the procedure of Nicholson et al. (8). This procedure was carried out for dimethyl fumarate and cinnamonic
trile in the region where $i_{pa}/i_{pc}$ is most sensitive to variations in $k_2$. The $i_{pa}$ values for fumaronitrile were
too small to allow precise calculations from cyclic voltammetric data. The results and some intermediate
factors used in the calculations are shown in Table III. The $k_2$ values obtained for dimethyl fumarate and
cinnamonictrile are 1.6 x 10$^{-2}$ and 7.9 x 10$^{-2}$ liters/mole-
sec, respectively.

Discussion

The results obtained here support the previous studies (1) and point to the major pathway in the electrohydrodimerization of these compounds as in-
volving initial production of the anion radical fol-
lowed by a coupling step. Other aspects of the mecha-
nism, the protonation steps, the nature of the poly-
merization reaction, and the reactions at the later
waves, which sometimes lead to secondary radicals
(10), still await elucidation.

In examining the results, we see that dimethyl fuma-
rate, which undergoes dimerization at the slowest rate
of the three compounds, shows the most scatter in
the $k_2$ value calculated from RRDE results and only
fair agreement with that obtained by cyclic voltam-
metry. Several factors contribute to this. Because the
radical ion disappearance is slow on the RRDE time
scale, $N_k$ values are close to those for an unperturbed
collection efficiency, and the observed slopes are rather
insensitive to small changes in $X_{TCT}$. Moreover, the
small value of $k_2$ necessitates use of high dimethyl
fumarate concentrations, which increases the polymer-
ization side reaction.

The RRDE results for cinnamonictrile fall into the
sensitive $N_k$ vs. CONI region for our electrode and the
reaction is unperturbed by polymerization. The $k_2$
values determined by RRDE measurements over a
wide range of $C$ and for differing $w$ show good precision
and agree very well with the value determined by
cyclic voltammetry. This good agreement between a
steady-state and transient technique also is suggestive
of lack of involvement of adsorption of parent or inter-
mediates in the reaction mechanism.

The fumaronitrile RRDE experiments were per-
formed near the upper limit of determinable $k_2$ values
with our RRDE. For this reaction, for concentrations
of 0.4 to 4 mM, $N_k$ values of only 0.020-0.006 (CONI
= 1) were found. For both the cinnamonictrile and
fumaronitrile reactions the data suggest some con-
tribution from a reaction of the anion radical with
parent, although in both cases this contribution was
relatively small. It is interesting that even this small
contribution can be noticed and accounted for in the
analysis of the data, although other processes removing
anion radical, such as a first order ECE reaction lead-
ing to RH$_2$, may also account for the small deviations
from a close fit to mechanism I.

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ion Section to be published in the June 1973 JOURNAL.

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ments, Univ. of Texas, 1971.
trohydrodimerizations [see (5-6) and references contained therein].

The following mechanisms are considered:

I. Dimerization EC (electrochemical-chemical) —
Species B, which is generated at the disk electrode by
\[ A + n_{e} \rightarrow B \]  
[1] 
dimerizes to a nonelectroactive product
\[ 2B \rightarrow X \]  
[2] 
At the ring electrode A is regenerated from B by the reaction
\[ B - n_{e} \rightarrow A \]  
[3] 
II. Second order ECE — Species B, produced at the disk as in Eq. [1], reacts with parent

\[ k_{b} \]  
[4] 
where C is immediately reduced at the disk
\[ C + n_{e} \rightarrow Z \]  
[5] 
At the ring electrode either (a) B alone is oxidized, as in Eq. [3], or (b) both B and C are oxidized. Nuances of ECE mechanism IIa (7-8) consider (c) the irreversible reaction represented in Eq. [4] or (d) the reversible reaction
\[ B + A \rightarrow C \]  
[6] 
followed by an irreversible oxidation-reduction charge transfer reaction
\[ B + C' \rightarrow Z + A \]  
[7] 
III. Second order EC — Species B, produced at the disk as in Eq. [1], reacts with parent to form a nonelectroactive product

\[ k_{c} \]  
[8] 
Again at the ring B oxidizes to A via Eq. [3].

