTIVE EFFECTS OF ALKYL GROUPS

烷基電子效應之研究

CHENG-HSIA WANG

王 澄 霞

Department of Chemistry

Alkyl groups have two electronic effects, inductive and hyperconjugative. The concept of inductive effect of alkyl groups, recognized since the earlier stages of the development of the electronic theory of organic chemistry, has appeared successful in accounting for both physical data and relative chemical reactivity. When the polar effects of alkyl groups are under consideration, electron releasing power by the inductive effect is in the order H<Me<Et<i-Pr<t-Bu. The inductive effect alone proved satisfactory in explaining the variation in the acid strengths of the phenylacetic acids[1] and in the relative rates of hydrolysis of alkyl halides[2].

There were also, however, reactions in which this general inductive order appeared to be disturbed. Thus electrophilic substitution of p-alkyltoluenes occurs mainly *ortho* to the methyl group instead of being directed by the larger alkyl groups[3] as would be demanded by the inductive effect alone. The disturbed and apparently random order of the electronic effect of alkyl groups was also revealed in the relative rate of chlorination of p-alkylbenzoxyphenols[4] and in the methylation of p-alkyldimethylanilines[5]. All of these observations necessitated another electronic characteristic of alkyl groups. This was suggested to be a resonance effect (now referred to as hyperconjugation) by Baker and Nathan[6] in 1935 after their kinetic study of the Menschutkin reaction between substituted benzyl bromide and pyridine, which revealed an inverted order of electron release for alkyl groups, that is, Me>Et>i-Pr>t-Bu>H. An extensive survey of hyperconjugation is not attempted here, since some excellent review articles on the subject have been published[10].

— 1 —

It was the purpose of this work to study the electronic effect of the alkyl groups by measuring the dissociation constants of 2-nitro-4-alkylphenols.

Although phenol (Ka ca. 10^{-10}) is much more acidic than any aliphatic alcohol (Ka ca. 10^{-16} to 10^{-20}) owing to resonance stabilization of its anion, the dissociation constants of p-alkylphenols (Ka ca. 10^{-11} to 10^{-12} in ethanol-water) are almost of the order of that of water, and are thereby rendered difficult to be measured accurately. Introduction of an *ortho* nitro group, an electron withdrawing group, tends to increase the acid strength of the alkylphenols by placing a positive fractional charge on the oxygen of the hydroxyl group, which repels the hydrogen atom as a proton. For this reason, accurate measurements of the dissociation constants of the 2-nitro-4-alkylphenols are easier than of the p-alkylphenols, and the results obtained in the present work are perhaps subject to less experimental error.

EXPERIMENTAL

Absolute methanol[7] and *absolute acetone*[8] were prepared from reagent grade methanol and U.S.P. acetone, respectively.

Preparation of 0.0990 N carbonate-free NaOH[9]

One hundred grams of C.P. sodium hydroxide was dissolved in 100 ml. of water in a Pyrex flask. The sodium carbonate remained in suspension and slowly settled to the bottom of the container. The solution was allowed to stand undisturbed for two weeks, until the carbonate had settled. The clear solution was pipetted out without disturbing the precipitated carbonate into a bottle which had been previously coated inside with paraffin.

Concentrated carbonate-free NaOH was diluted 250 times with carbonate-free water which was made by boiling distilled water for about ten minutes. About 0.4-0.5 g. of potassium acid phthalate (accurately weighed) was transfered into a 300-ml. flask. Fifty ml. of cold carbonate-free water was added and titrated with approximately 0.1 N NaOH (free from CO_2). The carbonate-free NaOH was tested by 0.5 N $BaCl_2$ solution, i.e., no white precipitate was observed.

Preparation of o-nitrophenol

o-Nitrophenol (Eastman Kodak) was crystallized three times from ligroin (b.p. 30-40°) affording long yellow needles, m.p. 45.3-46.0° (corr.).

2-Nitro-4-alkylphenols were all prepared by nitration of the corresponding p-alkylphenols. The crude (liquid except the p-methyl compound) 2-nitro-4-alkylphenols were then converted into the solid benzoates in order to purify them.

2-Nitro-4-methylphenol[10]

The crude 2-nitro-4-methylphenol: To a cooled solution of 36 g. (1/3 mole) of 4-methylphenol in 500 ml. benzene, a mixture of 128 ml. 70% nitric acid and 256 ml. water was added dropwise in a period of three and half hours with vigorous stirring at 2-3°. Then, 300 ml. of water was added. The aqueous layer was separated and extracted with 100 ml. of benzene. The combined benzene solutions were washed with dil. aq. sulfuric acid and dried over calcium sulfate. The yield of the phenol boiling at 100° at 7 mm. was 34.5 g. (67.6%).

