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A POLAROGRAPHIC STUDY OF NITRO COMPOUNDS

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Received November 18, 1954

In order to verify the structures of a group of substituted 4-nitro-5-phenylcyclohexenes and to determine if certain derivatives caused any steric hindrance to the nitro group, a polarographic study of these compounds was initiated. Since no literature exists on the behavior of cyclo aliphatic nitro compounds at the dropping mercury electrode, it was of interest also to compare their behavior with simple aliphatic and aromatic nitro compounds.

De Vries and Ivett (1) made a polarographic study of six aliphatic nitro compounds with the expectation of developing an analytical method for these compounds. They found that the half-wave potentials were very similar for all six compounds and that the diffusion currents were proportional to concentration if 0.05 *M* sulfuric acid was the supporting electrolyte. However, this proportionality did not hold in 0.05 *M* sodium sulfate. They attributed this non-linearity to the partial conversion of the nitro compound to the non-reducible *aci*-form in the neutral background.

Petru (2) reported more fully on the polarographic behavior of four nitroparaffins and showed that these compounds undergo a four electron irreversible reduction to the hydroxylamine at the dropping mercury electrode. Over a limited *p*H range, a second wave, which is attributed to the more irreversible reduction of the hydroxylamine to the alkylamine, was observed. At *p*H 10.38, a gradual decrease with time was observed in the nitro wave until a constant small diffusion current was reached. This small diffusion current was assigned to the equilibrium state between the reducible nitro compound and the non-reducible anion or *aci*-form which existed at the *p*H used. The rates of conversion of nitroparaffins and the positions of the equilibria were studied rather thoroughly by Miller, *et al.* (3).

Many investigations on the polarographic behavior of aromatic nitro compounds have been reported. Most of these compounds show two irreversible waves of four and two electrons, respectively, over a limited *p*H range. The half-wave potentials are quite sensitive to the alcohol content and to the concentration of maximum suppressor used in the supporting solution. The position of the hydroxyl group in relation to the nitro group in the nitrophenols has been shown to affect very appreciably the products of these electro chemical changes at the dropping mercury electrode (4, 5).

EXPERIMENTAL

All polarographic measurements were made with a Leeds and Northrup Type E Electrochemograph using a saturated calomel electrode as the reference electrode in all cases. The dropping mercury electrode had a drop time of 3.90 seconds in 0.1 *N* potassium chloride at 0.00 volts applied and delivered 1.30 mg. of mercury per second at the pressure of mercury used throughout this investigation. All polarographic measurements were made at 25° ± 0.1°.

Buffers having *p*H's of 2.88, 4.99, and 6.94, respectively, were prepared by adjusting solutions of dibasic sodium phosphate and citric acid with sodium hydroxide to approximately the desired *p*H. Sufficient 95% ethanol and water were added to make the buffer 25% by volume in alcohol and 0.2 *M* in both phosphate and citrate. The *p*H of the final buffer solution then was measured. Buffers of *p*H 10.52 and 12.2 were prepared in the same way so that the final solutions contained 25% by volume ethanol and were 0.2 *M* in glycine and 0.2 *M* in citrate. All *p*H measurements were made with a Number 7664 Leeds and Northrup *p*H meter.

The nitromethane and nitrobenzene were reagent grade chemicals but were redistilled before they were used. Most of nitrocyclohexane derivatives were prepared in the course of earlier research (6–8).

3-Ethyl-4-nitro-5-phenylcyclohexene (II). A Pyrex bomb was charged with 2.98 g. (0.02 mole) of β-nitrostyrene, 1.64 g. of hexadiene-1,3 (9), 1 ml. of dry thiophene-free benzene, and a trace of hydroquinone. The bomb was sealed and heated at 130° for 24 hours. The bomb contents were concentrated in a stream of nitrogen to give 4.5 g. of brown oil. The oil was dissolved in 15 ml. of benzene-petroleum ether (2:1) and chromatographed on 30 g. of alumina. Elution with benzene-petroleum ether (1:1) gave a colorless oil that crystallized upon trituration with ethanol to afford 0.642 g. of colorless needles, m.p. 88–89°. Two recrystallizations from ethanol raised the melting point to 93–95°. Although this material was analytically pure, the melting point was raised to a constant value of 99.5–100.5° upon rechromatographing the lower melting solid. The over-all yield of II, m.p. 99.5–100.5°, was 7.3%.

Anal. Calc'd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06.

Found: C, 72.68; H, 7.50; N, 6.09.

