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LOYOLA UNIVERSITY CHICAGO

ELECTROCHEMICAL CLEAVAGE OF PHENYLSULFONES

A THESIS SUBMITTED TO

THE FACULTY OF THE GRADUATE SCHOOL

IN THE CANDIDACY FOR DEGREE OF

MASTER OF SCIENCE

DEPARTMENT OF CHEMISTRY

BY

JOSEPH E. LOHR, JR.

CHICAGO, ILLINOIS

MAY, 1996

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LIST OF ABBREVIATIONS

4-PSBA 4-(phenylsulfonyl) butanoic acid

Ag Silver

AN Acetonitrile

AR Aromatic

BAS Bioanalytical Systems, Inc.

Bu Butyl

C Carbon

CH(PSTHP) 6-Cyclohexyl-5-(phenylsulfonyl)-3,4,5,6-tetrahydropyran-2-one

CV Cyclic Voltammetry

Disp Disproportionation reaction

DIW Deionized Water

DMF Dimethylformamide

DMSO Dimethyl Sulfoxide

ECEC E for electron transfer and C for chemical reaction showing the progressive steps in a scheme

Et Ethyl

F Faraday's Constant

GC Gas Chromatography

H Hydrogen

HPLC High Performance Liquid Chromatography

I Current

IR Internal Resistance

LC Liquid Chromatography

LCEC Liquid Chromatography Electrochemical Cell

M Moles

m milli

Me Methyl

N Nitrogen

Na-Hg Sodium Mercury Amalgam

NMR Nuclear Magnetic Resonance

P(PSTHP) 6-Phenyl-5-(phenylsulfonyl)-3,4,5,6-tetrahydropyran-2-one

Ph	Phenyl
Pt	Platinum
s	Seconds
SCE	Saturated Calomel Electrode
SET	Solution Electron Transfer
TBAF	Tetrabutyl-ammonium fluoroborate
TB(PSTHP)	6-tetrabutyl-5-(phenylsulfonyl)-3,4,5,6-tetrahydropyran-2-one
TEAP	Tetraethyl-ammonium perchlorate
TLC	Thin-Layer Chromatography
UV	Ultraviolet
V	Volts
v	Scan Rate

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CHAPTER I

Introduction and Background

I.A. Introduction

In general, the use of a sulfone group in synthesis concludes with its reductive elimination. Alternatively, substitution by an alkyl group can be effected by treatment with a trialkylborane. In some cases, however, it is desired to remove the sulfone group without reductive elimination or substitution. Numerous studies have shown electrochemical techniques useful in reduction of functional groups without elimination. In this study we will apply electrochemical techniques to remove a sulfone group which is utilized in chemical synthesis in previous steps. Prior studies uncovered a four carbon homologation reaction that utilized a sulfone to effect a dianion, and promote ring closure to produce lactones and lactams. Conventional reductive elimination pathways produced ring-opened products which in itself is an extension of available homologation reactions. The full utility of sulfones in synthesis can be greatly enhanced if the sulfone can be removed without formation of an alkene.

The purpose of this investigation is to study the electrochemical cleavage of phenylsulfones from molecules by a non-eliminative pathway, and as a consequence, to produce lactones and lactams by this method.

I.B. Background

I.B.1. Utility of Sulfone Group

Compounds that differ by a constant, such as a carbon and two hydrogens, are called homologs. A series of compounds each differing by the same constant moiety is called a homologous series. A reaction scheme that produces the next compound in such a series is called a homologation reaction. Homologations have been reviewed.[1] Reactions with one and two carbon homologs are abundant. Close examination shows that, like the well known Aldol condensation (Scheme 1), the reaction starts with the abstraction of the hydrogen ion alpha to the carbonyl group by a base. The carbanion then reacts with another carbonyl group.
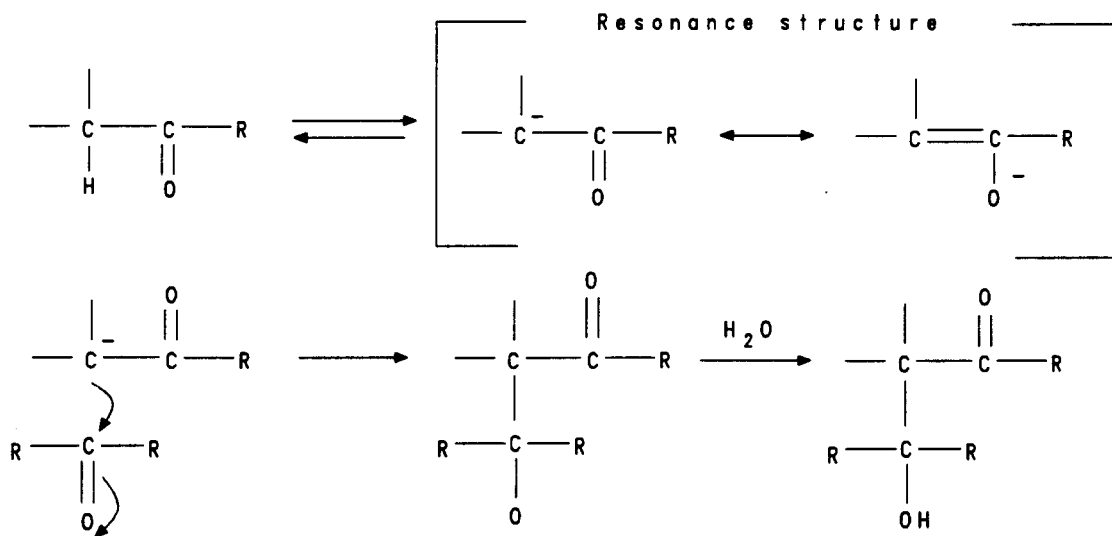
Scheme 1   Aldol Condensation
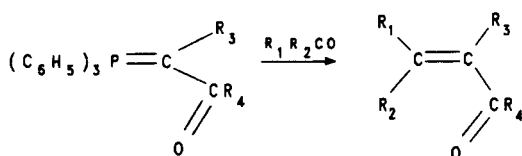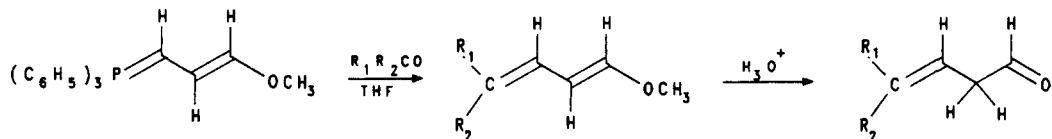
Scheme 2   Wittig Reaction

Some other homologation examples are the Perkin, Knoevenagel, Doebner, Claisen, Darzen, Tollens, and Dieckmann reactions.[2] Fewer three carbon examples exist and four carbon examples are limited to reactions such as the Wittig (Scheme 2) or the seldom used vinylogous Reformatsky (Scheme 3).

$$ROOCCH_2Br + Zn \longrightarrow (ROOCCH_2ZnBr) + \underset{R}{\overset{R}{>}}C=O \longrightarrow ROOCCH_2-\underset{\underset{R}{|}}{\overset{\overset{OH}{|}}{C}}-R$$

Two carbon extension

$$\underset{R}{\overset{R}{>}}C=O + \underset{R}{\overset{HAL}{\underset{|}{C}}}\overset{COOR}{\underset{R}{|}} \xrightarrow[H_3O^+]{Zn} R-\underset{\underset{R}{|}}{\overset{\overset{OH}{|}}{C}}-\underset{\underset{R}{|}}{\overset{\overset{COOR}{|}}{C}}-R$$

Four carbon extension

$$\underset{R}{\overset{R}{>}}C=O + ROOC-\overset{\overset{H}{|}}{C}=\underset{\underset{H}{|}}{C}-CH_2Br \xrightarrow[H_3O^+]{Zn} ROOC-\overset{\overset{H}{|}}{C}=\underset{\underset{H}{|}}{C}-CH_2-\overset{\overset{OH}{|}}{\underset{\underset{R}{|}}{C}}-R$$
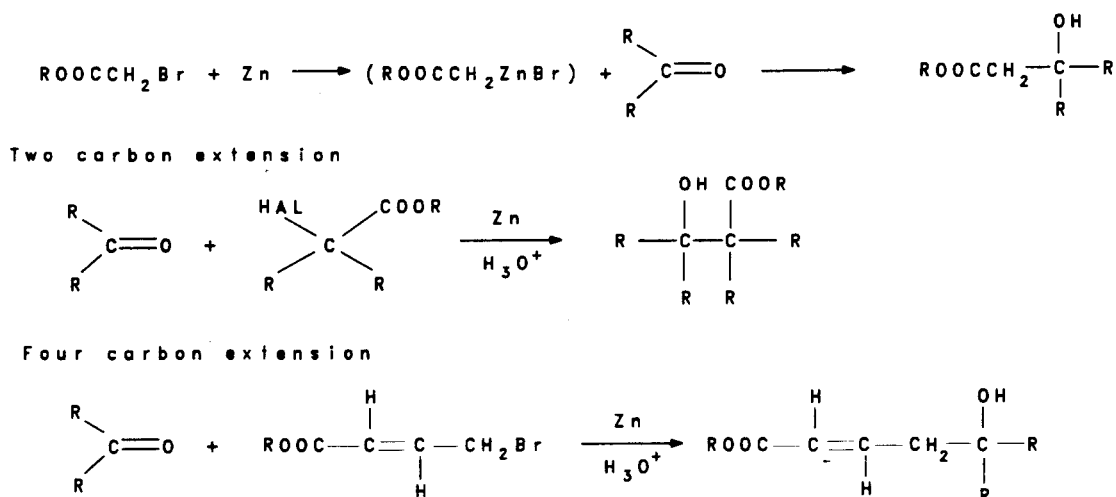
Scheme 3   Reformatsky Reaction

Similar reactions with ylides of sulfur, nitrogen, arsenic, and selenium are also known.[3] Sulfone groups have been shown to be versatile in chemical synthesis.[4] In a process similar to Aldol condensation, the sulfone group can be used as a lever to form carbon-carbon bonds in a controlled manner (Scheme 4) by acidifying the hydrogen on the alpha carbon enough to be removed by a base. Numerous reactions can now be directed at the alpha carbanionic center.

$$\underset{R}{\overset{PhSO_2}{\underset{\diagdown}{}}}\overset{\diagup H}{\underset{\diagdown H}{C}} \xrightarrow[R_1CH_2X]{base} \underset{H}{\overset{PhSO_2}{\underset{|}{C}}}-CH_2R_1 \begin{array}{c} \xrightarrow{reduction} RCH_2CH_2R_1 \\ \\ \xrightarrow[\text{if } R_1-OH \quad \text{elimination}]{} RCH=CH_2 \end{array}$$
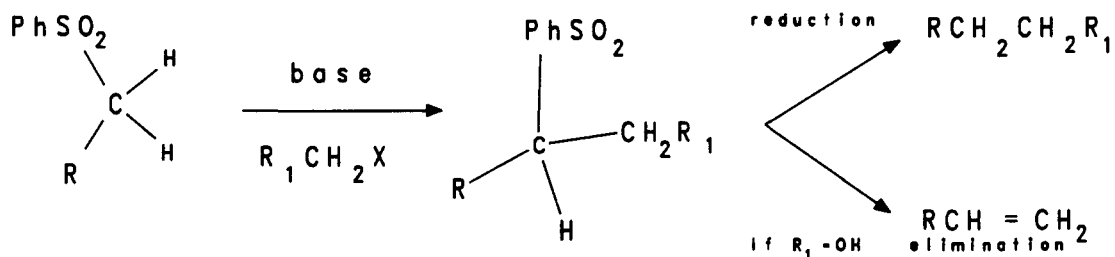
Scheme 4   Alpha Carbanionic Process

The α-sulfonyl carbanions can be produced by the action of ethylmagnesium bromide, lithium amide, or sodamide in liquid ammonia, which then can undergo reaction with aldehydes, ketones, isocyanates, and other electrophiles. The

presence of the SO$_2$ group thus facilitates substitution at the carbon alpha to the SO$_2$ through stabilization of a carbanionic center.[5] For example, in the Michael-type addition of nucleophiles to α,β-unsaturated carbonyl compounds, the β carbon acts only as an electrophile. The introduction of a benzenesulfonyl group to the β carbon with subsequent ketalization or acetalization produces a strong nucleophile and now various electrophiles can be introduced to the β carbon (Scheme 5).[6]
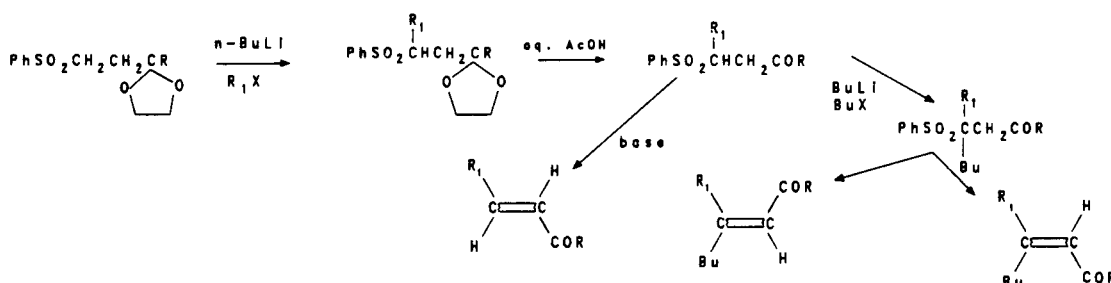
Scheme 5 Ketalization/Acetalization Reaction

The Ramberg-Bäcklund reaction[7] for example, converts an α-halosulfone to an alkene through formation of an α-carbanion that undergoes an intramolecular alkylation (Scheme 6).
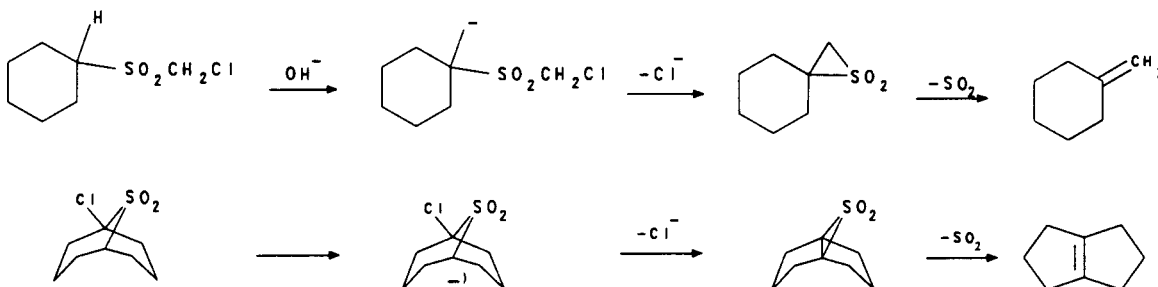
Scheme 6 Ramberg-Bäcklund Reaction

Similar results were obtained by treating the sulfone directly with KOH in carbon tetrachloride and avoids the preparation of the α-halosulfone in a separate step.

