

265. *The Polarography of Quinoline Derivatives. Part VIII.¹ The Reduction Waves of Certain 8-Substituted Quinaldines and Quinaldinic Acids.*

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The polarography of (a) quinaldine and of its 8-amino-, 8-chloro-, 8-hydroxy-, 8-methoxy-, 8-methyl-, and 8-nitro-derivatives, and (b) 8-hydroxy-, 8-methoxy-, 8-methyl-, and 8-nitro-quinaldinic acid, in buffered solutions of constant ionic strength, covering the approximate pH range 2—12, has been examined. The quinaldines give large maxima in acid solutions; in the pH range 7.5—12, all exhibit a wave that corresponds to a one-electron reduction of the quinoline ring system. Waves attributable to a 2-electron reduction of the ring system of the quinaldinic acid derivatives are measurable over the entire pH range examined. A wave presumed due to the reduction of the undissociated acid species persists in alkaline solutions and appears to be kinetically controlled in such solutions. An essentially linear relationship exists between the half-wave potentials of the 8-substituted quinaldines (at a fixed pH in the range 8—11), or of the 8-substituted quinaldinate ions (at pH 12), and the Hammett *para* sigma constants of the substituents.

A POLAROGRAPHIC study has shown that the order of increasing (negative) half-wave potentials of the anions of the isomeric quinolinemonocarboxylic acids is essentially the order of increasing electron densities at the points of attachment of the carboxylate group.¹ The study of disubstituted quinolines should yield further information concerning the relationship of half-wave potential to the nature and position of the substituent groups. In this connection, compounds of the type A'-X:A''-Y-quinoline, where A' and A'' are specified ring positions, X is a substituent common to the whole family, and Y is a variable substituent, should be useful. The related families of 8-substituted quinaldines and 8-substituted quinaldinic acids (A' = 2, A'' = 8, X = CH₃ or CO₂H) were selected for examination. Some members can precipitate metal ions and are potential analytical reagents.

As in previous studies,¹ deoxygenated well-buffered solutions of constant ionic strength were used to cover a pH range of about 2—12.

EXPERIMENTAL

Apparatus.—Apparatus and techniques were generally as described previously, but each run was made at an essentially constant room temperature within the range 22—26°. On open circuit in 0.5M-potassium chloride at 25° and with a mercury head of 45 cm., the characteristics of the dropping-mercury electrode were $m = 1.47$ mg. sec.⁻¹, $t = 4.1$ sec. In cases where a maximum occurred, the limiting current was measured on the plateau that followed the maximum. All potentials are with reference to the saturated calomel electrode.

Reagents.—8-Methoxyquinaldine, m. p. 125° (lit.,² 125°), 8-methylquinaldine, 8-hydroxyquinaldinic acid, m. p. 216—217° (lit.,² 211°), 8-methoxyquinaldinic acid, m. p. 160—161° (lit.,² 158—159°), and 8-methylquinaldinic acid, m. p. 135—136° (lit.,³ 132°), were prepared by the methods of Irving and Pinnington.² 8-Chloroquinaldine, m. p. 65—67° (lit.,⁴ 64°), was synthesized by the method of Bartow and McCollum.⁴ 8-Nitroquinaldine, m. p. 140—141° (lit. 129—131°,⁵ 137°⁶), was prepared by the method of Al'perovich *et al.*⁶ 8-Aminoquinoline, m. p. 54—55° (lit.,⁵ 57—58°), and 8-nitroquinaldinic acid, m. p. 174—176° (lit.,⁵ 180—181°), were made from 8-nitroquinaldine by the methods of Roth and Erlermeyer.⁵ 8-Hydroxyquinaldine, m. p. 73—74° (lit.,⁷ 74°), and quinaldine were purchased.

¹ Part VII, J. T. Stock, T. R. Williams, and F. J. Pinchin, *J.*, 1960, 3221.

² H. Irving and A. R. Pinnington, *J.*, 1954, 3782.

³ W. Mathes and W. Sauermilch, *Ber.*, 1954, 87, 1179.

⁴ E. Bartow and E. V. McCollum, *J. Amer. Chem. Soc.*, 1904, 26, 703.

⁵ R. Roth and H. Erlermeyer, *Helv. Chim. Acta*, 1954, 37, 1064.

⁶ M. A. Al'perovich, I. K. Ushenko, and L. N. Tyurina, *J. Gen. Chem., U.S.S.R.*, 1959, 29, 3384.

⁷ R. G. W. Hollingshead, "Oxine and its Derivatives," Butterworths, London, 1956, Vol. 3, p. 758.

