A POLAROGRAPHIC INVESTIGATION OF 5-NITROPHENYL-2-FURFURALS AND THEIR DERIVATIVES

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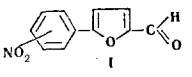
The polarographic behavior in dimethylformamide of the o-, p-, and m-isomers of 5-(nitrophenyl)-2-furfural and their benzoylhydrazones has been studied. These compounds give one one-electron and one three-electron wave of the reduction of the nitro group, the corresponding half-wave potentials being considerably more negative than the half-wave potentials of 5-nitro-2-furfural and the corresponding nitrobenzaldehydes. In the case of 5-(o-nitrophenyl)-2-furfural and its benzoylhydrazone, a hydrogen bond is formed between the nitro group and the furan ring or the amide grouping of the side chain, which leads to a considerable shift in the potentials in the negative direction. Because of the high electroreduction potentials, the benzoylhydrazones of the 5-(o-, p-, and m-nitrophenyl)-2-furfurals have no antibacterial and fungistatic activity.

The polarographic behavior of the 5-(o-, p-, and m-nitrophenyl)-2-furfurals (I) and their benzoylhydrazones (II) [1, 2] is of interest from the point of view of elucidating the ease of addition of an electron to the molecules of these compounds and characterizing some features of their electronic structure, and also for explaining the high antibacterial activity of these compounds.



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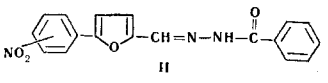


II

We have carried out a study of the electroreduction of these compounds at a dropping mercury electrode (DME) in N, N-dimethylformamide (DMF), in which all these compounds are fairly readily soluble and in which their electroreduction is not complicated by the adsorption of the electroactive substances on the DME; in addition, DMF possesses a high differentiating capacity (in this medium, the half-wave potentials of the nitro group depend strongly on the σ^0 constant of the substituents and the value of the ρ_π constant in the equation $\Delta E_{1/2} = E_{1/2}^X - E_{1/2}^H = \rho \cdot \sigma^0$ exceeds 0.60 V[3]. For comparison, we also recorded under identical conditions the curves of o^-, m^-, and p-nitrobenzaldehydes and their benzoylhydrazones and those of 5-nitro-2-furfural and its benzoylhydrazone and some of the simplest derivatives of 5-(p-nitrophenyl)furan in order to evaluate the conduction of the polar effect of a substituent through the bicyclic system. The half-wave potentials and the limiting currents of all the compounds studied are given in the table.

The influence of the chemical structure is shown particularly on the value of $E_{1/2}$ for the first wave.

In an aprotic medium (DMF), all the nitro compounds studied give two polarographic waves of the reduction of the nitro group, of which the first is a one-electron wave and the second a three-electron wave. The first stage of electroreduction leads to the formation of the corresponding anion radical and the second to the further reduction of the free anion radical to the hydroxylamine derivative [4, 5]. All three 5-(nitrophenyl)-2-furfurals are reduced at considerably more negative potentials than 5-nitro-2-furfural and the corresponding nitrobenzaldehydes. The same

Half-Wave Potentials $E_{1/2}$* and Limiting Currents i_{lim} of the Nitro Derivatives in Dimethylformamide (2×10^{-4} M solution of the depolarizer; support: 0.1 N solution of LiCl)

No.	Name of the compound	First wave		Second wave	
		$-E_{1/2}$, V	i_{lim}, μA	$-E_{1/2}$, V	i_{lim}, μA
1	5-Nitro-2-furfural	0.24	0.4	0.46	0.7
2	o-Nitrobenzaldehyde	0.41	0.9	0.55	2.4
3	m-Nitrobenzaldehyde	0.49	0.5	0.78	1.7
4	p-Nitrobenzaldehyde	0.35	0.5	0.60	0.7
5	5-(o-Nitrophenyl)-2-furfural	0.57	0.5	0.67	1.6
6	5-(m-Nitrophenyl)-2-furfural	0.52	0.5	0.79	2.0
7	5-(p-Nitrophenyl)-2-furfural	0.45	0.6	0.70	1.7
8	5-(p-Nitrophenyl)-2-acetylfuran	0.51	0.4	0.74	1.4
9	5-(p-Nitrophenyl)furan	0.58	0.4	0.87	1.1
10	5-(p-Nitrophenyl)furan-2-carboxylic acid	0.54	0.6	0.82	0.8
11	5-Nitro-2-furfural benzoylhydrazone	0.42	0.4	0.73	1.0
12	o-Nitrobenzaldehyde benzoylhydrazone	0.61	0.6	0.79	1.4
13	m-Nitrobenzaldehyde benzoylhydrazone	0.57	0.5	0.86	1.2
14	p-Nitrobenzaldehyde benzoylhydrazone	0.59	0.5	0.77	1.4
15	5-(o-Nitrophenyl)furfural benzoylhydrazone	0.64	0.5	0.76	1.6
16	5-(m-Nitrophenyl)furfural benzoylhydrazone	0.55	0.4	0.87	1.4
17	5-(p-Nitrophenyl)furfural benzoylhydrazone	0.54	0.4	0.84	1.4

*Relative to the bottom mercury electrode.