The Julia-Lythgoe coupling sequence produces olefins by the reaction of β-acyloxysulfones with Na-Hg amalgams (Scheme 7).[8-11] This reaction represents the common elimination pathway used for removal of a sulfone group after C-C bond formation has been achieved.
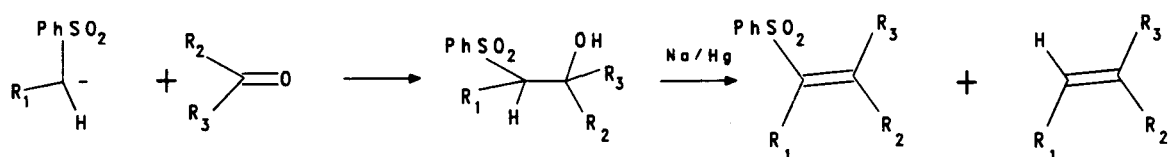
Scheme 7   Julia-Lythgoe Coupling Sequence

The method of Trost uses 4 equivalents of disodium hydrogen phosphate to control the pH and provide better yields of the desulfonation product in cases involving α-phenylsufonyl esters.[12]

I.B.2. Synthesis of Tetrahydropyran-2-ones

Carboxylic acid dianions have evolved as valuable intermediates for effecting carbon-carbon bond formation.[13-25] The easy availability and the reluctance to self condense has facilitated their use as carbon chain extenders. The sulfone carboxylic acid dianion shows utility of its own. Iwai reported[26] that the 3-sulfur functionalized propanoic acid dianion may be generated and added to carbonyl compounds (Scheme 8).
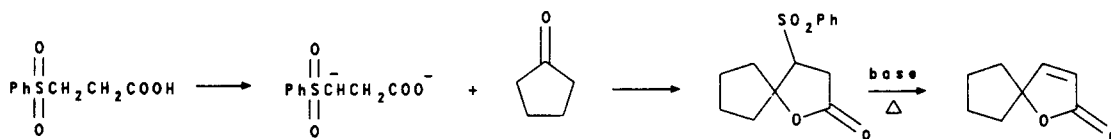
Scheme 8   Iwai Reaction

In an effort to extend the utility of dianion methods, Thompson and coworkers

investigated the reactions of the dianion of 4-(phenylsulfonyl)butanoic acid.

The reagent, 4-(phenylsulfonyl)butanoic acid (4-PSBA), is prepared in three

straightforward steps. First, ethyl-4-bromobutyrate, produced from butyrolactone,

was converted to the iodide. Second, the crude ethyl-4-iodobutyrate was reacted

with benzenesulfinic acid sodium salt in ethanol to produce a mixture of S- and O-

alkylated products. Third, the mixture was directly saponified to the butanoic acids

(Scheme 9).[27,28]
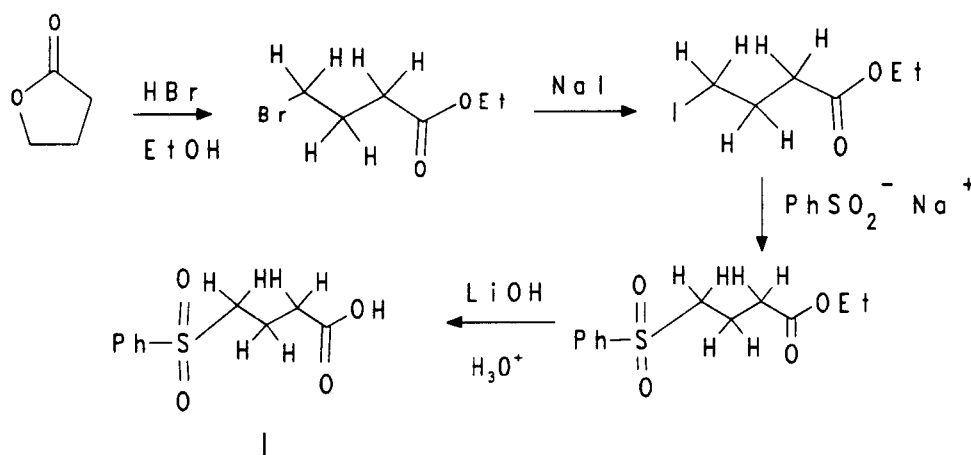
Scheme 9   Preparation of 4-PSBA

Acidification and extraction into diethyl ether deposited needles of pure **I**

upon standing; the sulfinate isomer remaining in solution. The dianion of 4-PSBA

was produced by treatment with two equivalents of n-butyllithium. The dianion adds

readily to a variety of aldehydes and ketones at -78°C. Cyclization to lactones was

produced by treatment of the intermediate 4-hydroxy acids with trifluoroacetic

anhydride (Scheme 10).
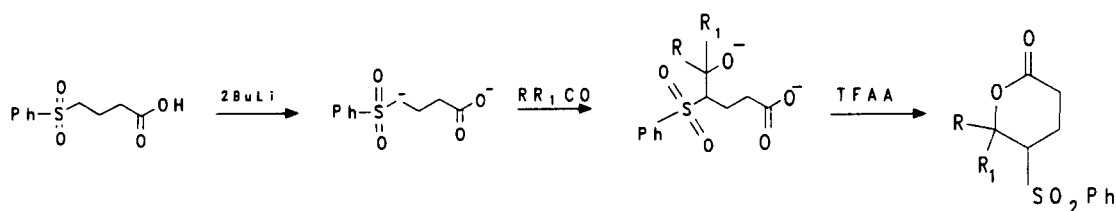
Scheme 10 Cyclization Reaction to Lactone

R groups for scheme 10

R	R₁
nBu	H
Ph	H
PhCH=CH	H
C₁₁H₂₃	H
Me	Me
Et	Et
-(CH₂)₅-	
Ph	Me

The pentanolides (6-membered lactones) were produced in yields of 62 to

89%. Selective removal of the phenylsulfone could lead to lactone rings bearing

unique substitution patterns.

For maximum utility of the sulfone group, a specific method for its removal

must be resolved. When the carbon group beta to the phenylsulfone group contains

an acyloxy group, chemical cleavage results in the reductive elimination pathway

to form the alkene as shown below to the right, rather than the reductive products

II or **IV** shown to the left (Scheme 11).
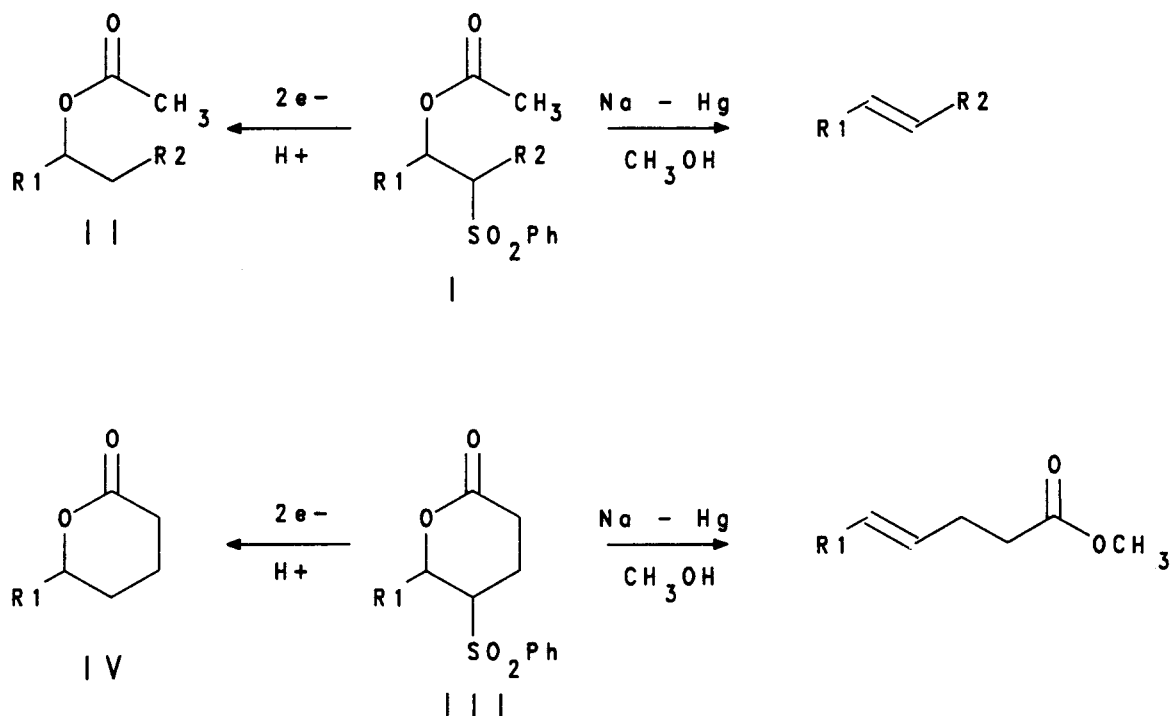
Scheme 11 Reduction/Elimination Reaction

Thompson and coworkers established the mechanism for converting 3,4,5,6-tetrahydropyran-2-ones to methyl 4-butanoates, which is initiated by a ring opening with methoxide to a hydroxysulfone intermediate with subsequent elimination of the sulfone. The resulting geometry of the olefins was consistent with the results of Lythgoe and coworkers (Scheme 12)[27,28].
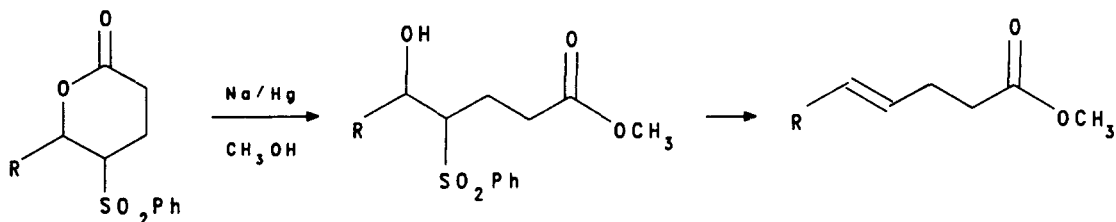
Scheme 12 Na-Hg Ring Opening & Elimination

A four carbon chain extension procedure has been devised from the phenylsulfonyl lactones (Scheme 11) and applied to the synthesis of a pheromone.[29]