3-Ethyl-5-(3-methoxyphenyl)-4-nitrocyclohexene (V). A Pyrex bomb was charged with 9.26 g. of *m*-methoxy-β-nitrostyrene, 10.0 g. (0.12 mole) of freshly distilled hexadiene-1,3 (b.p. 72–74°), 20 ml. of benzene, and a trace of hydroquinone. The bomb was cooled in a Dry Ice-acetone bath, evacuated to approximately 50 mm. of mercury, and then flushed with nitrogen. This process was repeated three times, the last time filling the bomb with nitrogen to a pressure of about 20 mm. less than atmospheric pressure. It then was sealed and heated at 100–110° for 65 hours. The contents of the bomb were treated as before to yield 5.78 g. (43%) of white crystals, m.p. 47–59°, which consisted of a mixture of Va and Vb. Fractional crystallization of 10.55 g. of this mixture from methanol gave 4.54 g. of Va, m.p. 76–78°, and 3.64 g. of Vb, m.p. 54–58°.

A sample of Va was recrystallized three times from methanol to give flat, rectangular prisms, m.p. 80–81°. When this material was chromatographed on alumina, only non-crystalline oils were obtained. Hydroxylation (*vide infra*) of this material gave a mixture of products, m.p. 138–148°, that could not be separated into pure components.

Anal. Calc'd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36.

Found: C, 69.38; H, 7.29; N, 5.22.

Recrystallization of Vb from petroleum ether gave colorless rhombs, m.p. 56–58°.

Anal. Calc'd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36.

Found: C, 69.21; H, 7.36; N, 4.98.

3-Ethyl-5-(3-methoxyphenyl)-4-nitro-1,2-cyclohexanediol (VII). By the procedure of Wildman and Norton (8), 1.34 g. of Vb, m.p. 56–58°, gave a 42% yield of VII, m.p. 132–134°. The material was recrystallized once from chloroform and once from water for analysis, m.p. 137.5–139°.

Anal. Calc'd for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74.

Found: C, 61.30; H, 6.94; N, 4.54.

The compound formed a pure dibenzoate in 77% yield, m.p. 163–164°.

A 0.0100 *M* solution of the nitro compound to be studied was prepared in 95% ethanol. The solutions for the polarographic measurements were made by pipetting 2.50 ml. of the

0.0100 M solution of the nitro compound into a 50 ml. volumetric flask, adding 0.05 ml. of 1% methyl cellulose, and then diluting to volume with the appropriate buffer. The resulting solution, which was 5.00×10^{-4} M in the nitro compound and contained 27.3% by volume of ethanol, was transferred to a thermostated polarographic cell and deaerated with a stream of nitrogen. The nitrogen was passed through an aqueous solution containing 27.3% ethanol before it entered the polarographic cell. The polarographic behavior of the compounds were thus recorded under identical experimental conditions of pH, alcohol content and concentration.

Due to limited solubility of some of the nitro compounds in the 27.3% by volume ethanol, it was necessary to compare the polarographic behavior of these compounds in solutions containing more ethanol. The solutions for these polarograms were prepared by diluting 1.0 ml. of the 0.01 M solution of the nitro compound with 5.0 ml. of ethanol and then with sufficient buffer to make 25.0 ml. Since the alcohol content was 36.8% by volume in these cases, no intercomparison was made between these results and those obtained from the lower alcohol content.

For the kinetic studies, the buffer of pH 12.2 and the nitro solutions were deaerated separately. As soon as the two solutions were mixed, the time of standing was recorded and a polarogram of the solution was recorded as soon as possible. The decrease in the diffusion current was followed at timed intervals.