Buffer solutions of ionic strength $0.5M$ ⁸ were checked polarographically for the absence of reducible impurities. Except in current-concentration studies, the solutions were $0.2mm$ with respect to the selected quinoline compound.

RESULTS

General Observations.—Quinaldine and its substitution products all give a large polarographic maximum in acid solutions. The maximum, probably due to catalytic hydrogen-ion discharge, becomes smaller as the pH is raised, and is not detectable at a pH greater than 9. Although the peak current is obtained at a potential that varies with the compound being examined, this potential is essentially independent of pH. The addition of gelatin, even at concentrations great enough to cause wave distortion or suppression, does not eliminate the maximum. With the exception of 8-nitroquinaldine, further examination was restricted to the pH range 7.5–12.

Any maxima given by the four 8-substituted quinaldine acids are minor. Measurable polarograms are obtained over the entire pH range 2–12. The half-wave potentials are generally much less negative than those of the corresponding quinaldines.

Quinaldine.—In alkaline solutions, quinaldine gives a single wave. Increase of pH causes the limiting current constant I_1 ($I_1 = i_{lim}/Cm^{2/3}t^{1/6}$, where the terms have their usual significance) to decrease and the half-wave potential to become more negative (Table 1).

8-Methoxy- and 8-Methylquinaldine.—The polarographic behaviour of these derivatives is generally similar to that of the parent compound (Table 1).

TABLE I.

Half-wave potentials (1st line) and limiting current constants (2nd line) of quinaldines.								
pH		7.8	8.4	8.8	9.2	9.7	10.6	11.8
Quinaldine	{	-1.20	-1.25	-1.29	-1.33	-1.45	-1.55	-1.60
		2.25	2.09	1.61	1.61	1.46	0.98	0.98
8-Methoxyquinaldine	{	-1.19 ^a	-1.23	-1.21	-1.28	-1.41	-1.53	-1.61
		2.22 ^a	2.22	1.86	1.44	1.28	0.48	0.33
8-Methylquinaldine	{	-1.15	-1.19	-1.21 ^b	-1.22	-1.28 ^c	-1.56 ^j	-1.60
		1.44	1.44	1.60 ^b	1.28	1.12 ^c	1.00 ^j	0.84
8-Aminoquinoline	{	(-1.34)	(-1.35)	(-1.39)	-1.43 ^c	-1.53 ^g	-1.60	-1.61 ^k
		1.12	1.12	1.44	1.02 ^c	0.81 ^g	0.59	0.50 ^k
8-Hydroxyquinaldine	{	-1.26	-1.32	-1.36	-1.39	-1.46 ^g	-1.56 ⁱ	-1.62
		2.24	2.40	1.92	1.61	1.77 ^g	2.26 ⁱ	1.97 ⁱ
8-Chloroquinaldine	{ A ...	(-1.15)	(-1.18)	-1.22	-1.25 ^c	-1.30	-1.34 ^h	-1.36
		1.60	1.44	1.28	1.28 ^c	1.12	0.80 ^h	0.16 ^l
	{ B ...	-1.71	-1.69	-1.71	-1.70	-1.70	-1.70	-1.70
		1.96	1.97	1.97	2.28	2.62	2.62	2.95
8-Nitroquinaldine	{ A ...				See text			
	{ B ...	-0.98	-1.10	-1.13	-1.17 ^d	-1.17 ^f	-1.17	-1.16 ^l
		1.25	1.88	2.20	1.88 ^d	1.41 ^f	1.09	0.63 ^l

^a pH 7.9; ^b pH 8.9; ^c pH 9.1; ^d pH 9.3; ^e pH 9.5; ^f pH 9.8; ^g pH 9.9; ^h pH 10.5; ⁱ pH 10.7; ^j pH 10.9; ^k pH 11.6; ^l pH 11.7.

8-Aminoquinaldine.—This compound exhibits a maximum that is large at a pH as great as 8, and is still detectable at pH 8.8. For solutions of pH less than 9, the half-wave potentials for 8-aminoquinaldine in Table 1 are estimated ones.

8-Hydroxyquinaldine.—The polarography of 8-hydroxyquinaldine in Britton-Robinson buffers has been reported by Fernando and Phillips.⁹ These workers found that the half-wave potential ($E_{1/2}$) follows the relationship $-E_{1/2} = 0.59 + 0.084$ pH. The present work (Table 1) indicates the relationship to be $-E_{1/2} = 0.53 + 0.094$ pH. Corsini and Graham¹⁰ claim that the waves obtained in solutions of pH less than 11 are complex and resist analysis. These workers state that the relationship $-E_{1/2} = 0.98 + 0.061$ pH holds, at least over the pH range

⁸ J. T. Stock, *J.*, 1957, 4532.