Although the 4-carbon homologation is a high yielding and interesting procedure, a new synthetic route that could produce compounds **II**

gamma-Valerolactone

alpha-Valerolactone

and **IV** would access lactones (and lactams) such as valerolactone which is a key substructure of many natural products. The full impact of this new synthetic route to compounds **II** or **IV** can be realized if the phenylsulfone can be removed without reductive elimination, by some electrochemical route like the ones shown in Scheme 13.
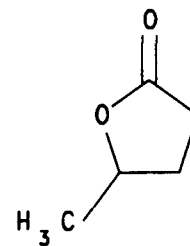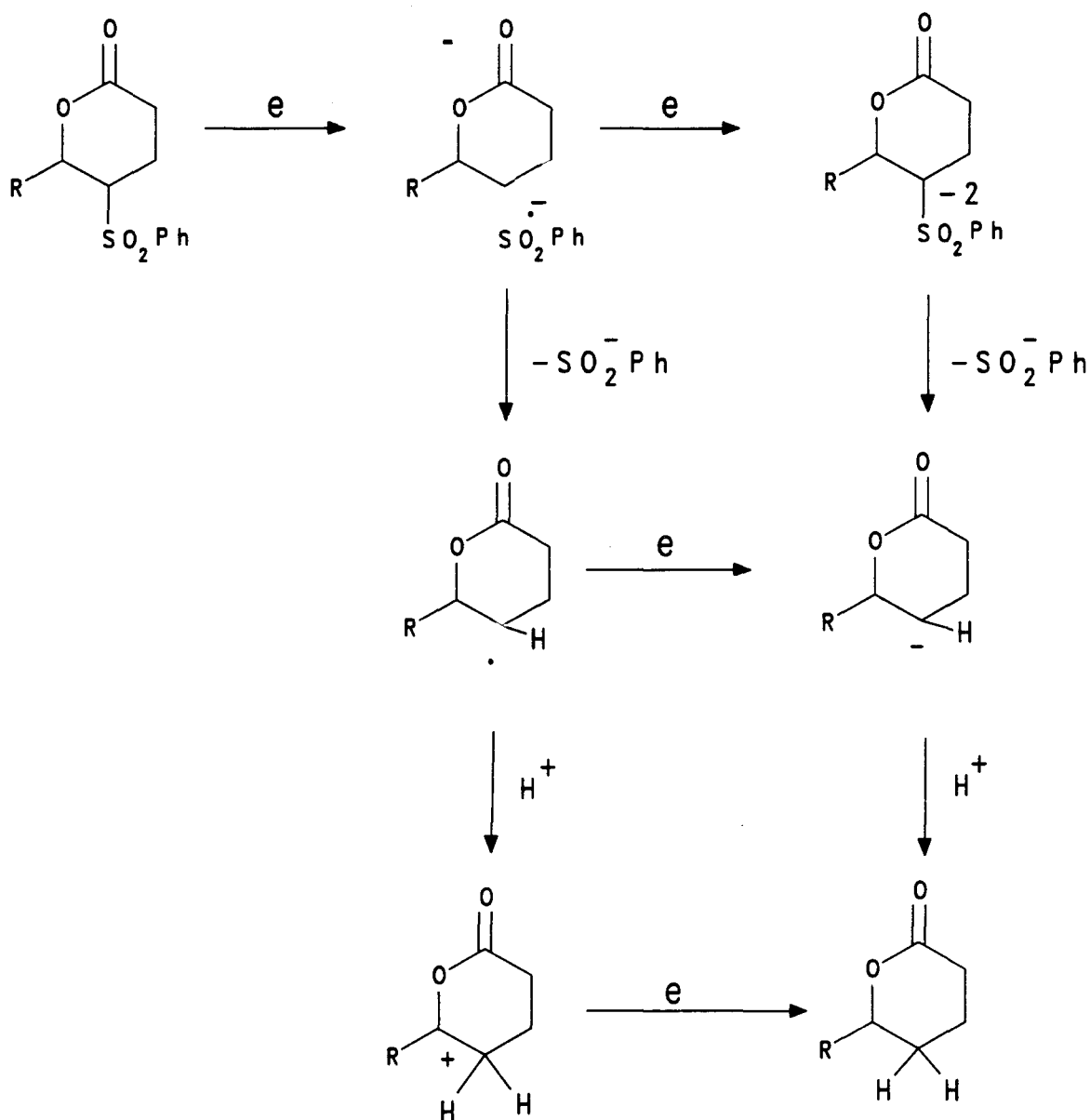
Scheme 13 Possible Electrochemical Routes

I.B.3. Conventional Cleavage

Sulfones are generally very stable compounds and fairly strong conditions

are needed to cleave the carbon-sulfur bond. Suter summarized that sulfones are

unaffected by the usual reducing agents.[30] His review of earlier works includes zinc

in dilute acid, hydrogen iodide, heating with yellow phosphorus or distillation from

12

zinc dust, to mention a few. Cleavage was produced by a variety of strong alkali with the conclusion that sodium ethoxide is the most satisfactory reagent. Heating a sulfone with alkali to temperatures up to 235°C produces an olefin and sulfinate (Scheme 14).
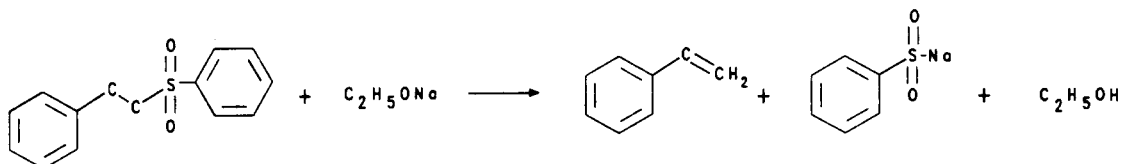
Scheme 14 Suter Alkali Reduction

Briefly, before the publication of Suter's book, investigations of the structure of natural compounds containing sulfur led to the use of Raney nickel catalyst in neutral or alkaline solution to remove sulfur (Scheme 15).
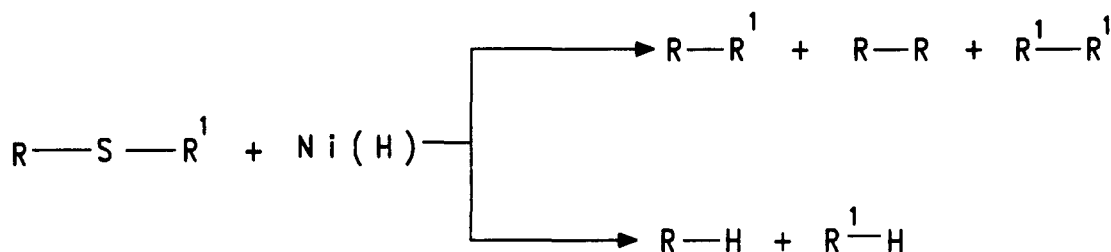
Scheme 15 Raney Nickel Cleavage

It was shown that aliphatic and aromatic sulfides, disulfides, sulfones and sulfoxides undergo cleavage by the hydrogen activated by Raney catalyst, provided sufficient Raney nickel was used to produce an excess of hydrogen.[31] In this case, the carbon-sulfur bond was changed to a carbon-hydrogen bond with no combination of radicals being observed. Dabby, Kenyon and Mason showed that sodium amalgam in alcohol converted diaryl and alkyl aryl sulfones to sulfinic acid and hydrocarbons.[32] They suggested that it was necessary for the sulfone to be

directly attached to an aromatic group for the reaction to proceed, based on the

inert reactions attempted with dialkyl and substituted aryl alkyl sulfones (Scheme

16).
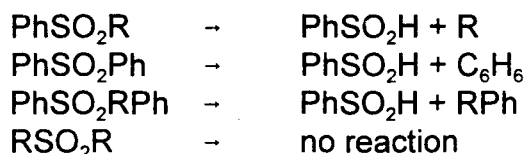
PhSO$_2$R   →   PhSO$_2$H + R
PhSO$_2$Ph   →   PhSO$_2$H + C$_6$H$_6$
PhSO$_2$RPh   →   PhSO$_2$H + RPh
RSO$_2$R   →   no reaction
Scheme 16 Dabby, Kenyon & Mason Reaction

Cleavage of alkyl aryl and unsymmetrical diarylsulfide to the hydrocarbon

and sulfinic acid was produced by using sodium in liquid ammonia or lithium in

methylamine.[33] Controlled addition, to avoid the presence of excess reducing

agent, was accomplished by refluxing the amine solvent containing the sulfides or

sulfone through an extraction thimble containing the metal.

Reaction of the methylsulfinyl carbanion with esters produces β-keto

sulfoxides, which can be converted to the β-ketones by reaction with aluminum

amalgam in tetrahydrofuran-water mixture.[34]

RCOCH$_2$SOCH$_3$ + Al-Hg + H$_2$O → RCOCH$_3$
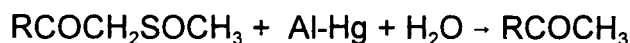
The milder conditions for this reaction are made possible by the presence of

the β-keto group, which activates the sulfone towards reduction. Sulfones and

sulfonamides were also shown to undergo this reaction.

Numerous publications are devoted to reduction of sulfur compounds using

amalgams, bases and the like. Julia first produced olefins by reduction of vicinal

acyloxy sulfones with sodium amalgam in alcohol in 1973 (Scheme 17).[35, 36]
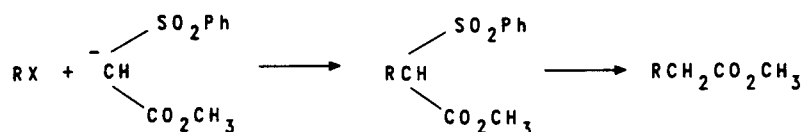
Scheme 17 Julia Reduction

As a synthetic pathway to olefins, β-acyloxy-sulfones were reduced with sodium amalgam in methanol-ethyl acetate to prepare a variety of conjugated dienes. Kocienski studied several elimination reactions and proposed that the reaction was stereospecific and followed an ECEC elimination mechanism.[37, 38] Kocienski noted that typical reaction products produced 80:20 trans to cis isomer distribution. He proposed that in the reductive elimination mechanism of benzoyloxy sulfone, the first step is the addition of an electron (E - Electrochemical), and the separation of phenylsulfinate (C - Chemical) to produce a radical stable enough to equilibrate to the less energetic form (Scheme 18).
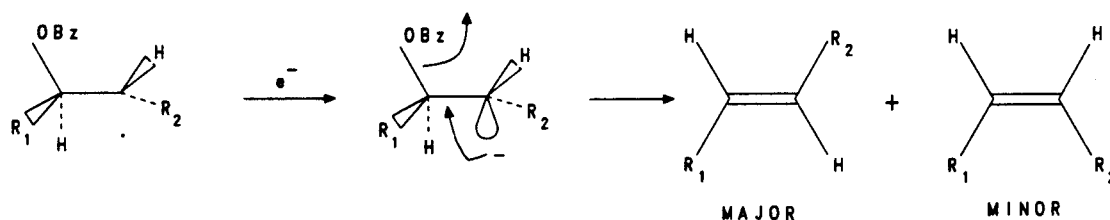
Scheme 18 Kocienski Reaction

After a second electron is added (E), the benzylate anion separates (C) to produce the olefin. Most studies produced olefins or other reductive elimination products.

Thompson noted that in the production of 3, 4, 5, 6-tetrahydropyran -2-ones, the 6 substituted 5 phenylsulfonyl analogs were substantially trans in orientation (Scheme 19).
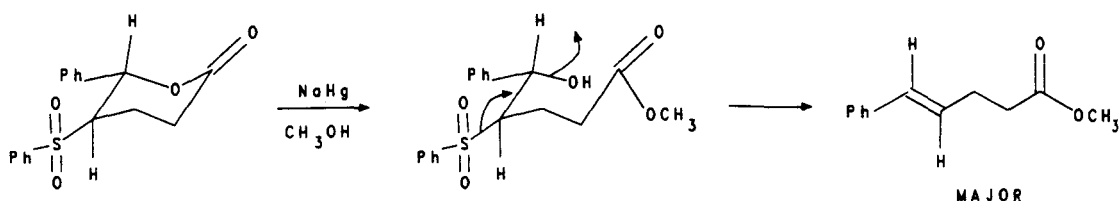
Scheme 19 Thompson Reduction

Subsequent conversion to methyl 4-butenoates with Na-Hg amalgam produced olefins in the 4:1 ratio consistent with results of previous work. The ring opening to the ester is expected from the methoxide produced. The hydroxy sulfone then undergoes elimination. This mechanism was further substantiated by the isolation of the hydroxy sulfone in one case, and by base induced methanolysis and subsequent treatment with amalgam to produce the same resulting isomer distribution. The cis isomer treated alone also produced 4:1 E to Z ratios, which also requires ring opening with rearrangement to the less energetic trans form before elimination as proposed by Kocienski.

I.C. Electrochemical Cleavage

I.C.1. Reaction Pathways

In order to remove the phenylsulfone group without reductive elimination, electrochemical cleavage is proposed. Generally electrochemical cleavage of phenylsulfones takes place at a mercury cathode in the potential range below -2 volts (vs. SCE)[39-49] according to the equation:

$$ArSO_2R + 2e^- + H^+ \rightarrow ArSO_2^- + RH$$

Horner and Neuman[49] proposed that the stability of the radical formed, after the transfer of one electron, would determine the position where the cleavage would take place. In the case of an aromatic sulfone, the strong electron withdrawing SO_2 group, together with the electron rich benzene ring, favor the electron transfer to the sulfone itself, resulting in cleavage to the phenylsulfinate ion. In their studies of diaryl and alkylaryl sulfones, the phenylsulfinate was detected as the preferred product as opposed to the alkylsulfinate.

Manoušek, Exner and Zuman[50] investigated substituted aryl methyl sulfones and found that aryl substitutions shifted reduction potentials more positive and electron withdrawing groups promoted the cleavage of the benzene sulfur bond (Scheme 20).
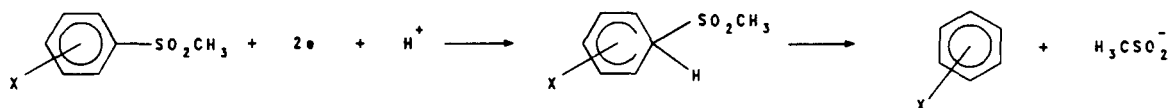
Scheme 20 Manoušek, Exner & Zuman Reduction

Simonet and Jeminet[39] expanded on the work of Manoušek, Exner and Zuman by adding more variety of substituents. They pointed out that another potential reaction is the reduction of the side chain (X) when the required potential is more positive than that of the sulfone.

