TABLE I

RELATIVE BASICITIES OF METHYLBENZENES

	Calcd.	Exptl.[3]
Benzene	0.0002	....
Methylbenzene (toluene)	.012	(*ca.* 0.001)
1,4-Dimethylbenzene (*p*-xylene)	.042	.05
1,2-Dimethylbenzene (*o*-xylene)	.050	.10
1,3-Dimethylbenzene (*m*-xylene)	1.3	1
1,2,4-Trimethylbenzene (pseudocumene)	2.6	2
1,2,3-Trimethylbenzene (hemimellitene)	3.1	2
1,2,4,5-Tetramethylbenzene (durene)	6.6	6.7
1,2,3,4-Tetramethylbenzene (prehnitene)	9.4	9.4
1,3,5-Trimethylbenzene (mesitylene)	151	156
1,2,3,5-Tetramethylbenzene (isodurene)	312	311
Pentamethylbenzene	484	484
Hexamethylbenzene (mellitene)	......	4950

figure, a line with a slope of 1.45 could be drawn through the remaining points in accordance with the least squares principle.

The relationship noted here between two reactions involving aromatic ring carbons is similar to previously observed relationships between reactions involving aromatic side chains[4] for which

$$\log k/k_0 = \rho\sigma$$

where k and k_0 are rate or equilibrium constants for a substituted and an unsubstituted compound, respectively, and ρ and σ are constants characteristic of the reaction and the substituent, respectively. Since σ for meta methyl is -0.069 and σ for para methyl is -0.170, it can be calculated that ρ for halogenation is $-\log 5/0.069 = -10.1$ or $-\log 870/0.170 = -17.3$ and that ρ for reaction with $HF \cdot BF_3$ is $-\log 3.1/0.069 = -7.1$ or $-\log 145/0.170 = -12.7$. The large differences between the ρ's calculated from the σ for meta methyl and the ρ's calculated from the σ for para methyl suggests that a set of σ-values different from those used to correlate reactions of aromatic side chains may be useful for correlating reactions of aromatic ring carbons.

(4) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

BARTLESVILLE, OKLAHOMA

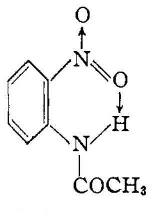
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA]

Polarographic Reduction and Indicated Tautomeric States of the Nitroacetanilides in Ethanol[1]

BY M. E. RUNNER[2] AND E. C. WAGNER

Study of the polarographic behaviors of *o*-, *m*- and *p*-nitroacetanilides and of the isomeric N-nitrophenyl-N'-phenylacetamidines in absolute ethanol buffers revealed (1) analogy between the two types considered as aquo-ammono and ammono-acids, (2) a tentative correlation between the *pK* characteristics of the buffers and induced tautomeric or ionic states of the nitro compounds, (3) the effects of the acetamino and acetimino groups in facilitating polarographic reduction of the nitro group, (4) a similar effect, in the ortho-nitro isomerides only, attributable to chelation, presence of which is suggested also by their relatively greater volatilities, and (5) four-electron polarographic reduction, with indecisive indication of six-electron reduction in acid media.

This paper reports the results of polarographic reductions of *o*-, *m*- and *p*-nitroacetanilides in absolute ethanol. Interpretation with respect to tautomeric states is similar to that applied in the similar study of the isomeric N-nitrophenyl-N'-phenylacetamidines[3] (of which the nitroacetanilides are the half-oxygen system analogs), and justifies the inference that the structure of *o*-nitroacetanilide permits chelation



Such involvement of the nitro group would be expected to increase its reducibility. Other inferential evidence for chelation in this compound is available in the finding[4] that in naphthalene it is less associated than its isomerides, and that its wet melting point depression is less than that of *p*-nitroaniline.[4,5]

The structures of the nitroacetanilides may undergo alterations induced by the *pK* of the environment, to test which of the polarographic examinations were made at intervals through the range *pK* 1 to 17. The use of absolute ethanol as solvent necessitated elaboration of a suitable system of buffers.[6]

Since the polarographic reductions of the N-ni-

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(1) This paper represents the first part of the Ph.D. Dissertation of Mervin E. Runner, University of Pennsylvania, 1950.

(2) Chemistry Dept., The Illinois Institute of Technology, Chicago 16, Illinois.

(3) M. E. Runner, M. L. Kilpatrick and E. C. Wagner, THIS JOURNAL, **69**, 1406 (1947).

(4) H. O. Chaplin and L. Hunter, *J. Chem. Soc.*, 375 (1938).

(5) W. Baker, *ibid.*, 1687 (1934).

(6) The buffers used, and the *pK* value calculated for each, are as follows: perchloric acid, 1; *o*-bromoaniline hydrochloride, 3; β-naphthylamine hydrochloride, 5; chloroacetic acid, 6; *m*-bromobenzoic acid, 8; benzoic acid, 9; *o*-chlorobenzylamine hydrochloride, 10; diethylbarbituric acid, 12; guanidine hydrochloride, 13; lithium ethoxide, 17. Lithium chloride was added in amounts such that in each case the total concentration of the supporting electrolyte was at an ionic strength 0.05. This system of buffers, used here recently in the polarographic examination of the isomeric nitrobenzimidazoles,[7] was developed for the present study by the junior author.