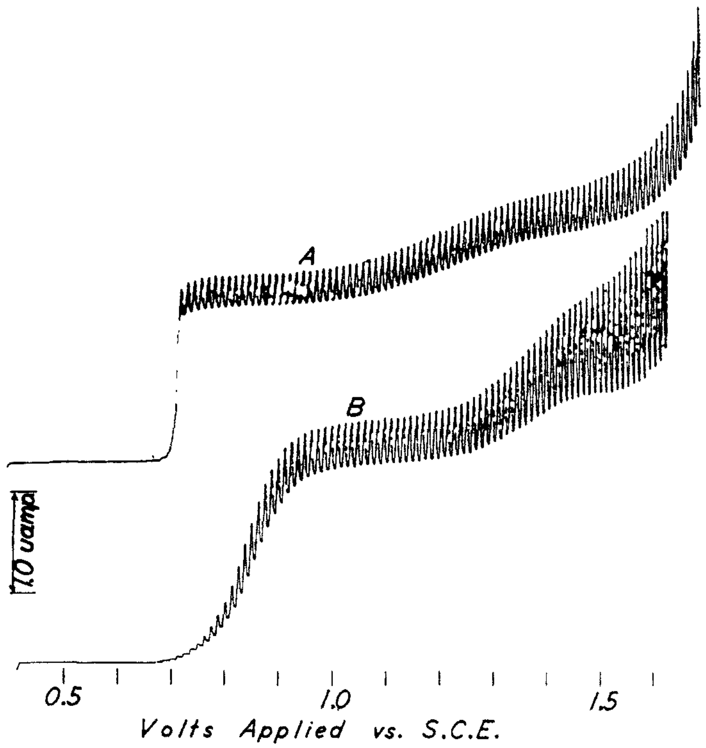


FIG. 1. CURVE A IS POLAROGRAM FROM 5-(4-METHOXYPHENYL)-4-NITROCYCLOHEXENE (Compound IV) in 27.3% by volume ethanol at pH 4.99. Curve B is polarogram from 5-(3-methoxyphenyl)-4-nitro-1,2-cyclohexanediol (Compound VI) in 27.3% by volume ethanol at pH 4.99.

RESULTS

A polarogram which is typical for the reduction in slightly acid solution of all 4-nitro-5-phenylcyclohexenes that did not contain hydroxyl groups is shown as Curve A in Figure 1. It is apparent that this compound at *p*H 4.99 shows two waves and undergoes two electrochemical reductions at the dropping mercury electrode. This polarographic behavior is quite similar to that previously reported for nitroparaffins and aromatic nitro compounds. It should be noted, however, that the first wave is much too steep for a reversible four electron reduction whereas the second wave is much too "drawn out" for a reversible two electron change. At all the other *p*H's used, only the first wave was observed and was similar in appearance to that shown in Curve A as long as the alcohol content was maintained at 27.3% by volume. When the alcohol was increased to 36.8% by volume, the first wave was less steep and identical to that shown in Curve B.

Curve B in Figure 1 is the polarogram obtained from 5-(3-methoxyphenyl)-

TABLE I

HALF-WAVE POTENTIALS AND DIFFUSION CURRENTS IN 27.3% BY VOLUME ETHANOL

	*p*H							
	2.88		4.99		6.94		10.52	
	$E_{1/2}$	i_d/C	$E_{1/2}$	i_d/C	$E_{1/2}$	i_d/C	$E_{1/2}$	i_d/C
5-(3-Methoxyphenyl)-4-nitrocyclohexene. Compound I	−0.646[x]	6.52	−0.698[x]	6.52	−0.793[x]	6.24	−0.987[x]	6.37
			−1.28[a]	3.38				
5-(4-Methoxyphenyl)-4-nitrocyclohexene. Compound IV	−0.650[x]	6.88	−0.708[x]	6.66	−0.785[x]	6.30	−0.983[x]	6.28
			−1.21[a]	3.10				
3-Ethyl-5-(3-methoxyphenyl)-4-nitrocyclohexene. Compound Va	−0.680[x]	6.03	−0.742[x]	5.95	−0.840[x]	[v]	−1.025[x]	[v]
			−1.18[a]	2.70				
5-(3-Methoxyphenyl)-4-nitro-1,2-cyclohexanediol. Compound VI	−0.785	6.28	−0.850	6.00	−0.890	6.04	−1.023	5.97
			−1.37[a]	2.92				
3-Ethyl-5-(3-methoxyphenyl)-4-nitro-1,2-cyclohexanediol. Compound VII	—	—	−0.864	5.90	−0.933	5.74	−1.08[c]	5.80
			−1.26[a]	2.66				
Nitromethane	−0.884	10.9	−0.896	11.0	−0.913	11.0	−0.988	[N]
Nitrobenzene	−0.304	9.47	−0.465	8.37	−0.500	8.17	−0.782	8.56
	−0.91[a]	4.50	−1.31[a]	4.20				

[x] = Abnormally large slope (See curve A in Fig. 1).

[c] = Ill-defined polarogram.

[N] = The diffusion current is insignificant since the compound was partially in the *aci*-form.

[a] = Second wave.

[v] = Concentration of compound in solution not known due to precipitation of some compound from solution.