I.C.2. Cyclic Sulfone Cleavage

Lamm and coworkers[42-47] investigated cyclic sulfones (Scheme 21) expecting to produce ortho substituted phenyl sulfones.
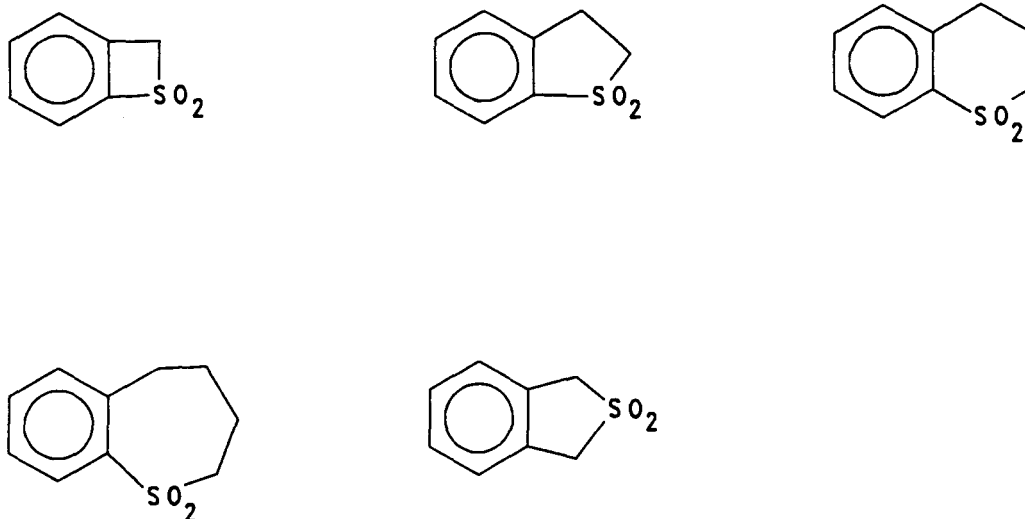
Scheme 21 Cyclic Sulfones

It was proven, however, that the position of the free electrons in the benzyl radical, at the time of bond breaking, is orthogonal to the benzene π bond system, and as a result, is not the preferred radical formed. In all cases, the benzene carbon-sulfur bond is broken to produce a benzene alkyl sulfone, in agreement with Horner's suggestion, when the molecular orientation is considered more closely.

I.C.3. Proposed Electrochemical Cleavage

J. Simonet summarized the electrochemical behavior of sulfones[51] by the following diagram (Scheme 22).

(d) Unsaturation in R₁ and/or R₂ activates the cleavage of the C-S bond, especially when the R₁SO₂⁻ is a good leaving group.

(a) R₁ reacts with electrons in the presence of an unsaturation directly bound to the sulfonyl group.

(c) Increased acidity of this hydrogen atom may lead to self-protonation reactions with electrogenerated bases (in aprotic solvents or in unbuffered solutions).

(b) Cleavage reactions are strongly favored when R₁SO₂⁻ is a good leaving group.

Scheme 22 Simonet Diagram Reprinted from Ref. (50). P 1003 by courtesy of Marcel Dekker, Inc.

In general, the cleavage of all aromatic sulfone compounds proceeds with the breaking of the C-S bond of the sulfone anion radical as the fast reaction step. This is illustrated with the organic molecule of interest in step 2, (Scheme 23).
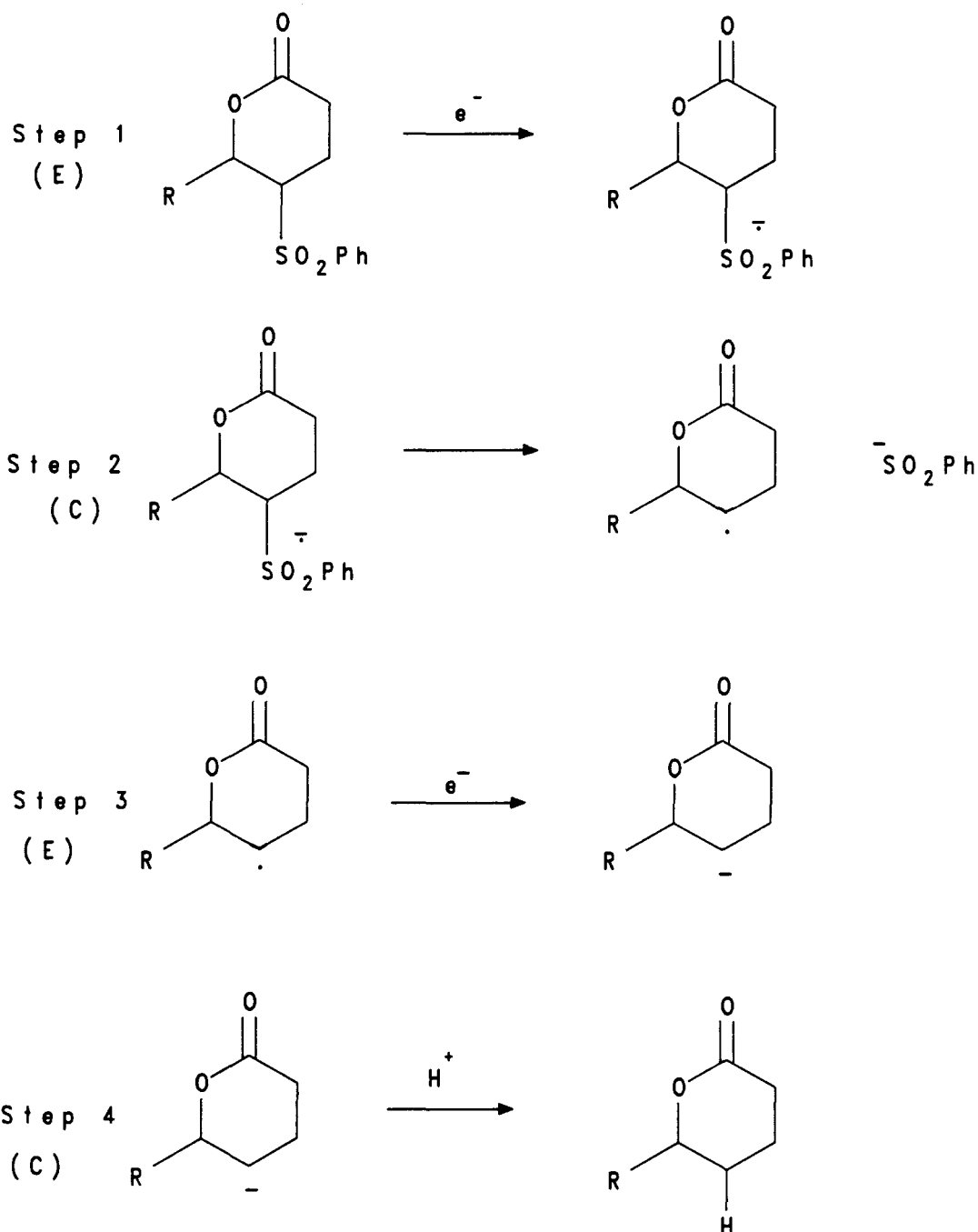
Scheme 23 Proposed Electrochemical Reduction

Step 1 only occurs at the cathode, this electrochemical step is followed by

a relatively fast decomposition of the sulfone anion radical in step 2. The rate of this

reaction determines the location of the formation of the lactone radical. In the case of very fast reactions, the lactone radical is formed near the cathode, and a second electron transfer is provided from the electrode itself in step 3. For slower reactions, the anion radical may migrate into the diffusion layer or even to the bulk solution itself. In these cases, the second electron transfer is effected by a second sulfone anion radical in what is known as a solution electron transfer or SET (Scheme 24).
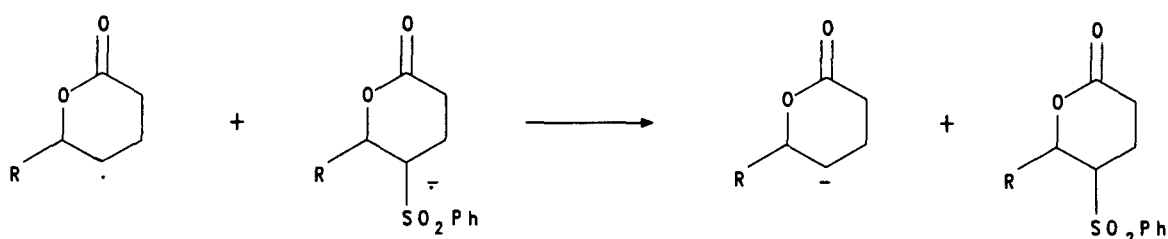
Scheme 24 Solution Electron Transfer Reaction

In this case, the ECE mechanism is replaced by a disproportionation process or "disp." Finally, in step 4, the strong base is protonated by the solvent or acidic impurities in the reaction mixture.

I.C.4. Cyclic Voltammetry

In cyclic voltammetry, a potential is applied to a working electrode and changed linearly with time from a point where no reaction occurs to potentials where reduction or oxidation occurs. Then the sweep is reversed, and the reactions of the intermediates and products formed by the forward scan may be observed.

Initially the potential is varied to find the area of response of interest. Once the response area of interest is defined, then the scan rate is varied. Graphic and mathematical analysis of the resulting curves can reveal mechanistic and kinetic information about the reaction being studied. The electroactivity of sulfones can

is made more reducing, the electron transfer process starts with characteristic increase in current flow where the observed current is dependent on the rate of electron transfer to the electroactive molecule. The concentration of the reactive specie is being depleted, especially at the surface of the electrode. At more negative potentials the current drops off as the electron transfer rate is now dependent on the rate of diffusion of new molecules to the electrode surface. The observed current is now dependent on the diffusion rate of the electroactive molecule under the reaction conditions being used.

Reversal of the sweep potential can produce complimentary information on the nature of the electrochemical process. If the diffusion of the anion is slow enough, and the scan rate is fast enough, then the potential change produces a near mirror image of the forward sweep (Figure 1). The analogy in the reverse sweep is the same. The layer near
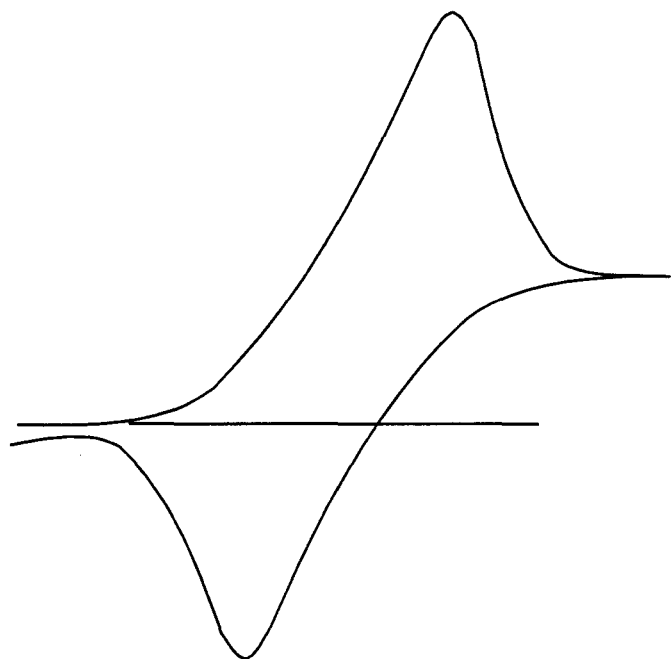
Figure 1 **Cyclic Voltammogram**

the electrode has been depleted of electroactive molecules and been replaced by sulfone anion radicals which are oxidized to produce a peak potential before the competition of the electrochemical rate, and the diffusion of radicals switches, and the current drops off to reflect the limiting of the current by the rate of diffusion of the radical. If, however, the diffusion rate is fast, and the sweep rate too slow, then the reverse scan only reflects the diffusion rate of the anion, and no reverse peak is observed (Figure 2).
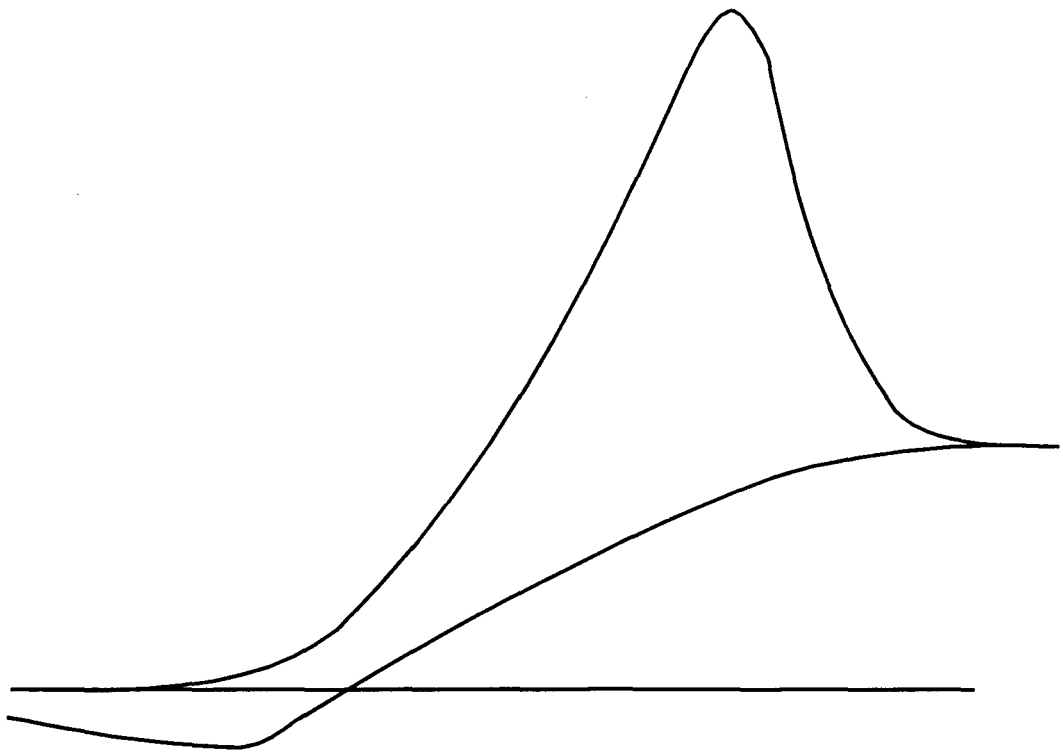
Figure 2   CV No Reverse Peak