(7) J. L. Rabinowitz and E. C. Wagner, THIS JOURNAL, **73**, 3030 (1951).

trophenyl-N'-phenylacetamidines were first studied[3] using 50% ethanol as solvent and a different system of buffers this work was repeated under the conditions outlined above for the nitroacetanilides. No significant difference, requiring modification of the interpretations of earlier results, was disclosed. To ascertain the extent of reduction in each case the approximate value of the diffusion coefficient, separately obtained for each compound, was used in the Ilkovic equation.[8] As a standard of comparison of half-wave potentials nitrobenzene was subjected to polarographic reduction under the same conditions.

Results and Discussion

Polarographic data for the nitroacetanilides are collected into Tables I and V; results at *pK* 3 and 12 are presented graphically in Figs. 1 and 2.

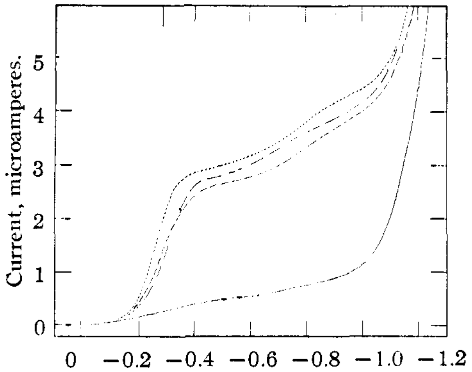

Fig. 1.—Nitroacetanilides *pK* 3: -----, ortho; ---, meta; —·—, para.

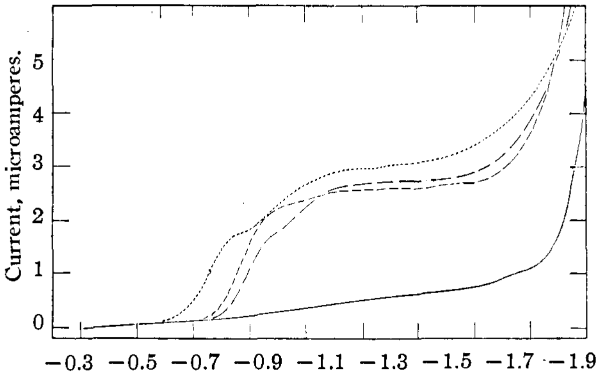

Fig. 2.—Nitroacetanilides *pK* 12: ----, ortho; ---, meta; —·—, para.

Data for the N-nitrophenyl-N'-phenylacetamidines appear in Table II. Data for nitrobenzene are implicit in the values of Table III, which lists the differences between values of the half-wave potentials of the isomeric nitroacetanilides and of the isomeric N-nitrophenyl-N'-phenylacetamidines as compared with those of nitrobenzene. In Table III the amounts by which the half-wave potentials of each compound are less negative than those of nitrobenzene are indicated by positive values, and *vice versa*.

Table I

Effect of Hydrogen Ion Concentration on the Reduction of 2 × 10^{-4} *M* Nitroacetanilides in Ethyl Alcohol

	Ortho-		Meta-		Para-	
pK	Diffusion current, μa.	Half-wave potential, volts	Diffusion current, μa.	Half-wave potential, volts	Diffusion current, μa.	Half-wave potential, volts
1	2.75	−0.12	2.25	−0.15	2.40	−0.18
3	2.52	− .26	2.18	− .28	2.35	− .29
5	2.25	− .38	2.00	− .43	2.05	− .45
6	2.36	− .53	2.05	− .62	2.10	− .66
8	2.45	− .53	2.10	− .63	2.18	− .68
9	2.45	− .60	2.15	− .70	2.11	− .73
10	2.48	− .55	2.25	− .62	2.25	− .67
12	1.50[a]	− .76[a]	2.03	− .88	1.40[a]	− .89[a]
	2.43[b]	−1.03[c]			2.15[b]	−1.10[c]
13	1.00[a]	−0.81[a]	2.15	− .84	2.20	−0.89
	2.68[b]	−0.96[c]				
17	2.66	−1.05	2.20	− .91	2.20	−1.01

[a] First wave. [b] Total wave. [c] Second wave.

Table II

Effect of Hydrogen Ion Concentration on the Reduction of 2 × 10^{-4} *M* N-Nitrophenyl-N'-phenylacetamidines in Ethyl Alcohol

	Ortho-		Meta-		Para-	
pK	Diffusion current, μa.	Half-wave potential, volts	Diffusion current, μa.	Half-wave potential, volts	Diffusion current, μa.	Half-wave potential, volts
1	1.83[a]	−0.06[a]	1.87[a]	−0.14[a]	1.87[a]	−0.14[a]
	2.84[b]	− .66[c]	2.89[b]	− .63[c]	2.89[b]	− .60[c]
3	1.58[a]	− .18[a]	1.65[a]	− .20[a]	1.65[a]	− .19[a]
	2.30[b]	− .86[c]	2.30[b]	− .82[c]	2.30[b]	− .77[c]
5	1.60	− .32	1.63	− .36	1.70	− .36
6	1.93	− .46	1.76	− .51	1.76	− .54
8	2.03	− .54	1.97	− .57	1.92	− .61
9	2.03	− .59	1.98	− .64	2.00	− .70
10	1.98	− .57	1.87	− .61	1.92	− .67
12	1.84	− .83	1.90	− .86	1.80	− .92
13	1.82	− .83	1.90	− .85	1.90	− .90
17	1.95	− .92	1.95	− .90	1.90	−1.02

[a] First wave. [b] Total wave. [c] Second wave.