Table I. Surface boundary conditions

<table>
<thead>
<tr>
<th>Boundary conditions (z = 0)</th>
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<tbody>
<tr>
<td>Mechanism</td>
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<tr>
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</tr>
<tr>
<td>I</td>
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<td>IIb</td>
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<tr>
<td>IIc</td>
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</table>

Digital Simulation

The general approach to the simulations and the notation to be used has been described in the previous communications (2-4). Two different types of experiments were simulated. In the first the disk was assumed to be held at a potential where the concentration of A at the disk surface was always zero and for mechanism II, the concentration of C at the disk surface was also zero. A second simulation concerned a constant current maintained at the disk, so that the flux of A (or the sum of the fluxes of A and C in mechanism II) was held constant at the disk. In both cases the boundary condition at the ring electrode was that the concentration of B was zero at the ring. In mechanism IIb, the concentration of C was also held at zero at the ring surface. Surface boundary conditions for the different experiments and mechanisms considered are given in Table I. As in previous simulations, the results are specific for the particular RRDE geometry considered. The electrode under consideration here had IR1 = 94, IR2 = 100, and IR3 = 166, where IR1, IR2, and IR3 are the number of simulation boxes necessary to represent the radius of the disk electrode, and the radii to the inner and outer edge of the ring electrode, respectively; these values yield a collection efficiency in the absence of kinetic perturbations of 0.555. Values of \( i_{r}, i_{d}, \) and \( N_{K} \) were calculated as functions of the dimensionless parameter \( XKTC \) in the controlled

\[ XKTC = (0.51)^{-2/3p^{1/3}D^{-1/3}C_{a}^{1/2}k_{2}} \]  
[10] 
potential simulation and as functions of \( XKTC \) and the flux at the disk in the constant disk current simulation. Because a basic assumption of mechanism II is that species C is more easily reduced than species A, it was first necessary to establish in the constant current simulation if the total flux at the disk, as defined by the current, was greater or less than the maximum flux possible for species C. If greater, a fraction of the total current was allocated sufficient to maximize the concentration gradient of C at the disk surface.
Fig. 1. Collection efficiency (NK) vs. XKTC for the EC dimerization mechanism (I), the ECE radical-parent coupling mechanisms (IIa and IIb), and the EC radical-parent coupling mechanism (III).

[FC(1,1) = 0] while the remaining current diminished the concentration of A. If less, a finite concentration of C remained at the surface and the concentration of A was not altered by the passage of current. In every instance the diffusion coefficients of species A, B, and C were assumed equal, although provision is included in the program for introducing a different value for each species.

Results

Controlled disk potential results.—The results of simulations where the disk potential is maintained on the limiting current plateau for reaction [1] and the ring maintained at a potential where [3] occurs at the mass transfer controlled rate are shown in Fig. 1. (Mechanisms IIc and IIId are not shown in Fig. 1 because of NK's dependence on two parameters (equilibrium constant and rate constant) instead of one for the mechanisms as shown but qualitatively they would show the same sort of behavior.) All curves yield a value of NK = 0.555 as XKTC approaches 0 (k2C approaches 0, or ω approaches infinity) and all show a similar decrease of NK with increasing XKTC. While these NK-XKTC curves are indicative of kinetic perturbations and could be used to determine k2 values once the mechanism is known, they are clearly not very useful in distinguishing among the various mechanisms under consideration. Further, the dependence of the disk limiting current on XKTC (Table II) is of value only in distinguishing case III from cases I and II. Case II, categorized as an ECE type, is unlike the simple ECE case in that n, the number of electrons per molecule of starting material, A, electrolyzed, equals one independent of the rotation rate. Case III, however, undergoes a change in n from n = 1 to n = 2 with increasing rotation rate and thus, exhibits a dependence of disk limiting current with varying XKTC values.