Cyclic voltammetry scans can be characterized by several parameters [52] measured off of the curve as shown in Figure 3.
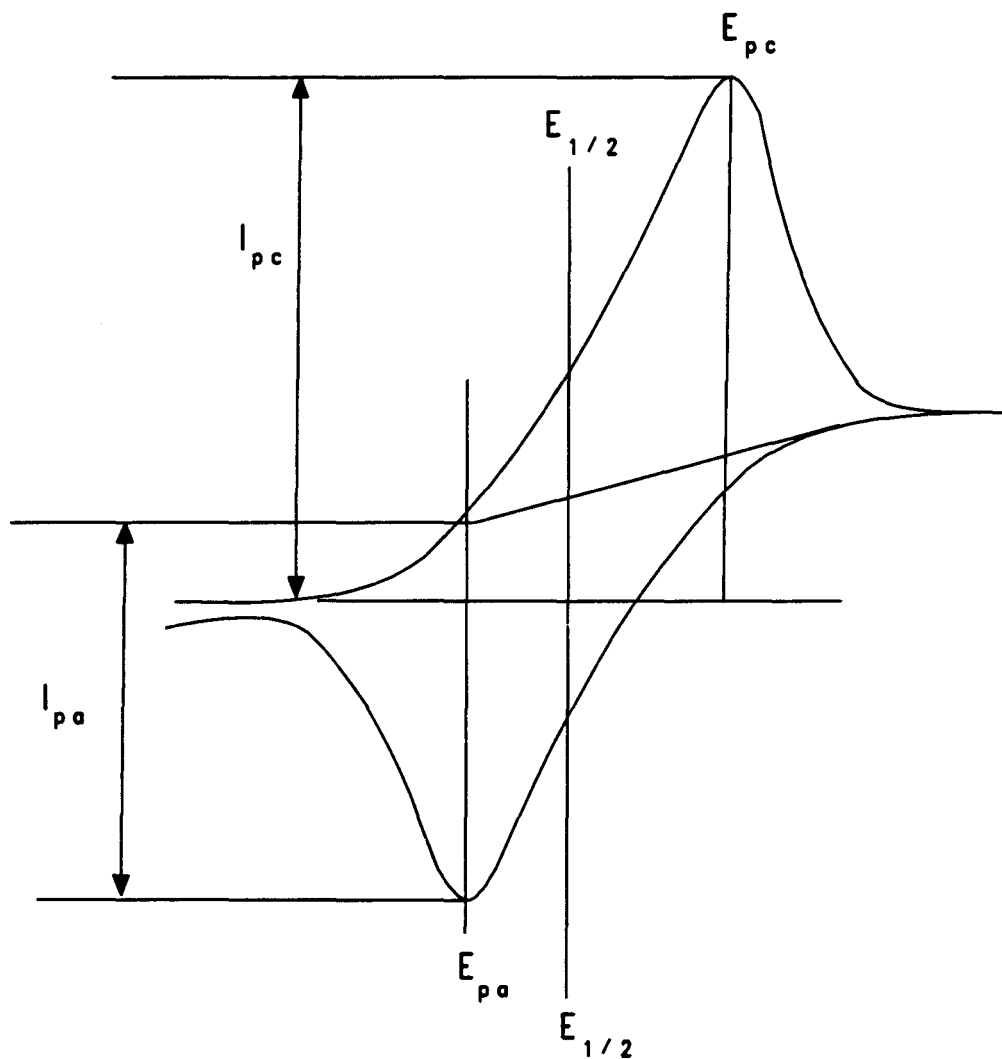
Figure 3   CV Annotated Curve

E_{pc} Cathodic peak potential

E_{pa} Anodic peak potential

i_{pc} Cathodic peak current

i_{pa} Anodic peak current

$E_{p/2}$ Cathodic half-peak potential

$E_{1/2}$ Half-wave potential (midway between E_{pa} and E_{pc})

$$E_{1/2} = E^{0'} + (\frac{RT}{nF}) \ln (\frac{D_R}{D_0})^{1/2} \quad [1.1]$$

Where D_0 is the diffusion coefficient of oxidation reaction.

D_R is the diffusion coefficient of reduction reaction.

$E^{0'}$ is the formal potential (dependent on ionic strength of solution used.)

For reversible reactions, the surface concentration of O and R, as calculated from the Nernst equation, differs very little from the actual concentrations because the electron transfer is rapid enough to maintain equilibrium. In these cases, the difference

$$\Delta E_p = E_{pa} - E_{pc} = \frac{57}{n} \, mV \qquad [1.2]$$

in the peak potential of the anodic and cathodic curves maintains a 57 millivolt per electron transferred spread, and is independent of scan rate (v). Similarly, the cathodic or anodic half-potential ($E_{p/2}$) is 56.5 millivolts per electron.

$$E_{p/2} - E_{pc} = \frac{56.5}{n} \, mV \qquad [1.3]$$

The half-wave potential $E_{1/2}$, well known from polarographic curves, is exactly half way between E_{pc} and E_{pa}.

If the reaction is not reversible, then ΔE_p is greater than 57 mV/n and increases with increasing scan rates. The rates of the anion radical formation and removal are substantially different, leading to depletion of one specie or the other by competing reactions. Solution electron transfer or chemical dimerizations are frequently observed in irreversible reactions.

In a diffusion-controlled reaction, none of these other competing reactions are present to any extent, and consequently, the current is limited only by the diffusion process. The test for diffusion control is made by comparing the peak current i_{pc} divided by the square root of the scan rate (v) for planar electrodes.

$$\frac{i_{pc}}{v^{1/2}} = constant \qquad\qquad [1.4]$$

Alternatively, a graph of peak current i_{pc} versus the square root of the scan rate (v) produces a straight line.

The current function, a dimensionless group, can be derived from the Cottrell equation and for reversible reactions should be about 0.446. The current function is calculated according to the equation:

$$\frac{i_{pc}}{nFAC_0(\dfrac{D_0nFv}{RT})^{1/2}} \qquad\qquad [1.5]$$

where i_{pc} is the peak cathodic current in amperes

A is the electrode area in cm^2

C_0 is the concentration of reactant in M/cm^3

D_0 is the diffusion coefficient in $cm^2/sec.$

v is the scan rate in volts/sec.

R, T and F are the conventional constants.

I.C.5. Chronocoulometry

According to Faraday's law, the amount of chemical reaction caused by the flow of current is proportional to the amount of electricity passed. In chronocoulometry a constant potential beyond the oxidation or reduction peak of interest is maintained and the current produced over time is observed. Integration of the resulting curve is the coulombs used in the reaction which is directly related to the number of electrons transferred by the equation:

$$Q=nFW/m \qquad\qquad [1.6]$$

where   Q = Coulombs

n = number of electrons

F = Faraday (96,487 coulombs)

W = Weight of sample

m = molecular weight of sample species.

For our purposes, a known amount of material is electrolyzed and the amount of current passed is used to calculate the coulombs consumed. From the above equation the number of electrons can be calculated. The transfer of two electrons adds to the evidence that an ECEC mechanism is taking place.

CHAPTER II

EXPERIMENTAL METHODS

II.A. Materials and Methods

II.A.1. Chemicals

Sodium sulfate, sodium chloride, sodium iodide, sodium benzenesulfonate, ethyl 4-bromobutyrate, n-butyllithium, tetrabutyl ammonium fluoroborate (TBAF), potassium ferricyanide and anthraquinone were used as obtained from Aldrich Chemical Co, Inc. Benzoquinone was used as obtained from Eastman Kodak Co. TB(PSTHP), CH(PSTHP) and P(PSTHP) (see below) were received initially as gifts from Dr. Chuck Thompson and were used as obtained. Solvents were purified
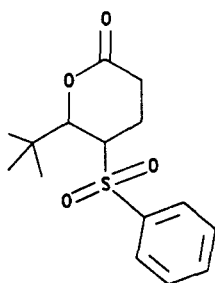
6-tetrabutyl-5-(phenylsulfonyl)-
3,4,5,6-tetrahydropyran-2-one
mwt 292.38
TB(PSTHP)
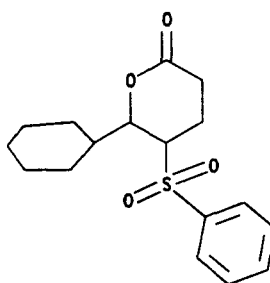
6-cyclohexyl-5-(phenylsulfonyl)-
3,4,5,6-tetrahydropyran-2-one
mwt. 318.43
CH(PSTHP)
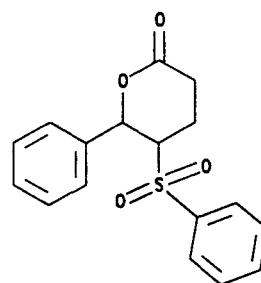
6-phenyl-5-(phenylsulfonyl)-
3,4,5,6-tetrhydropyran-2-one
mwt. 312.37
P(PSTHP)

and distilled prior to use according to procedures in the literature[53]. The 4-

(phenylsulfonyl) butanoic acid and subsequent analogs of 3, 4, 5, 6-tetrahydropyran-2-one were produced according to the Thompson and Frick paper.[12] Acetonitrile, dimethylsulfoxide and dimethylformamide were dried over alumina with a nitrogen purge in gas drying tubes. Nitrogen for purging purposes was passed through these tubes to saturate the nitrogen with solvent vapors before going into reaction flasks. Tetraethyl ammonium perchlorate (TEAP) was produced by reacting stoichiometric amounts of tetraethyl ammonium bromide with potassium perchlorate in water and recrystallizing several times until the filtrate did not test positive for potassium bromide when silver nitrate was added.[54]

II.A.2. Equipment

Electrochemical analysis was performed with three systems: 1.) EG & G Princeton Applied Research Model 273 Potentiostat/Galvanostat connected to a Houston Instruments Omnigraphic 200 recorder. 2.) EG & G Princeton Applied Research Model 175 universal programmer connected to an EG & G PAR XY recorder, a Wavetech 2MHz function generator Model 20, a Nicolet 4094 digital recording oscilloscope and a BAS System BA-1 containing a preamplifier PA-1, a microelectrode cell and a Faraday cage. 3.) EG &G Princeton Applied Research Versastat connected to an IBM XT computer running the PARC Headstart and R250 software.

Platinum (Pt) or carbon (C) was used as the working and counter electrodes and a standard calomel electrode (SCE), silver/silver chloride electrode (Ag/AgCl), or silver wire (Ag) reference electrode was used. Four-neck electrochemical cells

were used for cyclic voltammetry. A BAS microelectrode cell was used for microelectrode cyclic voltammetry. A BAS LCEC was used for chronocoulometry, and a homemade divided H-cell was used for electrolysis. Infrared scans were done on a Perkin Elmer Model 983 Infrared Spectrophotometer with the Model 7300 PC Series 7000 software. GC runs were produced on a Hewlett Packard Model 5890 fitted with a 30 meter DB-1 capillary column. HPLC was done on a Waters Model 710 with a 15 cm x 4.6 cm column packed with 5 micron C-18 Regis Spherisorb. A Waters 481 UV detector was used. Sample were weighed on a Mettler AE163 analytical balance. UV scans were done on Perkin Elmer Lambda 4C UV/VIS Spectrophotometer with the CUV3 application software. Proton NMR was conducted on JEOL GSX FT or a Varian VXR 300 MHz instrument. If needed, purified acetone or carbon tetrachloride was used as a solvent. TLC plates were aluminum sheets coated with 0.2 mm silica gel 60 F_{254}, obtained from Fisher Chemical Company, using diethyl ether or methanol. An ultraviolet lamp was used to identify the location of spots.

II.B. Procedures

II.B.1. Cyclic Voltammetry

II.B.1.a. Electrode Area

Purpose

To calculate the surface area of the electrode used.