Table III

Difference Between $E^1/_2$ for Each Nitro Compound and Nitrobenzene[a]

	Nitroacetanilides			N-Nitrophenyl-N'-phenylacetamidines		
pK	Ortho	Meta	Para	Ortho	Meta	Para
1	+0.09	+0.06	+0.03	+0.15	+0.07	+0.07
3	+ .10	+ .08	+ .07	+ .18	+ .16	+ .17
5	+ .10	+ .05	+ .03	+ .16	+ .12	+ .12
6	+ .15	+ .06	+ .02	+ .22	+ .17	+ .14
8	+ .16	+ .06	+ .01	+ .15	+ .12	+ .08
9	+ .12	+ .02	− .01	+ .13	+ .08	+ .02
10	+ .12	+ .05	0	+ .10	+ .06	0
12	+ .12	0	− .01	+ .05	+ .02	− .04
13	+ .03	0	− .05	+ .01	− .01	− .06
17	− .05	+ .09	− .01	+ .08	+ .10	− .02

[a] Positive values indicate amounts by which half-wave reduction potentials are less negative than those of nitrobenzene, *i.e.*, by which the compounds are easier to reduce than nitrobenzene.

Nitroacetanilides.—Except in media of *pK* above 12 *o*-nitroacetanilide is more readily reduced than the *m*- and *p*-isomers and nitrobenzene. The greater

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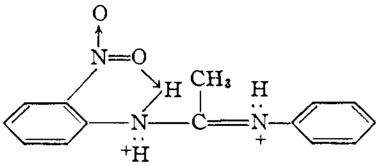
(8) D. Ilkovic, *Coll. Czech. Chem. Commun.*, **6**, 498 (1934); *J. chim. phys.*, **35**, 129 (1938).

susceptibility of the ortho-isomer to reduction, as compared with the meta-isomer and with nitrobenzene, may be attributed jointly to the influence of the acetamino group in decreasing the electron density of the nitro group and to the effect of internal hydrogen-bonding. The probability of chelation is increased by the observation that *o*-nitroacetanilide is more volatile than the meta- and para-isomers.[9]

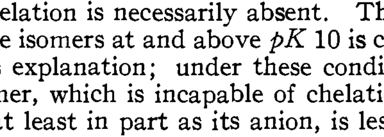
The difference between the half-wave potentials of *o*-nitroacetanilide and the para-isomer is greatest at *pK* 8 (+0.15 volt) and remains relatively large through *pK* 12 (+0.13 volt for first wave). At *pK* 17 the half-wave potential for *o*-nitroacetanilide is 0.04 volt more negative than that for the para-isomer, suggesting absence of chelation under strongly alkaline solutions. Solutions of the three isomers were colorless up to *pK* 12. At *pK* 13 and 17 the ortho- and para-isomers yielded, respectively, pale yellow and yellow solutions, but the solution of the meta-isomer remained colorless. The appearance of visible color may indicate appreciable conversion of the ortho- and para-compounds to the quinonoid-nitronic acid anions.

Within the range *pK* 1 to 10 (Table I) a single wave, representing a four-electron reduction, was observed for *o*-nitroacetanilide, with indication of a second wave at *pK* 1 and 3 obscured by discharge of hydrogen ion (Fig. 1). The diffusion current determined for *p*-nitroacetanilide under neutral conditions was 2.1 μa., indicating a four-electron process. For *p*-nitroacetanilide at *pK* 12 (Table I) the total wave approximates that at other *pK* values but appears as a double wave. At *pK* 12 and 13 the ortho-isomer (not the meta) likewise yielded a double wave (Table I and Fig. 2). Since the half-wave potential of the second wave for *o*-nitroacetanilide at *pK* 12 (−1.03 v.) approximates that obtained at *pK* 17 (−1.05 v.),[10] it is concluded that toward the anions of both buffers (lithium ethoxide at *pK* 17 and diethylbarbituric acid at *pK* 12) *o*-nitroacetanilide shows an acid behavior and may be present as the anion $NO_2C_6H_4NCOCH_3^-$. Similarly at *pK* 12 the second wave for *p*-nitroacetanilide indicates interaction with the buffer, but at *pK* 13, with guanidine as buffer there is no indication of such action. Since the double waves appear to be associated with the acid behavior of the amide linkage it cannot be assumed that a stabilization of the nitroso intermediate has occurred. The two-step reduction to the amino stage in acid media observed for the nitroacetanilides is similar to the behavior of nitrobenzene in aqueous media.[12]