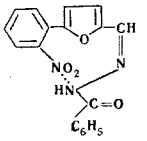
applies to the benzoylhydrazones of these aldehydes as compared with the benzoylhydrazone of 5-nitro-2-furfural and of the nitrobenzaldehydes.

Since the potential of electroreduction is determined by electron density on the nitro group, the influence of any electron-donating groups introduced into the molecule must oppose, and that of any electron-accepting groups facilitate, the electroreduction, and the polar effect of the substituent must be shown more clearly in the o- and p-positions and less clearly in the m-position. Because of this, m-nitrobenzaldehyde is reduced with greater difficulty than the o- and p-isomers by 80–150 mV. In the case of the benzoylhydrazones of m-, p-, and o-nitrobenzaldehydes, because of the opposite effects of the unshared pair on the nitrogen atom and the inclusion of the hydrazone size chain in conjugation, the influence of the substituent $>C = NNHCOPh$ has almost no effect on the potentials of the reduction of the nitro group. The $E_{1/2}$ values of the first wave of all three isomers are approximately the same, although they are considerably more negative than $E_{1/2}$ for the initial nitroaldehydes.

For the first stage of the electroreduction of the series of 2-substituted derivatives of 5-nitrofuran in DMF, the ρ_π constant was found to be $\rho_\pi = 0.60$ V, while the corresponding values of the ρ_π constant for the series of 5-(p-nitrophenyl)furans proved to be 0.18 V. Consequently, the introduction of a phenyl residue decreases the transfer of the polar effect by a factor of 0.30. The numerical value found agrees well with the coefficient of quenching by a bridging phenylene group given in the literature for other reaction series ($a = 0.27 \pm 0.03$) [10].

The considerable shift of $E_{1/2}$ for the first waves of the 5-(nitrophenyl)-2-furfurals to negative values (by 200 mV) in comparison with $E_{1/2}$ for the corresponding nitrobenzaldehydes is explained by the weakening of the transfer of the polar effect of the substituent through the furan ring: the fact that the transfer effect does actually take place is shown by the dissimilar electroreduction potentials of the nitroaldehydes and the benzoylhydrazones corresponding to them and also by the weakening of this transfer for the m-isomer as compared with the p-isomers.

The substantial differences between the half-wave potentials of 5-(o-nitrophenyl)-2-furfural and 5-(p-nitrophenyl)-2-furfural ($\Delta E_{1/2} = 100$ mV) and, particularly, between the $E_{1/2}$ values of the corresponding benzoylhydrazones ($\Delta E_{1/2} = 120$ mV) are particularly remarkable. This shift may be due to the formation of an intramolecular hydrogen bond between the nitro group and the amide grouping of the side chain or the furan ring. The fact that such association takes place is indicated by the low frequencies of the amide carbonyl in the IR spectrum of 5-(o-nitrophenyl-2-furfural benzoylhydrazone (1654 cm^{-1}) as compared with that of the p-isomer (1665 cm^{-1}) [2]. The polarographic results are in favor of the assumption that the amide group is associated with the nitro group and not with the oxygen atom of the furan ring.



The considerable increase in the potentials of the reduction of the benzoylhydrazones of the 5-(nitrophenyl)-2-furfurals as compared with their increase in 5-nitro-2-furfural benzoylhydrazone leads to a substantial lowering of the antibacterial and fungistatic activity of these compounds: the hydrazones of this series exhibit no well-defined activity of any kind. This is connected with the fact noted previously that for the appearance of antibacterial activity in a nitro compound its reduction potential must be within a definite, fairly positive, region of electrode potentials [6, 7].

EXPERIMENTAL

The compounds studied were synthesized by a published method [1, 2] and were purified by repeated crystallization.

All the compounds were polarographed in DMF, which was purified and dried in the following way. Benzene of "pure for analysis" grade was added to DMF (of "pure" grade) in a ratio of 1 : 10 by volume. The benzene–water azeotropic mixture was distilled off at 63–64° C and atmospheric pressure, and then the DMF was distilled in vacuum. The fraction with bp 49° C (18 mm) was taken for further treatment [8]. The DMF obtained was kept over anhydrous barium oxide for a day and was then redistilled in vacuum. The compounds studied (5×10^{-4} mole/l) and lithium chloride (0.1 g-eq) were dissolved in DMF purified and dehydrated in this way. The working solutions prepared contained about 0.003% of water (determined by the Karl Fischer reagent).

The solutions were polarographed (LP-60 polarograph) in a thermostatted cell at 25.0 ± 0.1° C. Purified nitrogen was passed through the working solution for 20 min. The polarograms were recorded from 0 V to the potential of the separation of the support (~1.7 V). The cathode was a DME with forced detachment of the drop (m = 0.76 mg/sec; t = 0.24 sec) and the anode was the bottom pool of mercury. The distance between the anode and the cathode was kept constant. The values of the potentials were determined graphically on graph paper with an accuracy of ±10 mV and the limiting current was measured relative to the support with an accuracy of ±5% (rel.).

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