Method

A three-electrode cell using a four-neck 100 ml round-bottom flask was set up (Figure 4).   A standard calomel electrode (SCE), a coiled platinum wire counter electrode, and a platinum wire sealed in glass (Joe E1) were used.   The platinum electrode,
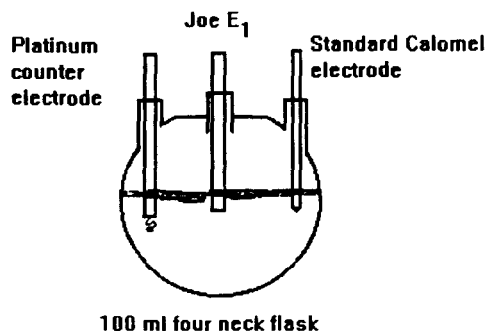
Figure 4   3-Electrode Cell

Joe E1, was rinsed with DIW, polished on a Buehler Ecomet III polisher-grinder using a Buehler Gamma Micropolish alumina 3, 0.05 micron, polishing solution, rinsed with DIW, sonicated for about five seconds in a Bronson 1200 sonicator, rinsed again with DIW and dried with a Kim Wipe tissue. The electrodes were each suspended by rubber pipette bulbs in respective necks of a four-neck flask. The fourth neck was available for adding or charging solution, nitrogen purge or the like. A model 273 potentiostat was set for 0.8 to -0.2 to 0.8 volts vs. SCE for E1, E2, E3 to produce the voltage ramp needed for cyclic voltammetry. The scan rates in both directions were set at 50 millivolts per second and the programmed delays at E2 and E3 were both set at 0 millivolts. (By default the delays were 100 milliseconds when 0 was selected.) Front panel controls were set to 10 microamps per volt output sensitivity, and single cycle was selected. The plotter was set in the X direction at 200 millivolts per inch and in the Y direction at 0.5 volt per inch. In the latter case, with the potentiostat set at 10 microamps, the resulting Y direction pen

movement represented 10 microamps/volt times 0.5 volts/inch or 5 microamps per inch of pen travel for I_p.

Initial scans were done on Potassium Ferricyanide in water with sodium sulfate as electrolyte. Potassium ferrocyanide was used because the diffusion coefficient, needed for the Randles-Sevcik equation, is well known and documented by several techniques. Scan rates were varied from 50 mv/s to 200 mv/s. Subsequent experiments were repeated using freshly prepared solutions, with scan rates of 5 mv/s to 360 mv/s. Results were recorded on an XY plotter. Curves were measured with a ruler, and peak current was measured by baseline extrapolation.

The Randles-Sevcik equation (Equation 2.1) was used to calculate the area of the platinum working electrode used, resulting in a value of .16 square centimeters for the electrode Joe E1.

$$I_p = Fn^{3/2}AD^{1/2}v^{1/2}C$$

[2.1]

Where C = concentration in M/cm^3

D = diffusion rate for $Fe(CN)_6^{-3}$ = 7×10^{-6} cm^2/second

A = area of electrode (to be determined) in cm^2

n = number of electrons transferred = 1

v = scan rate (varies)(V/s)

I_p = peak current in amperes (measured from graphs)

F = Faraday's constant 2.69×10^5.

II.B.1.b. Exploratory Cyclic Voltammetry of Unknowns

Purpose

To investigate the experimental conditions of an organic system.

Method

In an organic system, care must be taken to avoid moisture in the reaction. Glassware was washed and rinsed with alcohol, dried in an oven and immediately purged with dry nitrogen supplied from a cylinder. The solvents were placed in a gas drying cylinder over activated alumina and purged with nitrogen to remove any dissolved gasses. The dried solvents were used to make solutions of electrolyte and reactant. The gas drying cylinders, with the remaining solvent, were then used to saturate the nitrogen with solvent vapor to minimize evaporation in the reaction flask and avoid concentration changes when being used to purge the reaction flask (Figure 5).
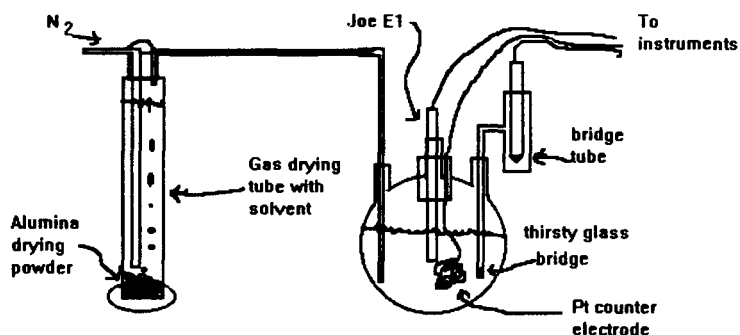
Figure 5   Reaction Setup

Initial runs were made with a SCE in a salt bridge tube with a thirsty glass bridge (Figure 6). Polishing was accomplished by mixing 0.05 micron aluminum oxide with the previously dried solvent and applying to a polishing pad. Actual polishing was done by hand, wetting the pad with solvent before each polish. One small pad was suitable for several polishings.

The system was tested by calculating the diffusion coefficient of anthraquinone using the Randles-Sevcik equation (see above). The value for the diffusion coefficient in the literature, $2.00 \pm 1 \times 10^5$ cm^2/sec., (typical for organic
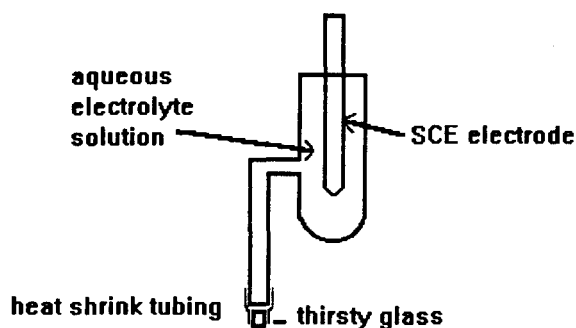
Figure 6 Thirsty Glass Bridge

systems, depending on solvent, electrolyte, etc.) was in good agreement with the calculated value.

Exploratory electrochemistry was carried out on the unknowns using the organic system described above. Solvents (DMF and AN) in conjunction with salts (TBAF and TEAP) were used. In exploratory cyclic voltammetry, a potential at which no current is observed is selected as the starting point and small voltage sweeps more positive or negative of that point applied. The magnitude of the range is successively increased. Potential was varied from 2 volts to -2 volts to try to identify the area of interest. Initial scans produced curves with many peaks. In an

attempt to identify and eliminate unwanted peaks, a scan of the solvent and electrolyte without the organic compound was made. Inspection indicated a possible peak of interest at about -2 volts. Scans were made varying potential limits, first by incrementally increasing the negative limit, and secondarily be decreasing the positive limit. Identity of the peak was confirmed by varying concentration and noting the increase in response in the area of interest. Once the potential limits were set, scan rate versus peak potential curves were run, and graphic analysis (i_p versus $v^{1/2}$) was done to show the linear relationship, indicating, possibly, a reversible reaction that was diffusion controlled.

II.B.1.c. Fast Scan Cyclic Voltammetry

Purpose

To capture reduction curves not obtained by slower scan rates.

Method

Microelectrode cyclic voltammetry was used when high speed scan rates were needed to capture the oxidation current before the reduction products diffuse away from the electrode double layer. When using faster scan rates, ohmic potential drop at conventional electrodes becomes a problem. Since the current generated is proportional to the square root of the scan rate, at fast scan rates (>10v/s) the solution IR becomes very large. With microelectrodes, the current is several orders of magnitude smaller and the IR drop is less significant.

An EG & G PARC Model 175, capable of scan rates to 10,000 volts per second was connected to a Nicolet 4094 oscilloscope. The Nicolet 4094

oscilloscope is capable of storing 4,094 data points in memory, averaging several points or sweeps together, and measuring the points after a scan is complete to obtain accurate peak current and voltage. Output, after a scan is captured, can be subsequently sent to the plotter for more permanent records. A Wavetech function generator was used to signal both the Model 175 and the Nicolet 4094 oscilloscope to start simultaneously. The BAS-PA1, a current-to-voltage converter, was used to drive in this case the "y" axis of the Nicolet 4094 oscilloscope. $K_3Fe(CN)_6$ in aqueous electrolyte, was used to calibrate the system. As expected, slow scan rates with a platinum electrode produce "S" type curves typical of microelectrode scans. Fast scan rates produce typical CV curves.

The synthetic organic system P(PSTHP) was tested initially using a silver/silver chloride standard electrode for reference. Ultimately, a silver electrode was used because it holds up to the solutions the best, and there is no water involved to contaminate solutions. This allows multiple runs to be made on the same solution. Scan rates were run from 1 volt to 5,000 volts/second. Concentrations were varied from 1 mM to 10 mM and electrolyte concentrations were from .125 M to 1 M. I_{pc} was plotted vs. $v^{1/2}$.

II.B.1.d. Chronocoulometry to Determine n

Purpose

To measure the number of electrons being transferred in the reduction of the organic material being studied by means of chronocoulometry.

Method

Chronocoulometry was done with an EG & G Princeton Applied Research AT computer-controlled Versastat. Initial tests were run on potassium ferricyanide using a home-made H cell. Several hours were needed to complete one run and
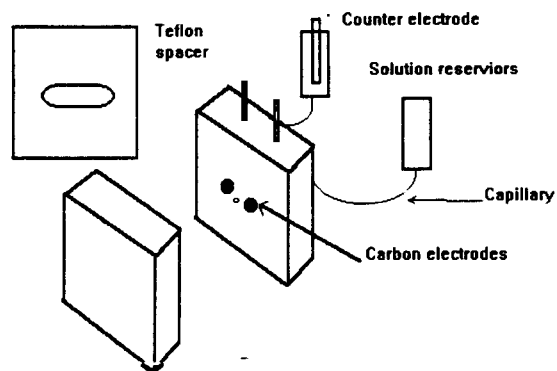

Figure 7   LCEC Cell

integration of the resulting curve was cumbersome. In an attempt to reduce the

solution volume and the electrolysis times, a home-made Teflon cell, holding

approximately 3 mls, was made and tried, and several thin layer cells were tried.

Ultimately, a BAS liquid chromatography electrochemical cell (LCEC), was used

(Figure 7). It was set up to contain, within the cell, one microliter of solution. Short

lengths of microtubing eliminate the need for salt bridges and produce the desired

results in less than five minutes. Material was introduced into the cell through the

capillary tubing. The counter electrode was isolated enough by the capillary tubing

to do chronocoulometry and get some fairly good curves. Analysis of potassium

ferricyanide solution calculates the value of n to be about .98 by the equation:

$$Q=nFW/m \qquad [2.2]$$

where   Q = Coulombs

n = number of electrons

F = Faraday (96,487 coulombs)

W = Weight of sample in grams

m = gram molecular weight of sample species.

Analysis of benzoquinone and anthraquinone shows the value of n to be about 1.7

to 2.0; which is consistent with a 2 electron reduction of the specie.

II.B.1.e. Preparatory Electrolysis

Purpose

To electrolyze sufficient material for further analysis.

Method

The H cell was made from two test tubes with side tubes for electrolysis of larger sample sizes. The two side tubes were connected by heat shrink tubing which contained a small piece of "thirsty glass" to produce a divided H cell (Figure 8). Conventional
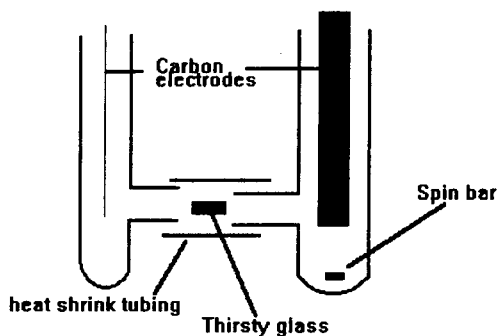
Figure 8   H Cell

sized carbon electrodes were used with Ag\AgCl reference. Conventional

electrodes in the H cell system produced acceptable CV curves. Initial trials with

the PARC model 273 potentiostat and large carbon electrodes gave both voltage

and current overload. These conditions were attributed to the cell and electrode

size. A 13.8 volt, 3 ampere power supply with center tap variable potentiostat as a

voltage divider was constructed. A voltmeter and ammeter were used to monitor the

desired values identified from previous CV curves (Figure 9). Electrolysis was

carried out on about 30 ml of solution. From previous work, one molar tetrabutyl ammonium fluoroborate (TBAF) in dimethylformamide (DMF) was used. A ten mM solution of P(PSTHP) was electrolyzed.

13.8 volt 3 amp supply
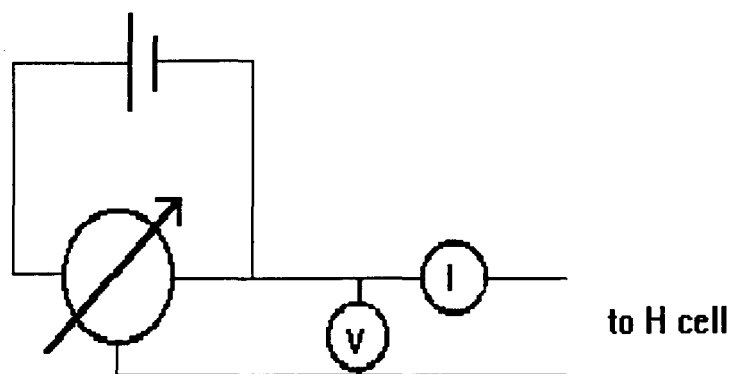
center tap
Figure 9 Electrolysis Schematic

II.B.1.f. Electrolysis Product Workup

Purpose

To separate the organic products from the reaction mixture for analysis and identification.