N-Nitrophenyl-N′-phenylacetamidines.—Results in absolute ethanol are virtually identical with those obtained earlier[3] in 50% ethanol and with a different set of buffers. At *pK* 1 and 3 reduction of the three isomers occurred in two stages, the first wave being two-thirds of the total wave, and reduction reached the amino stage. In less acid media (above *pK* 3) only one wave was observed, corresponding to a four-electron reduction. This behavior resembles that of nitrobenzene in aqueous solvents.[12] The half-wave potentials of the N-nitrophenyl-N′-phenylacetamidines in absolute ethanol through the *pK* range 1 to 9 are more positive than those in 50% ethanol[3] and are more so at lower *pK* values. This greater ease of reduction under acid conditions suggests the putative dipositive ion, in which any contribution of electrons to the nitro group is decreased. Reducibility is further enhanced by chelation in the case of the ortho-isomer



The relatively high reducibility of the ortho-nitro isomer through *pK* 10 may be ascribed to chelation of the monovalent cation[3] and the neutral molecule, with perhaps some contribution by the dipolar form



Above *pK* 10 the ortho-nitro isomer is less readily reduced than at lower *pK* values, though more readily than nitrobenzene. This may be attributed to an electron-donating tendency of the resonating anion (presence of which is indicated by color) in which chelation is necessarily absent. The behaviors of the isomers at and above *pK* 10 is consistent with this explanation; under these conditions the para-isomer, which is incapable of chelation but is present at least in part as its anion, is less readily reduced than its isomers and than nitrobenzene.

Both the N-nitrophenyl-N′-phenylacetamidines and the nitroacetanilides show in their reduction behaviors the results of analogous structural influences upon the nitro group, as is evident upon comparing their half-wave potentials with those of the nitroanilines.[11] Some representative half-wave potentials for *p*-nitroaniline through the neutral region will illustrate: at *pK* 8, −0.85 v.; at *pK* 9, −0.88 v.; at *pK* 10, −0.81 v. This is in contrast to the corresponding values for *p*-nitroacetanilide which are −0.68, −0.73 and −0.67 v. for these same media, respectively. The latter, however, agree closely with values for nitrobenzene, −0.69, −0.72 and −0.67 v., respectively in media of *pK* 8, 9 and 10. Table II reveals similar behavior in the case of N-*p*-nitrophenyl-N′-phenylacetamidine. It

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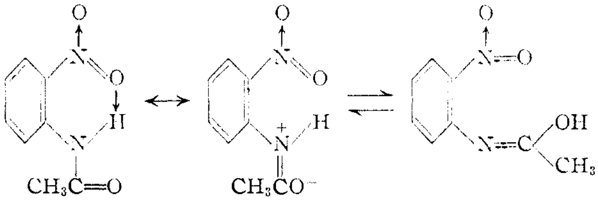
[9] Experiments performed by George R. Wolf, showed that at 228° the relative rates of sublimation are para:meta:ortho = 1:3:32.

[10] The half-wave potential (−1.05 v.) is identical with that obtained for *o*-nitroaniline at *pK* 17,[11] suggesting that lithium ethoxide may cleave the acetamino group: $NO_2C_6H_4NHCOCH_3 + {}^-OC_2H_5 = NO_2C_6H_4NH^- + CH_3COOC_2H_5$. This seems improbable because the half-wave potentials of *m*- and *p*-nitroacetanilides at *pK* 17 (−0.91 v. and −1.01 v., respectively) differ significantly from those of *m*- and *p*-nitroanilines at *pK* 17 (−0.95 v. and −1.11 v., respectively). The apparently anomalous behaviors at *pK* 12 and 13 may involve the specific characters of the buffers, for the half-wave potential of *o*-nitroacetanilide (second wave) approximates that for *o*-nitroaniline, while the values for *m*- and *p*-nitroacetanilides and the corresponding nitroanilines show no such similarity. The value found for the diffusion current for *o*-nitroacetanilide at *pK* 17 (2.66 μa., Table I) appears to exclude a conclusion that the compound reduced at *pK* 17 is actually *o*-nitroaniline, for which compound the experimentally determined value for the diffusion current at the same concentration is 3.00 μa.

[11] M. E. Runner, Dissertation, University of Pennsylvania, 1950, Part II.

[12] J. Pearson, *Trans. Faraday Soc.*, **44**, 683 (1948).

appears that the effects of the acetamino and the amidine groupings (respectively, aquo-ammono and ammono acids) are opposite to those of the amino group of the nitroanilines. The former decrease the electron density of the nitro group, an effect which in the N-nitrophenyl-N′-phenylacetamidines and nitroacetanilides is modified by the tautomeric forms of these systems, and which in the ortho-nitro isomers is further influenced by chelation; for *o*-nitroacetanilide



The +T effect of the acetamino group is slight compared with that of the unsubstituted amino group; it appears that the electron-donating ability of the amino group is annulled by presence of the acetyl substituent.

Diffusion Coefficient Measurements.—Diffusion coefficients were measured by use of a porous membrane between two homogeneous bodies of solution, with the diffusion gradient confined within this membrane.[13]

The diffusion cell and the procedure were those described by McBain and Liu.[14] The equation of King and Cathcart[15] for diffusion between two solutions of unequal volumes is used in the simplified form[16] $KDt_E = \log [c'/(c' - c)]$, in which D is the diffusion coefficient, K is a constant determined by the dimensions of the sintered glass membrane, t_E is the elapsed time of the diffusion experiment, c and c' are the concentrations of nitro compounds in compartments B and A of the diffusion cell after time t_E. Values of these terms are listed in Table IV, with values for KD in column six. From values for KD and the cell constant ($K = 0.50$) were calculated the diffusion coefficients listed in column three of Table V; values of the diffusion current constants, calculated from the Ilkovic equation,[8] appear in columns six and seven. The diffusion currents (i_d) in column four are selected from Tables I and II.