2-Nitro-4-methylphenylbenzoate: A mixture of 14.3 g. of the phenol (87.7 mmoles), 8.77 ml. of benzoyl chloride and 2 drops of conc. sulfuric acid was boiled for few minutes. After standing overnight at room temperature the reaction mixture solidified; the solid was recrystallized twice from ethanol. The yield of benzoate was 73% (16.45 g.), m.p. 98-100°.

Pure 2-nitro-4-methylphenol: The benzoate (6.52 g., 0.04 mole), 4.488 g. of potassium hydroxide (0.08 mole), 100 ml. of water, and 50 ml. of ethanol were mixed in a 250-ml. Erlenmeyer flask. The mixture was refluxed for about ten hours. Three hundred ml. of water was added and the mixture was acidified with conc. HCl. The solution was extracted with ether and the ether layer was extracted with 7.56 g. of $NaHCO_3$ (0.09 mole) and washed with a small amount of water. The ether layer was dried over calcium sulfate, and distilled. The main fraction, 11.30 g., was collected at 81-81.5° at 2 mm. The purified phenol, faintly yellow prisms, melted at 30.4-32° (corr.) with previous softening. *2-Nitro-4-ethylphenol, 2-nitro-4-isopropylphenol,* and *2-nitro-4-t-butylphenol* were prepared according to the same procedures as in the preparation of 2-nitro-4-methylphenol.

Measurement of the Dissociation Constants

· The dissociation constants at 25° were determined in the five aq. organic solvents by measuring the pH's of 40, 50 and 60% neutralized solutions using a Beckman Model G pH meter. The pH meter was set at regular short intervals against 0.05 M potassium biphthalate (pH 4.01) during each set of measurements.

The samples to be measured were thermostated at $25\pm0.1°$.

In order to prepare the samples for pH measurements, approximately 5 x 10^{-5} to 3 x 10^{-4} mole of the phenol (the amount varying with solvent) were weighed into 50 ml. volumetric flasks and partially neutralized with aq. carbonate-free NaOH (0.0990 N). The calculated amount of absolute methanol or acetone was then added to correct for the lack of organic solvent in the standard base, and the mixture was made to volume with the appropriate mixed aq. organic solutions. The resulting solution was approximately 0.0004 M to 0.0048 M in the phenol, and the concentration of the phenoxide ion varied over the same range. A minimum of four independent measurements were made for each compound in each of the five solvents.

The pKa's at $25\pm0.1°$ were calculated from the pH's of the partially neutralized solutions using the Henderson equation[11];

pKa=pH+log (conc. acid)/(conc. salt)

Results and Discussion

The dissociation constants of the 2-nitro-4-alkylphenols at 25° were determined in five aq.-organic solvents with the results recorded in Table I and II. In Table III are recorded pertinent data on the solvents used. The compounds were too little soluble to determine the dissociation constants in water alone.

Table I

Mean pKa±av. deviation at 25° for 2-nitro-4-R-C_6H_4OH

Solvent	R=H	Me	Et	i-Pr	t-Bu
10% Acetone	6.29±0.005	7.67±0.003	7.63±0.003	7.48±0.005	7.52±0.003
24.5% Acetone	7.57±0.005	7.89±0.005	7.86±0.003	7.71±0.003	7.76±0.003
40% Acetone	8.00±0.005	8.38±0.003	8.38±0.007	8.21±0.003	8.27±0.005
30% MeOH	7.61±0.005	7.92±0.005	7.89±0.003	7.78±0.003	7.84±0.007
50% MeOH	7.89±0.060	8.21±0.060	8.21±0.020	8.09±0.002	8.14±0.040

Table II

Ka x 10⁻⁸ at 25° for 2-nitro-4-R-C_6H_4OH where

$Ka \times 10^{-8}$ at 25° for 2-nitro-4-R-C_6H_4OH where

Solvent	R=H	Me	Et	i-Pr	t-Bu
10% Acetone	51.3	2.14	2.34	3.31	3.02
24.5% Acetone	2.69	1.29	1.38	1.95	1.74
40% Acetone	1.00	0.417	0.417	0.617	0.537
30% MeOH	2.45	1.20	1.29	1.66	1.45
50% MeOH	1.29	0.617	0.617	0.813	0.708

Table III

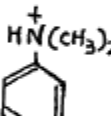Data on solvents used for dissociation constants studied
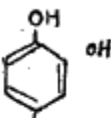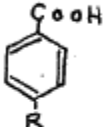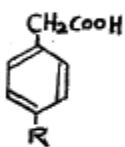
Solvent	% By wt. of organic component	Dielectric Constant, 25°	D_{25}^{25}	D_4^{25}	Moles org. component per mole H_2O
Acetone-H_2O	10.0	73.0	0.9879	0.9850	0.034
	24.5	64.3	0.9666	0.9638	0.101
	40.0	54.6	0.9406	0.9378	0.206
MeOH-H_2O	30.0	64.3	0.9529	0.9501	0.241
	50.0	54.9	0.9198	0.9171	0.563

The data indicate that the p-alkyl groups decrease the acidity of o-nitrophenol in all solvents studied in the order Me≥Et>t-Bu>i-Pr. This is also the order of electron release by the alkyl groups and shows the simultaneous operation of the hyperconjugation and the inductive effect. Hyperconjugation appears to be predominating in these systems; the observed order is a hyperconjugation order with the i-Pr and t-Bu compounds reversed.