Method

Conventional methods for solvent extraction, recrystalization and filtration were used to reduce and or remove the electrolyte from the products. The final procedure was quenching with 10 parts ethyl ether, to one part reaction mixture, cooling and gravity filtering using Watman 1 paper. The ether solution was used for TLC and GC as is , and was concentrated down on a Buchi for NMR tests.

II.B.1.g. GC Product Analysis

Purpose

To identify reaction products by gas chromatography.

Method

Six samples were prepared utilizing the "standardized" extraction method devised earlier.

1. unelectrolyzed reaction mixture

2. extracted unreacted mixture 1

3. extracted and washed unreacted mixture 1

4. reaction mixture after electrolysis

5. extracted 4

6. extracted and washed 4.

GC runs were carried out on a Hewlett Packard Model 5890 fitted with a 30 m DB-1 capillary column. The Helium carrier flow rate was 300 mL/minute, the hydrogen flow rate was 30 mL/minute, and the air flow rate was 15 mL/minute. The injector temperature and the flame ionization detector temperature were set at 275°C. The column was prepared by baking at 250°C overnight. The oven was set at 50°C and the ramp was established at 20°C/minute to a maximum of 250°C. Sample injections were 0.5 to 1.0 microliter. Solvent peaks were excluded from the peak integration by setting a 2.5 minute delay.

II.B.1.h. Thin Layer Chromatography

Purpose

To utilize a quick test during electrochemical experiments to see if the desired reaction was being accomplished.

Method

TLC aluminum sheets coated with 0.2 mm of silica gel was cut into strips approximately one inch wide and four to five inches long. A line, in pencil, was drawn about one-half inch from the end. Three marks, equidistant at 90 degree angles to the line, were used to locate the sample spots. Capillary tubes, drawn out of soft glass heated in a Bunsen flame, were used to place spots of sample solution on the marks. A spot of standard, or background, such as electrolyte in solvent, was, for example, placed on the left hash mark. The electrolyzed or organic unknown in solvent was placed on the right hash mark. The combination of the left and right test solutions was placed on the middle hash mark as a control. Tall form, pint jars were used to develop the plates. About one-quarter inch of solvent was placed in the bottom of the jar, and the TLC plate set on end to allow the flow of solvent to travel the length of the strip. The wet appearance of the silica gel was clearly visible, and the plate was removed before the liquid line reached the top. Plates were allowed to air dry, lying flat and viewed under ultraviolet light. The visible spots of organic material were marked with a pencil under the ultraviolet light for a more permanent record.

II.B.1.i. HPLC Analysis of Products

Purpose

To separate the organic products from the reaction mixture for analysis and identification.

Method

TLC plates were produced using washed and unwashed material, and six solvents to identify a solvent system for HPLC analysis. Best separation of peaks was obtained using methanol, for the peaks showing up under ultraviolet light. Anhydrous methanol was used as a solvent. HPLC was conducted on a Waters Model 710 with a 15 cm x 4.6 cm column packed with 5-micron C-18 Regis Spherisorb material. Methanol flow rate was 1.5 ml/minute. The injection sample was 20 microliters and a Waters 481 UV detector set at 210 mm was used.

CHAPTER III

RESULTS AND DISCUSSION

Calibration of equipment was done using potassium ferrocyanide with sodium sulfate as electrolyte in water (Figure 9). The data in Table 1, measured from the curves in Figure 10, was used to produce the cathodic and anodic graphs in Figure 11. The data from Figure 10 and the graphs from Figure 10 show that the system was reversible and diffusion controlled. Applying the Randles-Sevcik equation to this data, the area of the electrode Joe E1 was found to be 0.16 cm^2 and was used in subsequent experiments to calculate diffusion coefficients of unknowns.

Table 1
Test Solution 10mM Fe(CN)$_6^{-3}$ in 1.2M Na$_2$SO$_4$ No N$_2$ Purge

Model 273 Potentiostat					Plotter Settings			
Voltage:			vs. SCE in DIW		X Direction 1x200xmv			
E1, E3			0.8		Y Direction 1x5xua			
E2			-0.2					

Curve Number	Scan Rate	Cathode				Anode			
		Peak Current		Peak Voltage		Peak Current		Peak Voltage	
		Inches	Microamps	Inches	Millivolts	Inches	Microamps	Inches	Millivolts
417	10.0	0.688	3.44	3.250	150.00	0.719	3.59	3.000	200.00
412	25.0	1.313	6.56	3.250	150.00	1.313	6.56	2.906	218.75
413	50.0	1.563	7.81	3.250	150.00	1.500	7.50	2.813	237.50
414	100.0	2.094	10.47	3.313	137.50	1.938	9.69	2.813	237.50
418	150.0	2.438	12.19	3.250	150.00	2.625	13.13	2.500	300.00
415	200.0	2.750	13.75	3.313	137.50	2.594	12.97	2.750	250.00

5µ/inch

200mV/inch

5 mV/s

0.62

2.94

0.94

12.5 mV/s

2.94

100 mV/s

2.25

3.12

1.14

3.00

25 mV/s

1.69

125 mV/s

2.5

3.12

50 mV/s

2.00

3.10

75 mV/s

3.12
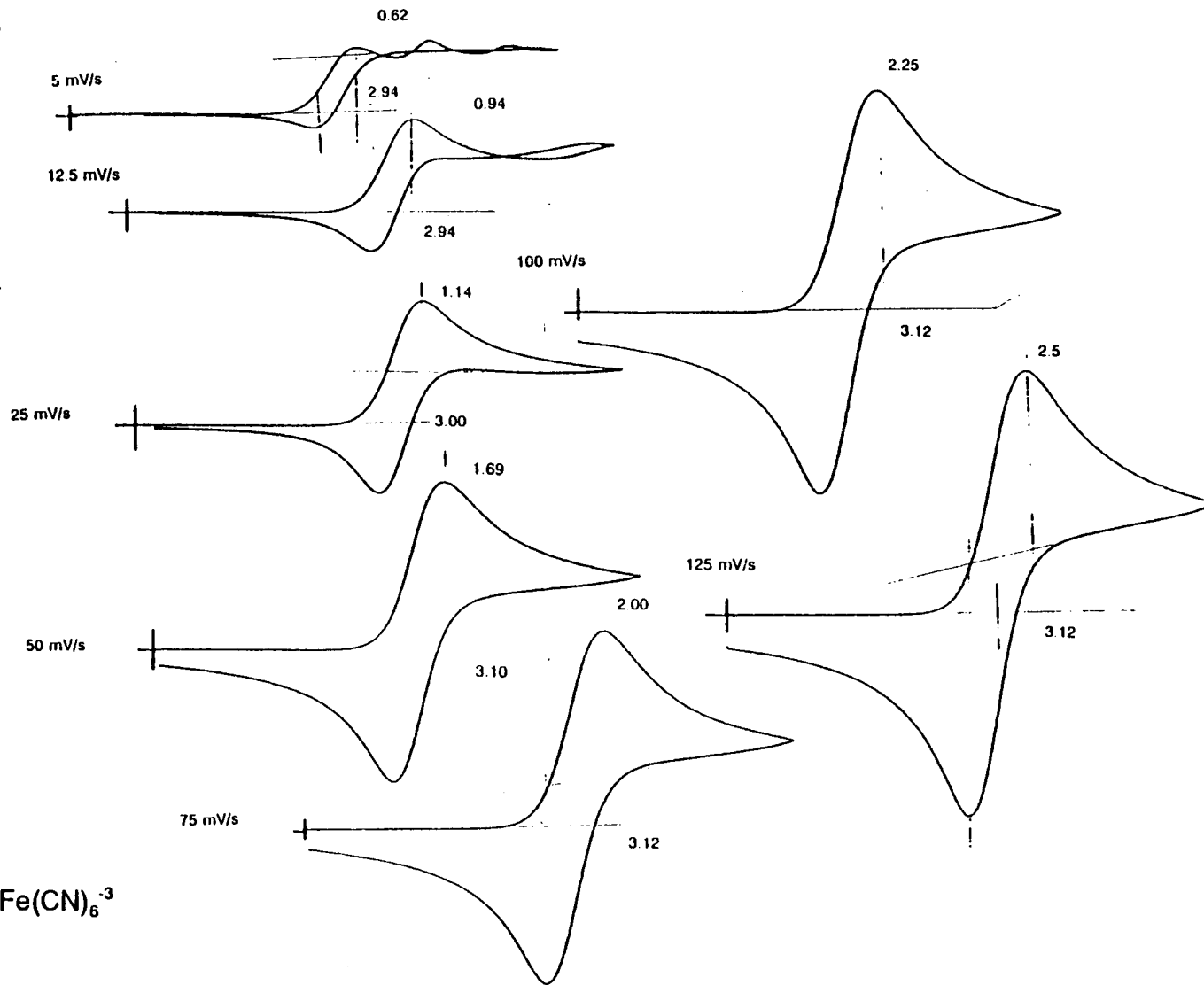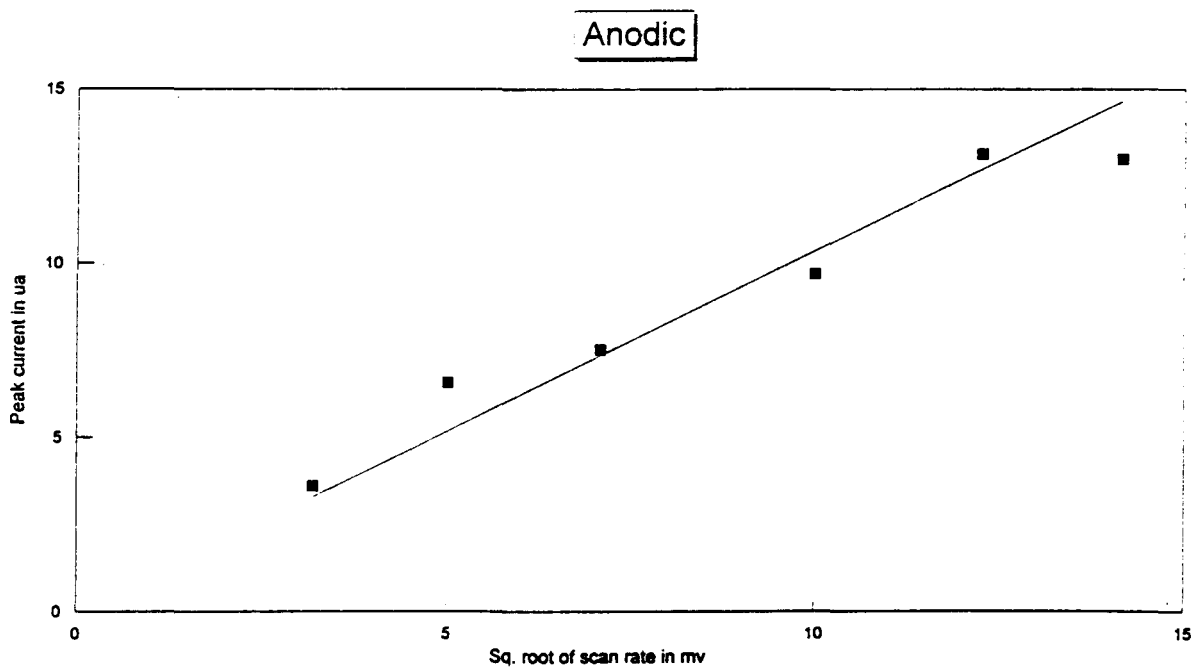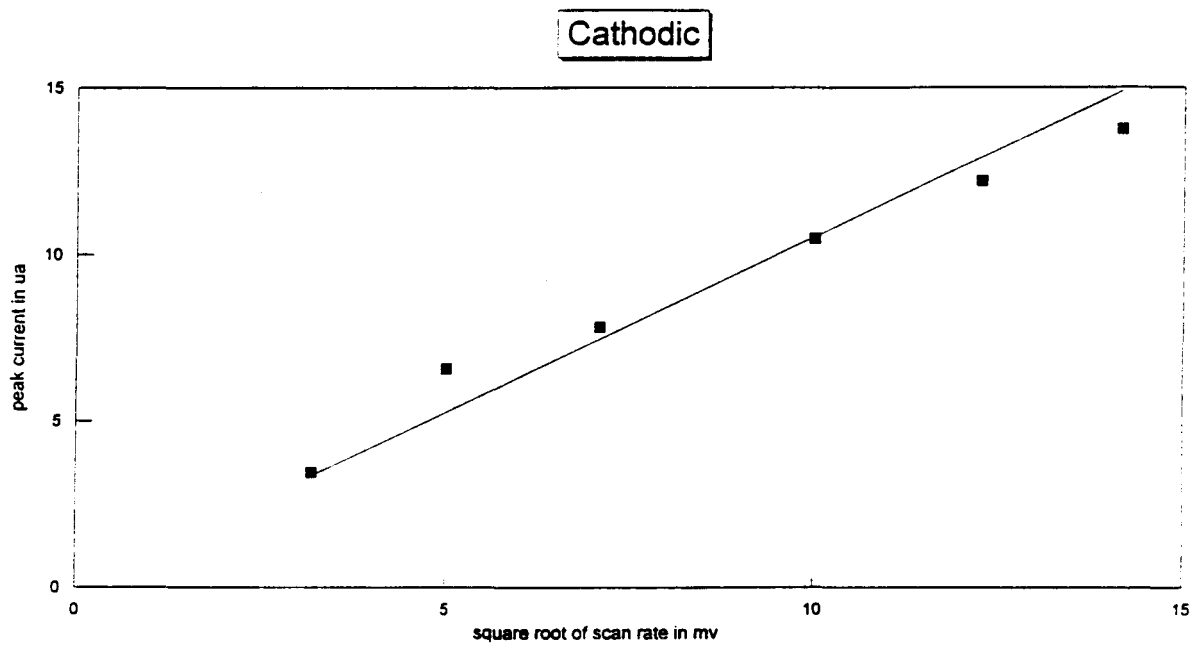
Figure 10   CV of Fe(CN)$_6$$^{-3}$

43

Figure 11   Analysis of Fe(CN)$_6^{-3}$ Cvs

The three analogs were run in acetonitrile with TEAP as electrolyte, a common solvent electrolyte system for organic work. All of the compounds showed similar electrochemical activity. Peaks were found above -2.1 volts (Figure 11) consistent with values reported in the literature.[30] Comparison of the reduction peaks at a scan rate of 50 mV/s are shown in Table 2.