TABLE IV

DIFFUSION COEFFICIENT MEASUREMENTS IN ETHYL ALCOHOL

Cell constant $K = 0.50$

Compound	c' i_d in μa.	c i_d in μa.	t_E $\times 10^{-5}$, sec.	Temp., °C.	KD $\times 10^5$
o-Nitroacetanilide	7.0	2.4	0.432	25	0.422[a]
m-Nitroacetanilide	5.8	1.4	.405	24	.322[a]
p-Nitroacetanilide	6.5	1.3	.270	27	.359[a]
N-*o*-Nitrophenyl-N′-phenylacetamidine	6.0	1.5	.432	23	.289[b]

[a] In medium pK 8. [b] In medium pK 9.

The diffusion coefficient found for *o*-nitroacetanilide is considerably greater than that for the *p*-isomer at pK 8, and the values for the diffusion current are consistently greater for the ortho-isomer (Table I). The concurrently large diffusion coefficients and diffusion currents for *o*-nitroacetanilide may be fortuitous, for the increased wave heights may be due to secondary reduction of products formed at the mercury drop surface by condensations or rearrangements of reduction intermediates, as observed for certain nitro compounds by Wawzonek.[17] The extent of such effect would be influenced by the concentration of nitro compound, hence the relationship of diffusion current and concentration may not be linear. For this reason the experimentally measured diffusion coefficient for *o*-nitroacetanilide is probably too high.

The diffusion currents for the N-nitrophenyl-N′-phenylacetamidines are the same for the three isomers, hence the diffusion coefficient for the *o*-nitro isomer serves for the others. The determined values for the diffusion current constants (Table V, columns six and seven) appear to confirm the four-electron character of the reduction (Table V, column five), and are approximately double the diffusion current constant for maleic acid.

TABLE V

THE EXTENT OF REDUCTION AND DIFFUSION COEFFICIENTS IN ETHANOL AT 25°

$c = 0.2$ millimole; $m^{2/3}t^{1/6} = 1.684$ mg.$^{2/3}$ sec.$^{-1/2}$

Compound	pK	D (found) $\times 10^5$ (cm.^{2}/sec.)	i_d, μa.	n, electrons	Diffusion current constants a	b
o-Nitroacetanilide	8	0.84	2.45	4	7.28	7.02
m-Nitroacetanilide	8	.65	2.10	4	6.24	6.17
p-Nitroacetanilide	8	.69	2.18	4	6.47	6.36
N-*o*-Nitrophenyl-N′-phenylacetamidine	9	.60	2.03	4	6.03	5.93
Maleic acid	1	..	1.10	2	3.27	..

[a] $K = i_d/(cm^{2/3}t^{1/6})$. [b] $K = knD^{1/2}$ (found).

Experimental

Materials.—Lithium chloride (Merck and Co., Inc., reagent grade) was purified by precipitation with ammonium carbonate, washing the lithium carbonate five times by decantation and finally with suction, and dissolving in hydrochloric acid; the solution was evaporated slowly in a large evaporating dish, with continuous stirring to avoid formation of lumps, and finally to dryness. The still hot powdery salt was transferred to a desiccator and was kept over calcium chloride. The lithium metal used in preparation of lithium ethoxide dissolved in absolute ethanol without residue.

The buffer acids were commercial materials excepting *o*-

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(13) J. H. Northrop and M. L. Anson, *J. Gen. Physiol.*, **12**, 543 (1929).

(14) J. W. McBain and J. H. Liu, THIS JOURNAL, **53**, 59 (1931).

(15) C. V. King and W. H. Cathcart, *ibid.*, **58**, 1639 (1936).

(16) The simplification results from certain approximations applied to the original equation and from elimination of any volume variation with respect to the solutions in each of the two compartments (V_A the volume of buffered solution of nitro compound, and V_B the volume of buffer solution). Specifically, if $V_B \ll V_A$ the term $(1 + V_B/V_A)c \cong c$ and the term $V_AV_B/(V_A + V_B) \cong V_B$, the equation becomes $(DK'/V_B)t_E = \log [c_0/(c_0 - c)]$ in which c_0 is the concentration in compartment A at the start. Since $c_0 \cong c'$, and since K'/V_B can be written as K if V_B is made a fixed volume, the equation reduces to the form given above, and the volume V_A need not be known; this volume, for the cell used, was approximately 100 ml., and the volume V_B was 15 ml. in all experiments. The values of c' and c were measured polarographically and are reported as diffusion currents since only ratios, and not actual concentration, serve to determine the log term. It may be assumed from the general behavior of nitro compounds that concentrations are proportional to diffusion currents, and this was found to be the case when 4×10^{-4} molar solutions of the nitroanilines were examined in media of pK 1, the waves being exactly double those obtained for each of the three isomers at 2×10^{-4} molar concentration.[11]

(17) S. Wawzonek, *Anal. Chem.*, **21**, 63 (1949).

chlorobenzylamine hydrochloride, which was prepared from 20 g. (0.124 mole) of *o*-chlorobenzyl chloride and 750 ml. of saturated ammonia water (20 g. NH_3 at 10°) by heating for ten hours at 100° in an autoclave (175 lb. per sq. in.). The amine was extracted in ether, the extract was dried and saturated with hydrogen chloride, and the amine salt was crystallized twice from aqueous HCl; the m.p. was 215°. Chloroacetic acid was distilled under reduced pressure, the first runnings being rejected. The acids of neutral charge type were recrystallized from ethanol, excepting *m*-bromobenzoic acid for which acetone–water was used.