Controlled disk current results.—Experiments involving disk currents at values below the limiting one are more diagnostic in deciding among the various reaction schemes under consideration here, because the relative fluxes of A and B from the disk can be varied. Simulations in this case are of NE at different values of the relative disk current, CONI, where

\[ CONI = \frac{i_d}{i_{d,1}} \]

and \( i_{d,1} \) is the limiting disk current, and for different values of XKTC. In this case a separate NK vs. CONI curve must be given for each value of XKTC. Results for the mechanisms under consideration here are given in Fig. 2-7. Note that for a first order decomposition of B, NK is independent of CONI, at a given value of XKTC, because both the velocity of the following reaction and the amount of B reaching the ring are proportional to disk current. The trend of NK with CONI is

![Fig. 2. Collection efficiency (NK) vs. 1-CONI for mechanism I and XKTC equal to (a) 0.1, (b) 0.5, (c) 2.0, and (d) 10.0, where CONI = \( \frac{id}{i_{d,1}} \) and \( i_{d,1} = (0.51)^{-2/3}v^{1/3}D^{1/3} \).](image)

![Fig. 3. Collection efficiency (NK) vs. 1-CONI for mechanism IIa and XKTC equal to (a) 0.1, (b) 0.5, (c) 1.0, and (d) 2.0.](image)
Because the product of the appropriate dimensionless simulation parameters for case IID is qualitatively similar to case I because the velocity of the following reaction assumes an overall second order dependence on B concentration. Transitional behavior, exemplified by curves b, c, and e (Fig. 6), occurs at intermediate values of CK. Quantitatively, the behavior of case IID differs from that of case I, for all values of CK, because the product of the appropriate dimensionless simulation parameters for case IID (i.e., CK and XKTC), which defines the velocity of the reactions consuming species B (and thus the magnitude of NK) has a squared dependence on the bulk concentration of A, whereas for case I, the reaction velocity is described by only one dimensionless simulation rate parameter, XKTC.

Discussion

The results show that the RRDE should be useful in studying different mechanisms of following reactions. Since RRDE studies involving steady-state NK measurements are relatively free from adsorption and double layer charging effects, the experimental results will be subject to fewer complications than transient methods. Digital simulation methods are capable of treating rather complex reaction schemes involving higher order chemical reactions. Variations of the mechanisms considered here, such as the simultaneous decreases and the kinetic perturbation of the following reaction becomes less. Hence, for case I, NK -> N as CONI -> 0 and NK approaches its minimum value as CONI -> 1. For cases IIa, IIb, IIc, or III, which involve coupling with the parent, the rate of the following reaction is a function of both A and B concentration at the disk. Hence, as t4 approaches t41 (CONI approaches 1) the A concentration decreases and the following reaction rate decreases. For these cases NK approaches its maximum value at a given value of XKTC as CONI -> 1. As CONI approaches 0, the concentration of A is essentially constant and the reaction of B approaches pseudo-first order conditions. When product C is also electroactive at the ring electrode (mechanism IIb), the trend is the same as for mechanism IIa but the NK values are larger because t4 is larger. Although case IID exhibits qualitatively different behavior depending on the value of the equilibrium constant for [6] and the rate constant for [7] as shown in Fig. 6, some trends are evident. For values of CK (CK = bulk concentration of A x equilibrium constant (K) for reaction [6]) greater than or equal to 0.10 and XKTC values resulting in collection efficiencies in the normal working range for the simulated RRDE (0.02 < NK < 0.54), NK approaches its maximum value as CONI -> 1. As CONI -> 0, the concentration of C is essentially constant and the reaction consuming B approaches pseudo-first order behavior. For CK values less than or equal to 0.001 (e.g., K = 1 when C = 1 mM), the NK variation with CONI is qualitatively similar to case I because the velocity of the following reaction assumes an over-all second order dependence on B concentration. Transitional behavior, exemplified by curves b, c, and e (Fig. 6), occurs at intermediate values of CK. Quantitatively, the behavior of case IID differs from that of case I, for all values of CK, because the product of the appropriate dimensionless simulation parameters for case IID (i.e., CK and XKTC), which defines the velocity of the reactions consuming species B (and thus the magnitude of NK) has a squared dependence on the bulk concentration of A, whereas for case I, the reaction velocity is described by only one dimensionless simulation rate parameter, XKTC.
occurrence of two of the reaction paths, can be treated by straightforward extensions of the described programs. For example, in studies of hydrodimerization reactions with the RRDE (9) it was sometimes necessary to consider the possibility of parallel reaction pathways of the intermediate radical ion (equivalent to substance B here) by both coupling and ECE mechanisms. The results in that work provide experimental confirmation of these theoretical results.