⁹ Q. Fernando and J. P. Phillips, *J. Amer. Chem. Soc.*, 1952, **74**, 3103.

¹⁰ A. Corsini and R. P. Graham, *Canad. J. Chem.*, 1963, **41**, 1636.

11.2—14.2. The large value of I_1 in strongly alkaline solutions differentiates 8-hydroxyquinaldine from quinaldine and its 8-methoxy-, 8-methyl-, or 8-amino-derivatives (Table 1).

8-Chloroquinaldine.—This compound gives two waves, the first, A, being similar to that given by the other quinaldines. A pronounced maximum is visible when the pH is less than about 8. The half-wave potential of the second wave, B, is independent of pH (Table 1).

8-Nitroquinaldine.—This compound gives two waves over the pH range 2—12. The first wave, A, is well formed, has $I_1 = 7.1 \pm 0.4 \mu\text{A}$, and its half-wave potential is given by $-E_{\frac{1}{2}} = -0.04 + 0.058 \text{ pH}$. The second wave, B, carries a pronounced maximum when the solution is acid. Under alkaline conditions, wave B is similar to the single wave obtained with most of the other quinaldines (Table 1).

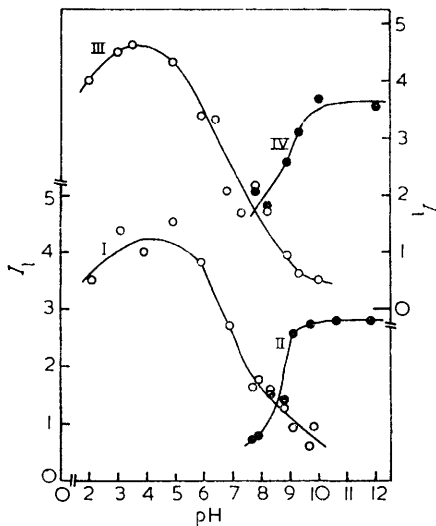


FIG. 1.

FIG. 1. Limiting current constant-pH relations for 8-methoxy- and 8-methylquinaldinic acid.

Curve I, left ordinate, 8-methoxyquinaldinic acid, wave A; II, wave B; III, right ordinate, 8-methylquinaldinic acid, wave A; IV, wave B.

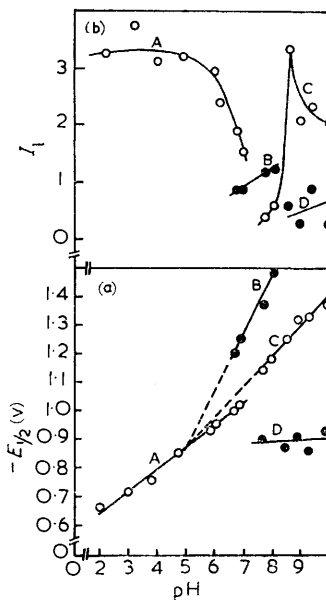


FIG. 2.

FIG. 2 Half-wave potential-pH (a) and limiting current constant-pH (b) relations for 8-hydroxyquinaldinic acid.

8-Methoxy- and 8-Methyl-quinaldinic Acid.—These compounds show close polarographic similarity. In each case, three waves can be detected. Wave A, visible when the pH does not exceed 10, obeys the relationship $-E_{\frac{1}{2}} = 0.45 + 0.074 \text{ pH}$ (methoxy) or $-E_{\frac{1}{2}} = 0.050 + 0.066 \text{ pH}$ (methyl). Measurable in the pH range 8—12, the second wave, B, has $-E_{\frac{1}{2}} = 1.59 \pm 0.01 \text{ v}$ (methoxy) or $-E_{\frac{1}{2}} = 1.62 \pm 0.01 \text{ v}$ (methyl). In the approximate range pH 6.5—8, wave B carries a small prewave C that has $-E_{\frac{1}{2}} = 1.30 \pm 0.02 \text{ v}$ (methoxy) or $-E_{\frac{1}{2}} = 1.28 \pm 0.01 \text{ v}$ (methyl). The variation with pH of the values of I_1 for waves A and B is shown in Fig. 1. In approximately neutral solutions, an increase in the mercury head increases the heights of waves A and B. At pH 10, the height of wave A, but not that of wave B, is independent of this head.¹¹

8-Hydroxyquinaldinic Acid.—In acid solutions, 8-hydroxyquinaldinic acid gives a single wave A, for which the relationship $-E_{\frac{1}{2}} = 0.51 + 0.077 \text{ pH}$ holds over the pH range 2.0—6.8. In a solution of pH 4.5, the limiting current measured at a potential of -1.15 v is proportional to the concentration of hydroxyquinaldinic acid. Although not greatly affected by pH change within the limits pH 2—5, the limiting current decreases rapidly as the pH is raised above 6.