The three isomeric N-nitrophenyl-N′-phenylacetamidines were pure specimens as used in the previous study.[3] The three isomeric nitroacetanilides were recrystallized from 95% ethanol to a state of purity.

Commercial absolute ethanol was purified by the method of Lund and Bjerrum,[18] and was distilled under an atmosphere of dry nitrogen. In the preparation of solutions the absolute ethanol was transferred through a closed system from the receiver of the distillation outfit to a volumetric flask containing the solute. Each solution was transferred by pressure of nitrogen to a storage-dispensing flask equipped with a 10-ml. buret which could be filled and drained without exposure of the solution to air. From the purification of the alcohol through the final polarographic measurements the liquids were kept and handled under an atmosphere of dry nitrogen. The nitrogen (99.6% water-pumped tank nitrogen) was passed successively through vanadous sulfate solution for removal of oxygen,[19] concd. sulfuric acid, calcium chloride, ascarite and finally dehydrite.

Absolute Ethanol Buffers.—At an ionic strength of 0.05 the acids used have the following *pK* values (negative logarithms of their dissociation constants): perchloric acid, *pK* 1 (calculated)[20]; *o*-bromoaniline hydrochloride, *pK* 3[21a]; *β*-naphthylamine hydrochloride, *pK* 5[21a]; chloroacetic acid, *pK* 6[22]; *m*-bromobenzoic acid, *pK* 8[23]; benzoic acid, *pK* 9[23]; *o*-chlorobenzylamine hydrochloride, *pK* 10[21b]; diethylbarbituric acid, *pK* 12[24]; guanidine hydrochloride, *pK* 13[25]; lithium ethoxide, *pK* 17 (calculated).[26] When needed the buffers were prepared in 25-ml. portions by mixing the stock solutions (0.1 molar lithium ethoxide, 0.15 molar lithium chloride, 0.001 molar solutions of the nitro compounds as required) in a 50-ml. erlenmeyer flask fitted with a glass tube side-arm leading inward and to the bottom. The preparation of buffer *pK* 9 will illustrate. The flask, containing 0.001 mole of benzoic acid, was swept out with nitrogen introduced through the side-arm, there were added 5 ml. of 0.15 *M* lithium chloride, 5 ml. of 0.1 *M* lithium ethoxide, 5 ml. of 0.001 *M* nitro compound and 10 ml. of ethanol, and solution was effected while bubbling nitrogen through the mixture. The electrolysis cell was rinsed with 10 ml. of the solution, and was then charged with a measured 10-ml. portion for the examination, all while passing a stream of nitrogen. Before it entered the electrolysis cell the nitrogen was bubbled through 10 ml. of dry ethanol. Although oxygen is about nine times as soluble in alcohol as in water it was found that the special precautions used in storing and handling the solutions made a degassing period of five minutes adequate.

Discussion of Buffers.—Values of the dissociation constants of weak acids (neutral molecule type) at ionic strengths other than 0.05 were converted to values at 0.05 by use of the extrapolation formula[27] $\log K_c = \log K_0 + (5.9\sqrt{\mu})$. Substitution of 0.05 for the ionic strength (μ) leads to the useful form $pK = pK_0 - 1.32$, in which K_0 is the thermodynamic dissociation constant at an ionic strength of zero. For dilute solutions of cation type acids (RNH_3^+) no correction is needed for change of *K* with ionic strength. The dissociation constant for guanidine hydrochloride was determined in aqueous solution[25]; for an acid of this type little change is to be expected in ethanol. Acids whose *pK* values are between 13 and 17 at ionic strength 0.05 are not known.

Since in the half-neutralized solution of a weak acid the dissociation constant is equal to the hydrogen ion concentration, the *pK* values given above indicate definite points on a scale of acidity for ethanol and are to be so interpreted whenever a hydrogen ion concentration is designated. Thus from the autoprotolysis constant for ethanol (7.28×10^{-20}) the neutral point can be calculated as $pK = 9.6$. Lithium ethoxide was used to prepare the half-neutralized solutions, yielding a final concentration of uni-univalent buffer salt of 0.02 molar. Lithium chloride was added to bring the final salt concentration to 0.05 molar. Perchloric acid solution (*pK* 1) was used in 0.05 molar concentration and without lithium chloride because the anodic wave for chloride ion interfered seriously with the waves for compounds of low reduction potential. The availability of perchloric acid only as an aqueous solution (72%, 12.15 *M*) necessitated presence of approximately 0.1 molar water in the buffer. This appears to be the only solution of *pK* 1 available for the purpose, since the use of anhydrous hydrochloric acid is limited owing to discharge of chloride ion. The buffer of *pK* 17 was 0.02 molar lithium ethoxide + 0.03 molar lithium chloride.