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Electrochemical Reduction of Allopurinol

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ABSTRACT

Allopurinol (1H-pyrazolo [3,4-d] pyrimidin-4-ol) is electrochemically reduced at the dropping mercury electrode by way of a single polarographic wave. Above pH 2, the electrode reaction is a 2e-2H + reduction of allopurinol to give 6,7-dihydroallopurinol as the sole product. At lower pH (i.e., pH 0) the single polarographic wave involves 4e and is due to reduction of allopurinol to 2,3,6,7-tetrahydroallopurinol. Under the conditions of prolonged electrolysis, however, the latter product slowly decomposes to give 4-carbamido-5-aminopyrazoline (2,3). The mechanism of these reactions has been elucidated by polarography, coulometry, cyclic voltammetry at the pyrolytic graphite electrode, mass electrolysis and isolation of products. The products have been identified by u.v., IR, NMR, mass spectrometry, and elemental analysis.

Pyrazolo [3,4-d] pyrimidines have been found applicable in clinical biochemistry as carcinostatic agents. Allopurinol (1H-pyrazolo [3,4-d] pyrimidine-4-ol) is a well-known inhibitor of the enzyme xanthine oxidase (1), and, hence, inhibits the formation of uric acid by oxidation of purines in organisms containing this enzyme (2,3). This property of allopurinol makes it possible to use lower doses of otherwise highly toxic 6-thiopurine in the treatment of leukemia (4). Allopurinol also substantially alters pyrimidine metabolism (5).

Because of the importance of understanding the oxidation-reduction behavior of biologically important compounds which interact with oxidation-reduction enzymes, we have begun a detailed and systematic study of the electrochemistry of the allopurines. The structure of allopurinol and the numbering employed in this paper is that used in "Chemical Abstracts," and is shown below.

\[ \text{Experimental} \]

**Chemicals.**—Allopurinol was obtained from Aldrich and was found to be chromatographically homogeneous. The other chemicals were of reagent grade. Argon (Linde) used for deoxygenating was equilibrated with water; no other purification was necessary. Buffer solutions used had an ionic strength of 0.5M except sulfuric and acetic acid solutions which were 1M in strength.

**Apparatus.**—The electrochemical apparatus has been described elsewhere (6-8). All potentials are referred to the SCE at 25°C. The dropping mercury electrode had normal m and t values.

**Ultraviolet absorption spectra** were recorded on a Perkin Elmer-Hitachi Model 124 spectrophotometer. Infrared spectra were recorded on a Beckman IR-8 using KBr pellets. NMR spectra were recorded on a Varian Model T-60 spectrometer. Mass spectra were recorded on a Hitachi Model RMU-6E spectrometer.

**Coulometry and macroscale electrolysis.**—For coulometry a measured volume (usually 100 ml) of background solution was introduced into the working electrode compartment of a three compartment cell. This solution was electrolyzed at the appropriate potential until an electronic current integrator gave a constant and small count. Then a weighed amount of allopurinol was introduced into the working electrode compartment sufficient to make the solution ca. 1 mM. After dissolution electrolysis was recommenced at the same potential, stirring rate, and flow rate of argon. Many macroscale electrolyses were carried out in the same fashion except that solutions were ca. 5-6 mM in allopurinol and an integrator was not employed. Completion of the electrolysis was confirmed by disappearance of the characteristic u.v. absorption and polarographic wave of allopurinol, and by characteristic cyclic voltammetric behavior at the pyrolytic graphite electrode.