The results can be compared with those obtained in the studies of the acidities of other alkyl substituted aromatic acids.
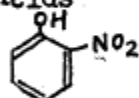
Table IV

pKa's for phenols and aromatic carboxylic acids and anilinium ions

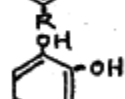| Acids		R=H	Me	Et	i-Pr	t-Bu
(phenol, OH / OH, R)	in 40% dioxane at 25° (12)	10.90	11.3	—	—	11.4
(COOH, R)	in H_2O at 25° (13)	4.20	4.37	4.35	4.35	4.40
(CH_2COOH, R)	in H_2O at 25° (13)	4.312	4.370	4.373	4.391	4.418
($\overset{+}{H}N(CH_3)_2$, R)	in 50% by vol. EtOH-H_2O at 20° (14)	4.22	4.77	4.69	4.78 / 4.77	4.65

In Table V the order of electron release observed in the 2-nitro-4-alkylphenols is compared with that observed in other acids.
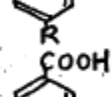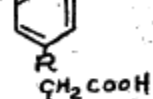
Table V

Acids

| Acid	Order
(OH, NO_2, R)	R= Me ≥ Et > t-Bu > i-Pr > H
(OH, OH, R)	R= t-Bu > Me > H
(COOH, R)	R= t-Bu > Me > Et = i-Pr > H
(CH_2COOH, R)	R= t-Bu > i-Pr > Et > Me > H (pure inductive order)
($\overset{+}{N}H(CH_3)_2$, R)	R= Me = i-Pr > Et > t-Bu > H
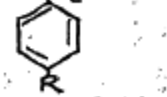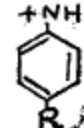
The hyperconjugation effect (relative to the inductive effect of alkyl groups) seems to be operating more strongly in the 2-nitro-4-alkylphenols than in the other neutral acids for which data are available.

The data in Table I and II indicate that the acidities of the 2-nitro-4-alkyl-phenols decrease as the water content of any one solvent pair is decreased. This trend is a general one for uncharged acids[15]. For example, Ka for acetic acid at 25° drops from 1.25×10^{-5} to 8.34×10^{-6} when the solvent is changed from 10% by weight methanol to 20% by weight methanol.[15] Because the ionization of a neutral acid involves the creation of charged species, i.e.,

$$HA + Base \rightarrow H^+ Base + A^-$$
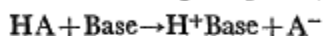
this decrease in acid strength is expected for solvent of lower solvating power.

References

1. Dippy, J. F. J., *Chem. Revs.*, 25, 151 (1939).
2. Bateman, L.C., Cooper, K.A., Hughes, E.D., and Ingold, C.K., *J. Chem. Soc.*, 925 (1940).
3. Battegay, M.M. and Haeffely, P., *Bull. Soc. Chim.*, 35, 981 (1924).
4. Jones, B., *J. Chem. Soc.*, 1414 (1938).
5. Davis, W.C., *ibid.*, 1965 (1938).
6. Baker, J.W. and Nathan, W.S., *ibid.*, 1844 (1935).
7. Fieser, F., "experiment in Organic Chemistry," 2nd Ed., Bost. D. C. Heath, p. 360, 1941.
8. Conant, J.B. and Kirner, W.R., *J. Am. Chem. Soc.*, 46, 245 (1924).
9. Pierce, W.C. and Haenisch, E.L., "Quantitative Analysis," John Wiley and Sons, Inc., New York, 3rd Ed., 127, 181, 124.
10. Schultz, *Ber.*, 40, 4324 (1907).
11. Glasstone, S., "Text Book of Physical Chemistry," D. Van Nostrand Co. Inc., N. Y., p. 982 (1940).
12. Corse and Ingraham, *J. Am. Chem. Soc.*, 73, 5706 (1951).
13. Baker, J.W., Dippy and Pagl, J. Chem. Soc., 1774 (1937).
14. Cule, W. and Davies, J. Chem. Soc., 1865 (1938).
15. Harned, H.S. and Owen, B.B., "The Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Co., N. Y., p. 581, 1943.
16. Dewar, M.J.S., "Hyperconjugation," Ronald Press, N. Y., 1962.