The value of the total ionic strength (0.05) was purposely set as low as practicable to permit higher accuracy in reporting the dissociation constants. The buffer capacity was relatively high, the concentration of buffer being 100 times that of the nitro compound.

The Electrolysis Cell.—The Lingane and Laitinen H-type cell[28] was connected with the permanent external anode through a 10-mm. sintered glass disc of fine porosity, since it was not possible to use an agar plug with alcohol solutions. To exclude water and potassium ions from the anode the saturated aqueous potassium chloride solution was replaced by a saturated solution of lithium chloride in ethanol. The appreciable viscosity of the lithium chloride solution prevented streaming through the sintered glass disc. The solid lithium chloride in the anode chamber required no replacement throughout the work. The potential of this reference electrode, tested frequently against an aqueous saturated calomel electrode connected through a potassium chloride salt bridge,[29] remained constant at 0.050 ± 0.002 volts at 25°. When not in use the electrolysis cell was kept filled with saturated lithium chloride solution.

Polarograph.—All polarograms were recorded automatically by a Leeds and Northrup Electrochemograph, the e.m.f. applied at the half-wave potential being obtained by manual operation of the polarizer unit in order to secure values free from effects due to recorder lag. The resistance of the cell and circuit, including the dropping mercury electrode in 0.05 *M* lithium chloride in ethanol, was found (using an Industrial Instruments, Inc. conductivity bridge) to be 8000 ohms. All half-wave potentials were corrected for the *IR* drop of the circuit, and in the tables are referred to the aqueous saturated calomel electrode. Residual current values for each buffer were determined in blank runs (conditions as in reductions but with nitro-compound omitted), and were used to correct the diffusion current values recorded in the tables.

The dropping electrode, an 8-cm. section of Corning Marine Barometer tubing, had an $m^{2/3}t^{1/6}$ value of 1.684 mg.$^{2/3}$ sec.$^{-1/2}$ at 50-cm. head of mercury. All measurements not otherwise designated were obtained at 25 ± 0.1°.

Diffusion Coefficient Measurements.—Calculations were made using the simplified form of the equation of King and Cathcart[15] given above.[16]

All measurements of *c* and *c′* were made with a constant head of mercury and a constant drop-time, eliminating the necessity for calibrating the dropping mercury electrode. Diffusion measurements were made at room temperatures and values of *D* were corrected to 25° (2% per °C.). In

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[18] H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931).

[19] L. Meites and T. Meites, *Anal. Chem.*, **20**, 984 (1948).

[20] This solution was 0.05 *M* in perchloric acid. The *pK* value was calculated as follows: $pK = -\log(C_2H_5OH \cdot H^+) = -\log 5 \times 10^{-2} = 1.3$.

[21] (a) L. D. Goodhue and R. M. Hixon, THIS JOURNAL, **56**, 1329 (1934); (b) *ibid.*, **57**, 1688 (1935).

[22] A. J. Deyrup, *ibid.*, **56**, 60 (1934).

[23] J. H. Elliott and M. Kilpatrick, *J. Phys. Chem.*, **45**, 466 (1941).

[24] I. M. Kolthoff, *ibid.*, **35**, 2732 (1931).

[25] N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932).

[26] This solution was 0.02 *M* in lithium ethoxide and was calculated from the autoprotolysis constant expression for ethanol as follows: $(C_2H_5OH \cdot H^+)(C_2H_5O^-) = 7.28 \times 10^{-20}$; $(C_2H_5O^-) = 0.02$, hence $(C_2H_5OH \cdot H^+) = (7.28 \times 10^{-20})/0.02 = 3.64 \times 10^{-18}$; $pK = -\log(C_2H_5OH \cdot H^+) = 17.4$.

[27] M. Kilpatrick, *Chem. Revs.*, **30**, 159 (1942).

[28] J. J. Lingane and H. A. Laitinen, *Ind. Eng. Chem., Anal. Ed.*, **11**, 504 (1939).

[29] H. A. Laitinen, *ibid.*, **13**, 393 (1941).

each case a preliminary diffusion period of 5 to 10 hours preceded introduction of a fresh solution in compartment B for a diffusion experiment. The initial concentration c_0 in compartment A was 5×10^{-4} molar.

To determine the cell constant for work with ethanol solutions 2×10^{-4} *M* maleic acid was examined at *pK* 1 (0.05 *M* perchloric acid). The wave height obtained indicated a diffusion current of 1.10 microamperes and a two-electron reduction; it was approximately one-half the wave obtained under like conditions for *m*-nitroacetanilide. Calculation of *D* for *m*-nitroacetanilide from the Ilkovic equation[8] with $n = 4$ yields the result 0.66×10^{-5} cm.^{2} sec.$^{-1}$ at *pK* 8. From the value of *KD* for *m*-nitroacetanilide at 24° the cell constant was calculated to be $K = 0.50$.