¹¹ W. R. Turner, Ph.D. Thesis, The University of Connecticut, 1964.

Except near pH 7, a second wave, B, can be distinguished within the pH range 6.6—7.9. The third and fourth waves, C and D, respectively, are visible when the pH is at least 7.6. Although all four waves presumably coexist when the pH is near 7, they cannot be separately identified under these conditions. When measured at a potential of -1.40 v, the total current of the composite wave obtained in 0.5M-ammonium acetate (pH 7.0) increases linearly with the concentration of hydroxyquinaldinic acid. The dependence on pH of $E_{1/2}$ and I_1 for the various waves is shown in Fig. 2. Two waves, visible in a solution of pH 12, have $-E_{1/2} = 1.37$ and 1.76 v, respectively, and $I_1 = 0.80$ and $1.17 \mu\text{A}$, respectively.

8-Nitroquinaldinic Acid.—This compound gives three waves. Wave A, measurable over the range 2—12, has $-E_{1/2} = -0.04 + 0.050$ pH. Wave B, which cannot be detected when the pH exceeds 9, has $-E_{1/2} = 0.22 + 0.086$ pH. This wave is difficult to measure, especially in acid solutions. Here the wave tends to merge into a third wave C, which can be distinguished over the pH range 2—12. When the pH does not exceed 7, the relationship $-E_{1/2} = 0.45 + 0.10$ pH holds for wave C. In the pH range 8—10, $-E_{1/2} = 1.30 \pm 0.05$ v for this wave. The effect of pH change on the I_1 values for the various waves is shown by Table 2.

TABLE 2.

Limiting current constants of 8-nitroquinaldinic acid.										
pH	2.1	3.1	3.9	5.0	5.9	6.9	7.9	8.9	9.9	12.0
Wave A	6.25	6.87	6.87	5.93	5.63	5.00	6.25	6.25	5.93	6.57
„ B	—	0.62	0.94	—	1.00	1.88	1.25	0.94	—	—
„ C	2.25	3.75	3.75	4.68	2.50	1.25	0.96	1.60	2.23	1.27

DISCUSSION

Quinaldines.—If the waves are diffusion-controlled and the diffusion coefficients of the various species are each assumed to be 8×10^{-6} , the value calculated for quinaldine acid,¹² n , the uptake of electrons per molecule, can be calculated for each fully-developed wave.¹³ Except where indicated, the results given in Table 3 are for the average values of I_1 over the pH range 7.8—10.

TABLE 3.

Electron uptake in the reduction of quinaldines.							
Compound...	Quinaldine	8-Methoxy-	8-Methyl-	8-Amino	8-Hydroxy	8-Chloro	8-Nitro
n	1.0	1.0	0.8	0.6	1.1	0.8 (A) 1.2 (B)	1.0 (B) 4.1 (A) *

* Average for pH 2—12.

Wave A of 8-nitroquinaldine has properties attributable to the reduction of a nitro-group.¹⁴ Wave B of this compound, wave A of 8-chloroquinaldine, and the single waves given by the other quinaldines, are attributed to the one-electron reduction of the heterocyclic ring.¹⁵ The sum of the limiting current constants of 8-chloroquinaldine indicates that the overall reduction involves 2 electrons per molecule. Hydrogen ion is presumably involved directly in the electrode reaction associated with wave A, but not in that associated with wave B.

Regarded as a nucleophilic attack by an electron on the quinoline ring system, the reduction of a substituted quinaldine should be facilitated by an electron-withdrawing substituent, and made more difficult by a substituent that is electron-releasing. When measured at a fixed pH value in the range 8—12, the half-wave potentials of the compounds (except of quinaldine itself) fall generally in the expected order. Fig. 3 shows the approximately linear relationship that exists between half-wave potential and the Hammett *para*-sigma constant of the substituent group.¹⁶⁻¹⁸

¹² J. T. Stock, *J.*, 1944, 427.

¹³ I. M. Kolthoff and J. J. Lingane, "Polarography," Interscience, New York, 1952, 2nd edn., Vol. 1, ch. III and IV.

¹⁴ Ref. 13, Vol. 2, ch. XLII.