TABLE II

HALF-WAVE POTENTIALS AND DIFFUSION CURRENTS IN 36.8% BY VOLUME ETHANOL

	*p*H							
	2.88		4.99		6.94		10.52	
	$E_{1/2}$	i_d/C	$E_{1/2}$	i_d/C	$E_{1/2}$	i_d/C	$E_{1/2}$	i_d/C
5-(4-Methoxyphenyl)-4-nitrocyclohexene. Compound IV	−0.666	6.20	−0.725 −1.26[a]	6.28 3.12	−0.832	6.08	−1.025	6.17
3-Ethyl-5-(3-methoxyphenyl)-4-nitrocyclohexene. Compound Va	−0.694	5.85	−0.750 1.27[a]	5.80 2.78	−0.875	5.88	−1.055	5.78
3-Ethyl-4-nitro-5-phenylcyclohexene. Compound II	−0.684	6.20	−0.770 −1.21[a]	6.20 3.17	−0.887	5.85	−1.067	5.75
3-Methyl-4-nitro-5-phenylcyclohexene. Compound III	−0.705	6.49	−0.770 −1.24[a]	6.30 2.78	−0.881	—	−1.055	6.04

[a] = Second wave.

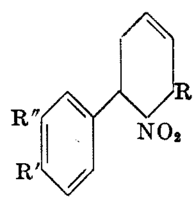
4-nitro-1,2-cyclohexanediol (VI) at *p*H 4.99 and is typical of all polarograms obtained from hydroxyl derivatives of the nitrocyclohexenes with a background containing 27.3% by volume ethanol. The same type of polarograms were obtained from nitromethane and nitrobenzene, except that nitromethane never gave a well defined second wave whereas nitrobenzene shows a second wave over nearly the entire acid region.

The half-wave potentials of 5×10^{-4} M solutions of five different 4-nitro-5-phenylcyclohexenes and of nitromethane and nitrobenzene in 27.3% by volume ethanol in four different buffers are given in Table I. In addition, a value of i_d/C is given for each compound at each *p*H. Similar data for four nitrophenylcyclohexenes in 36.8% ethanol are given in Table II.

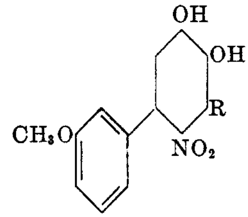
In alkaline solution, the diffusion current of aliphatic nitro compounds decreases with time of standing, and the rate of decrease varies considerably with different nitro compounds. Thus, by following the rate at which the diffusion current decreases with time, it is possible to deduce the rate of the conversion of the nitro compound to its *aci*-form. No previous work has been reported on the rate at which sterically hindered nitro compounds are converted to their corresponding anions, and thus no comparison has been made between such compounds and unhindered nitro compounds.

The rate of conversion to the *aci*-form for each of the 4-nitro-5-phenylcyclohexenes listed in Table I was studied at *p*H 12.2 at 25° in 27.3% by volume ethanol. The rate of conversion for the compounds listed in Table II was also studied at *p*H 12.2 at 25° but in 36.8% by volume ethanol. The results of these kinetic measurements are plotted in Figure 2, and the times required for one-half of each compound to ionize, as well as the rate constants, are tabulated in Table III.

DISCUSSION



Compound I R = H; R′ = H; R″ = OCH_3; m.p. 68–68.5°
Compound II R = C_2H_5; R′ = H; R″ = H; m.p. 99.5–100.5°
Compound III R = CH_3; R′ = H; R″ = H; m.p. 85.5–86.5°
Compound IV R = H; R′ = OCH_3; R″ = H; m.p. 76.5–77.5°
Compound Va R = C_2H_5; R′ = H; R″ = OCH_3; m.p. 80–81°



Compound VI R = H; m.p. 118–118.5°
Compound VII R = C_2H_5; m.p. 137.5–139°

Most nitro compounds yield polarograms similar to that shown in Curve B of Figure 1. However, when media containing 27.3 % by volume alcohol was used, compounds I, IV, and V gave waves whose slopes were much greater than those from similar compounds containing hydroxy groups. However, in 36.8 % by volume ethanol, the polarographic behavior of all compounds was normal. It is believed that this difference in the shape of the polarographic waves in the lower alcohol media is due to an adsorption effect at the dropping mercury electrode, and this prevented valid comparison of the polarographic data. Since at least three of the compounds to be studied were not sufficiently soluble in 27.3 % alcohol, a considerable number of polarograms were made from 36.8 % alcohol where all nitro compounds behaved similarly and thereby permitted comparisons of half-wave potentials to be made.