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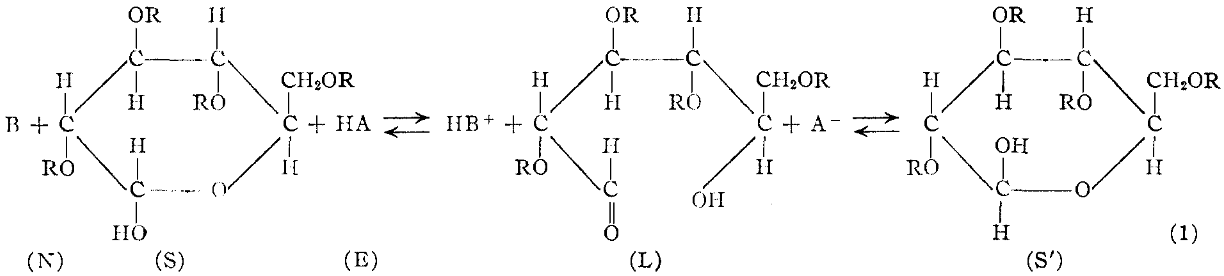
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Concerted Displacement Reactions. VII. The Mechanism of Acid–Base Catalysis in Non-aqueous Solvents[1]

BY C. GARDNER SWAIN AND JOHN F. BROWN, JR.

The mutarotation of α-D-tetramethylglucose (S) catalyzed by phenol–pyridine or other acid (E)-base (N) mixtures in benzene solution is first order in N, first order in S, and first order in E, hence third order over-all. This kinetics requires what we previously defined as a "concerted" mechanism. This involves no intermediate in which the sugar has either gained or lost a proton. A proton must be gained from the acid (E) only *in the same step* that proton transfer to the base (N) occurs, and this gives the aldehyde (L) directly.

The mutarotation of sugars is a convenient model reaction for studies of homogeneous catalysis. Previous studies have demonstrated that the rate-determining step is the formation of the free aldehyde (L), which then rapidly recyclizes[2,3]; that catalysis is general with respect to both acids and bases[4,5]; and that both a base (B) and an acid (HA) must be present in order for the reaction to proceed.[5,6]



(1)

Equation 1 represents the mutarotation of α-D-glucose or α-D-tetramethylglucose (S) to the β-D-isomer (S′). We choose the symbols N, S and E because the base is a nucleophilic reagent, the compound undergoing displacement is the substrate, and the acid is an electrophilic reagent. The open-chain aldehyde intermediate is much less stable than S or S′, and rapidly cyclizes partly back to S and partly to S′. Hence, the rate constant measured experimentally is proportional to the rate constant for the rate-determining step S → L.

There are, however, two different viewpoints as to the manner in which the proton transfers occur. One[6,7] holds that there is a *concerted* attack of the acid and the base (two separate molecules) upon the sugar to give L directly; the other, first stated in its present form by Pedersen,[8] holds that the proton transfers occur *successively*, so that either the conjugate acid (cation) or the conjugate base (anion) of the sugar (S) is an intermediate in the conversion S → L.

Our recent independent measurements of the complexing of pyridine and phenol in benzene solution[9] permit us to correct for the association and complexing phenomena involved when pyridine and phenol are used as catalysts for the mutarotation of tetramethylglucose, and to distinguish between these two viewpoints for the first time.

Results.—The mutarotation of α-D-tetramethylglucose (S) catalyzed by monofunctional acids (E) and monofunctional bases (N) in benzene solution at 25° is third order. The measured rate constant is

$$k_1 = \Sigma k_3[\mathrm{N}]\,[\mathrm{E}] \qquad (2)$$

This is the first time that third-order kinetics has been proved for the mutarotation of a sugar in an inert solvent.

If any form of the Pedersen mechanism[8] were valid, different kinetics would result. Let the conjugate base of L be represented by J^- (let $\mathrm{L} = \mathrm{HJ}$).

$$\mathrm{B} + \mathrm{HA} \overset{K_3}{\rightleftarrows} \mathrm{HB}^+ + \mathrm{A}^- \qquad (3)$$

$$\mathrm{S} + \mathrm{HA} \overset{K_4}{\rightleftarrows} \mathrm{HS}^+ + \mathrm{A}^-;\ K_4 \ll K_3 \text{ or } 1 \qquad (4)$$

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(1) For previous papers see *Record of Chemical Progress*, **12**, 21 (1951); THIS JOURNAL, **73**, 2813 (1951). For more complete experimental data related to this paper and Paper VIII, see J. F. Brown, Jr., Ph.D. Thesis, M. I. T., July, 1950.

(2) T. M. Lowry, *J. Chem. Soc.*, **127**, 1383 (1925).

(3) H. Fredenhagen and K. F. Bonhoeffer, *Z. physik. Chem.*, **181**, 392 (1938); K. Goto and T. Titani, *Bull. Chem. Soc. Japan*, **16**, 403 (1941); K. Wiesner, *Coll. Czech. Chem. Comm.*, **12**, **64** (1947).

(4) J. N. Brönsted and E. A. Guggenheim, THIS JOURNAL, **49**, 2554 (1927).

(5) T. M. Lowry and G. F. Smith, *J. Chem. Soc.*, 2539 (1927).

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(7) C. G. Swain, THIS JOURNAL, **72**, 4578 (1950).

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