¹⁵ J. T. Stock, *Proc. 1st Internat. Polarographic Congr.*, Prague, 1951, 371.

¹⁶ L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 184.

¹⁷ H. H. Jaffé, *Chem. Rev.*, 1953, 53, 191.

¹⁸ P. Zuman in "Advances in Polarography," ed. Longmuir, Pergamon, New York, 1960, Vol. 3, p. 812.

Quinaldinic Acids.—As in the case of quinaldinic acid itself,¹² the overall reduction of 8-methoxy- and 8-methyl-quinaldinic acid occurs with the uptake of 2 electrons per molecule. Since pH increase causes the height of wave A to diminish as that of wave B increases, these two waves are probably attributable to the reduction of the acid and of its anion respectively.¹⁹ If the waves are diffusion-controlled and the diffusion coefficient of an acid does not differ greatly from that of the acid anion, the apparent ionization constant K'_a can be estimated from the relationship $pK'_a \sim Q$, where Q is the pH at which waves A and B have the same I_1 value. Inspection of Fig. 1 gives 8.6 and 7.8 as the pK'_a values for 8-methoxy- and 8-methylquinaldinic acid, respectively. These values are about 3 units greater than expected for compounds closely related to quinaldinic acid (actual ionization constant $\sim 10^{-5}$).²⁰ The difference is attributed to the kinetically-controlled

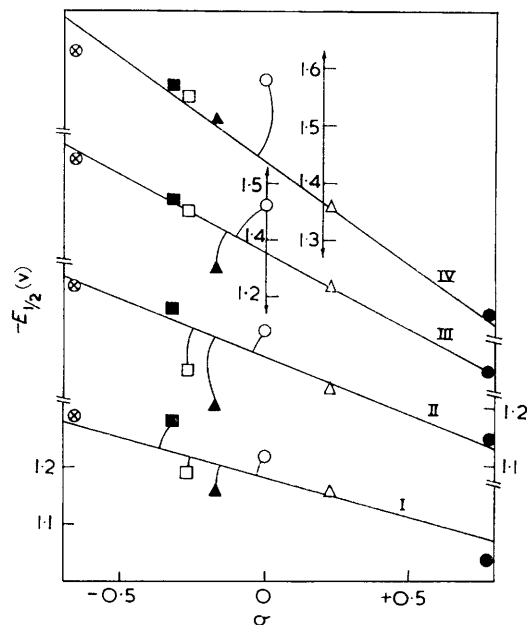


FIG. 3. Half-wave potential-Hammett sigma constant relations for quinaldines. Curve I, left ordinate, pH 8; II, right ordinate, pH 9; III, left-centre ordinate, pH 10; IV, right-centre ordinate, pH 11. 8-position groups:

- NO₂; △ Cl; ○ H; ▲ CH₃;
- OCH₃; ■ OH; ⊗ NH₂

formation of additional acid from the anion at the surface of the mercury drop.¹⁹ The invariance of the height of wave A with changing mercury head when the pH is 10 is indicative of the essentially kinetic nature of this wave under these conditions.

The overall reduction of 8-hydroxyquinaldinic acid appears to involve 2 electrons per molecule. Constant-potential coulometry⁸ supports this conclusion. When the pH is low, the behaviour of the hydroxyquinaldinic acid is similar to that of the 8-methoxy- and 8-methyl-compounds. Under alkaline conditions, the 8-methoxy- and 8-methyl-compounds each give a principal wave B that has a pH-independent half-wave potential. The half-wave potential of the analogous principal wave C of 8-hydroxyquinaldinic acid is markedly pH dependent. In view of the presence in 8-hydroxyquinaldinic acid of an additional ionizable and hydrogen-bonding group (hydroxyl), the polarography of 8-hydroxyquinaldinic acid is unlikely to resemble closely that of the other quinoline derivatives.

The properties of wave A of 8-nitroquinaldine are almost the same as those of wave A of 8-nitroquinaldine. Averaged over the pH range 2—10, the sum of the I_1 values of waves B and C is consistent with an uptake of 2 electrons per molecule of this compound.

If the half-wave potentials, at a pH of 12, of quinaldinic acid¹² and these four

¹⁹ I. M. Kolthoff and J. J. Lingane, Ref. 13, Vol. 1, pp. 268—276.

²⁰ "Stability Constants," Chemical Society, London, 1957, Pt. 1, p. 73.

8-substituted derivatives are plotted against the Hammett *para*-sigma constants of the substituent groups, the points lie reasonably about a straight line. The point for 8-hydroxyquinaldinic acid shows the greatest deviation.

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