The reduction of the nitrocyclohexenes at the dropping mercury electrode generally is quite similar to that observed for the nitroparaffins. There is, however, a decidedly greater effect of *p*H on the half-wave potential of the nitrocyclohexenes than found for the simple nitroparaffins.

Compounds II, III, Va, and VII all show more negative half-wave potentials than similar compounds which do not contain a substituent in the 3 position. This is attributed to a blocking action by the alkyl group to the electro chemical reduction of the nitro group. The magnitude of this steric hindrance on the half-wave potential would be expected to be small and was found to vary between 20 and 45 mv. Due to the small differences observed in the half-wave potentials, it probably is impossible by this comparison to distinguish between a methyl and a larger alkyl substitutent adjacent to the nitro group. However, it always is possible to detect the presence of a substituent at this position.

The diffusion currents of the nitrocyclohexenes were as expected—considerably less than nitromethane or nitrobenzene. The accuracy of the diffusion currents of the first wave given in Tables I and II is probably no better than

TABLE III

DATA FROM KINETICS MEASUREMENTS

$pH = 12.2$

	$t_{1/2}$ min.	k(min)$^{-1}$	Ethanol % by Vol.
5-(3-Methoxyphenyl)-4-nitrocyclohexene. Compound I	16	0.043	27.3
5-(4-Methoxyphenyl)-4-nitrocyclohexene. Compound IV	19	.040	27.3
	35	.021	36.8
5-(3-Methoxyphenyl)-4-nitro-1,2-cyclohexanediol. Compound VI	16	.046	27.3
3-Ethyl-4-nitro-5-phenylcyclohexene. Compound II	2160	.00032	36.8
3-Ethyl-5-(3-methoxyphenyl)-4-nitrocyclohexene. Compound Va	75	.0069	36.8
3-Ethyl-5-(3-methoxyphenyl)-4-nitro-1,2-cyclohexanediol. Compound VII	No change	in 48 hours	27.3
3-Methyl-4-nitro-5-phenylcyclohexene. Compound III	123	.0056	36.8

5%, and because of the diffuseness of the second wave, the accuracy of the diffusion currents for this wave is probably less than 5%. Where the second wave was well enough defined for measurement, the ratio of the diffusion currents of the first and second waves was always close to 2 to 1.

Miller, *et al.* (3), studied the kinetics of the conversion of nitroparaffins to the *aci*-form and found that an equilibrium was reached between the *aci* and reducible forms. Furthermore, the rate of attainment of this equilibrium was comparatively rapid—about 30 minutes at *p*H 10. The nitrocyclohexenes show a somewhat different behavior in that if they are converted at all to the *aci*-form, the conversion proceeds much more slowly and apparently to completion. The rate of this change is markedly different for the hindered and unhindered nitro groups but always follows a first order rate equation.

If it is assumed that the nitro group in compounds I, IV, and VI is unhindered, the data in Table III indicate that the rates of conversion of these compounds to the *aci*-form are practically identical. However, when a methyl or ethyl group is present at the 3 position and a phenyl group at the 5 position, the conversion of the nitro group at position 4 is greatly retarded. If the rates of conversion of compounds I, II, and III are compared, it is obvious that the nitro group must be much more hindered in compound III than in I and somewhat more in II than in III. A similar comparison can be made for compounds VI and VII where VII contains the more hindered nitro group. Furthermore, it is possible to show that, in general, the more negative the half-wave potential is over that of the unhindered compound, the more slowly the conversion of the nitro compound occurs. However, the differences in the rates of conversion are much more indicative of the degree of steric hindrance than are the differences in the half-wave potentials. Since the conversion of nitromethane to its unreducible form is instantaneous at *p*H 12.2, the nitro groups of compounds I, IV, and VI must be considered hindered to some extent.

Compound Va does not appear to conform to the above statements. Although the physical constants of the sample would suggest a pure compound, the fact that hydroxylation of Va yields a mixture of cyclohexanediols casts suspicion on its purity. Further evidence for the heterogeneity of Va may be inferred from the results of the catalytic reduction of the olefinic bond. Reduction of an ethanolic solution of Va with palladium catalyst gave neutral material, m.p. 70–92°, which could be only partially purified. Vb affords one pure diol (VII) in 42% yield upon hydroxylation. The remaining organic material from the hydroxylation of Vb is the same mixture of cyclohexanediols as is obtained from Va. The purity of VII can be shown by its polarographic behavior (*vide supra*), as well as the fact that VII gives a pure benzoate derivative and one amine upon catalytic reduction with Raney nickel. The polarographic study of these nitrocyclohexenes should

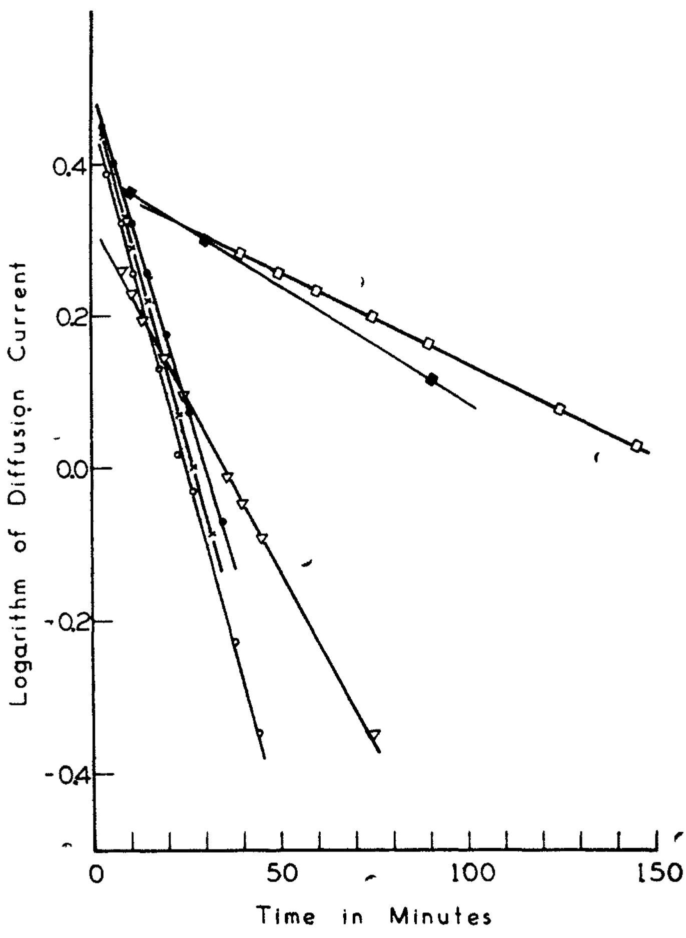


FIG. 2. RATE OF CONVERSION OF NITROPHENYLCYCLOHEXENES TO THEIR *Aci*-FORM. Open circles: Compound VI in 27.3% by volume ethanol. Crosses: Compound I in 27.3% by volume ethanol. Closed Circles: Compound IV in 27.3% by volume ethanol. Triangles: Compound IV in 36.8% by volume ethanol. Closed Squares: Compound Va in 36.8% by volume ethanol. Open Squares: Compound III in 36.8% by volume ethanol.

not only provide information which verifies their structure, but also suggest a method for determining the purity as well. If a compound was not pure, the plot of log of concentration *versus* time as shown in Figure 2 would give a curved line which would result from two or more separate first order reactions which were occurring simultaneously. If Va is taken to be impure, the fact that it gives a straight line plot must mean that one isomer present in the mixture is not converted to its *aci*-form (*e.g.* VII). The rate of conversion of the second isomer in the mixture is such that it probably is a less hindered *cis-trans* isomer of V, although the possibility that it is a position isomer of V (ethyl in the 6-position) can not be ignored.

It should be possible to separate hindered nitrocyclohexenes from the unhindered isomers by treating the mixture with a rather strongly alkaline buffer for an extended period of time and then extracting the solution with an organic solvent. Only the hindered nitro compound would be extracted because the less hindered compound would be in the *aci*-form and therefore would not be soluble.

SUMMARY

A polarographic study of compounds related to 4-nitro-5-phenylcyclohexene is described. The half-wave potentials of 5×10^{-4} *M* solutions in 27.3 % by volume ethanol of five nitrocyclohexenes, nitromethane, and nitrobenzene have been determined at *p*H 2.88, 4.99, 6.94, and 10.52. A value of i_d/C has been found for each compound at each *p*H. Similar data for four of the nitrocyclohexenes in 36.8 % ethano are presented. The rates of conversion of the nitro compounds to the *aci*-form at *p*H 12.2 have been determined.

In general, it has been shown that the half-wave potentials of hindered nitrocyclohexenes are more negative than those of the unhindered derivatives. Steric hinderance appears to be a major factor in the ease of conversion of nitrocyclohexenes to their *aci*-form.

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