Table 2
Comparison of Reduction Peaks

Analog	Peak Potential in Volts	
	Reduction Peak 1	Reduction Peak 2
cyclo-hexyl	-2.1	-2.5
phenyl	-2.1	-2.4
tert-butyl	-2.4	>-2.8

This data showed that the tert-butyl compound was harder, having a more negative potential, to reduce than the cyclo-hexyl or phenyl compounds. The cyclo-hexyl and phenyl analogs are very similar having shown two reduction peaks at nearly the same potentials. Faster scan rates showed some reversibility for the first electron transferred. Closer inspection of the first electron transfer of the phenyl analog (Figure 12) showed that a reversible cyclic voltammetric curve can be obtained at faster scan rates with microelectrodes if the second reductive peak is avoided by reversing the scan at -2.2 volts. This suggested that the anion radical can be stabilized in acetonitrile with TEAP.
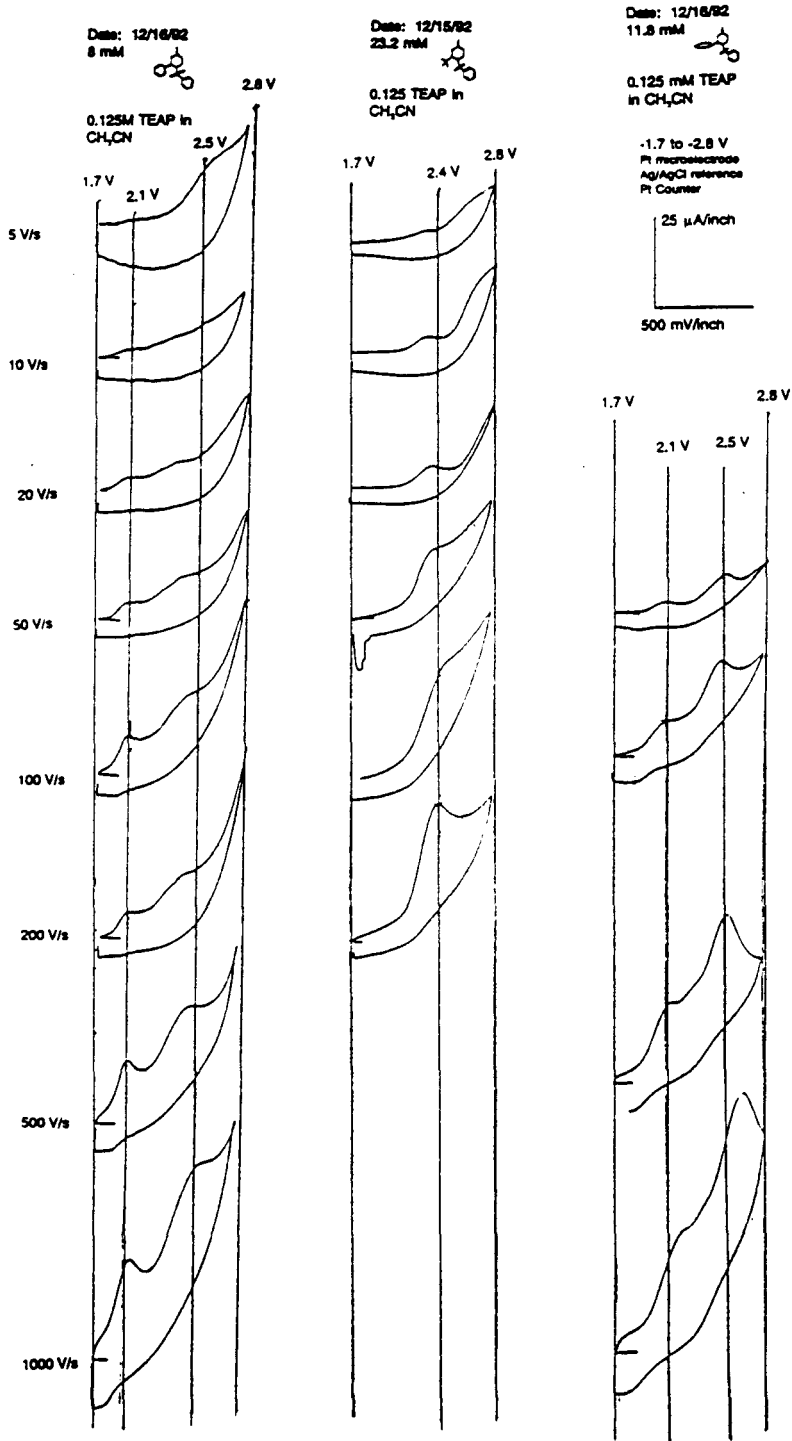
Figure 12   Comparison of 3 Analog Unknowns

Date: 10/13/92
22 mMg

0.125M TEAP in
CH₃CN
Pt microelectrode
Ag/AgCl reference
Pt Counter
-1.7 to -2.2 V

20µA/inch

100 mV/inch

1.7 V   2.0V   2.2 V

10 V/s

50 V/s
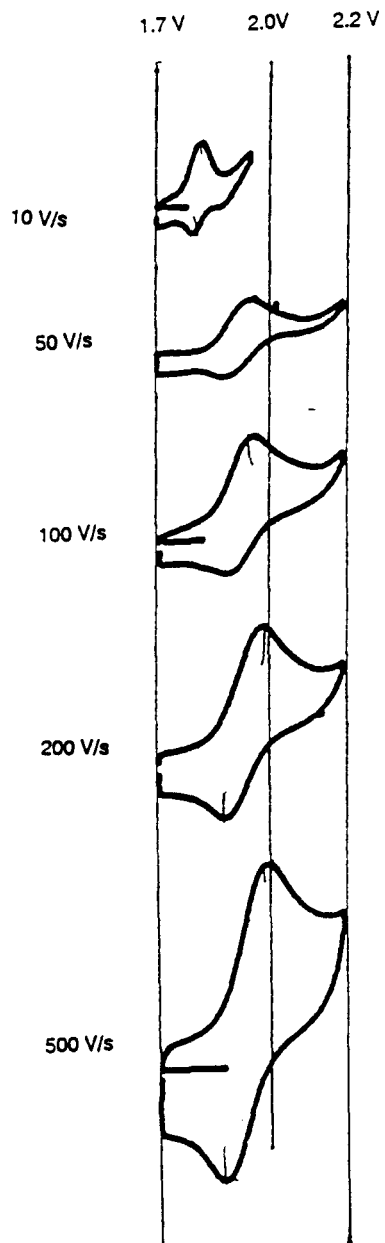
100 V/s

200 V/s

500 V/s

Figure 13   CV of First Reversible Peak

Cyclic voltammetry of the phenyl analog (Figure 13) in a thin layer cell clearly showed a one electron transfer at -2.1 volts with a second electron transferred at -2.4 volts. Chronocoulometry at point D , -2.1 volts (Figure 14), confirms a one electron transfer and a total of two electrons transferred at point E, -2.4 volts (Figure 15). This confirmed that the first peak in Figure 12 was related to a one electron transfer which can be stabilized at high scan rates.

Since the first electron transfer is reversible and diffusion controlled, the Randles-Sivcik equation can be used to calculate the diffusion coefficient. Using for the number of electrons, n = 1, and for the electrode area 0.16 cm^2, the computed diffusion coefficient of the phenyl analog is about 4.25 X 10^{-5} cm^2/s. Comparing this to literature values for organic systems of 2±1 x 10^{-5} cm^2/s, depending on solvent, electrolyte, etc., the faster value is not unexpected based on the cyclic voltammetry curves lacking return peaks.

These results clearly showed that a reversible one electron transfer product can be found for the cyclo-hexyl and phenyl analogs. For the tert-butyl analog, the reaction was more difficult to achieve, requiring a more negative potential, and an irreversible product was found. The data suggest that the tert-butyl substituent was influencing the reduction of the compound. This can be postulated to be an electronic effect, due to changes in the LUMO, or due to a kinetic effect which required a conformational change before an electron transfer could occur.
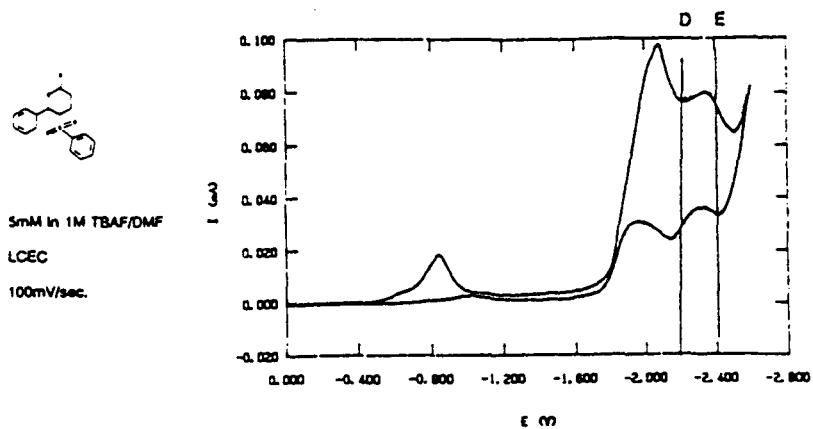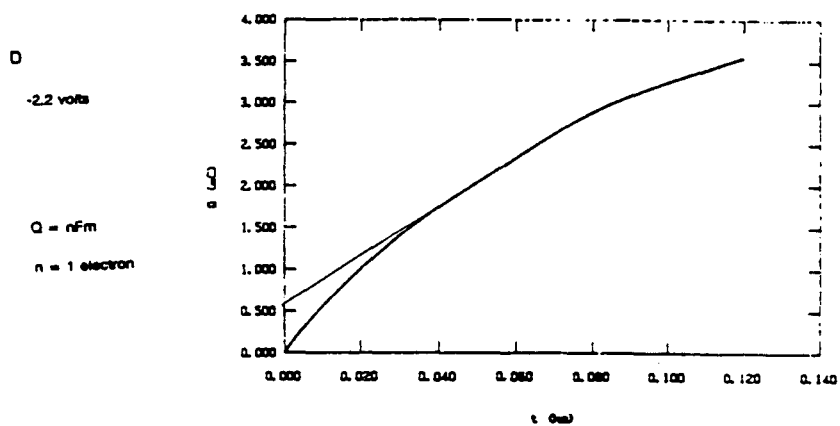
SmM in 1M TBAF/DMF

LCEC

100mV/sec.

Figure 14   CV Using LCEC

D

-2.2 volts

Q = nFm

n = 1 electron

Figure 15   Chronocoulometry at -2.2 Volts
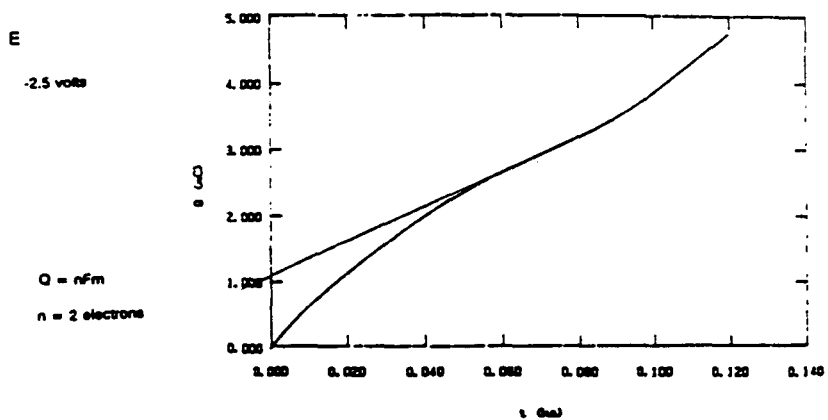

E

-2.5 volts

Q = nFm

n = 2 electrons

Figure 16   Chronocoulometry at -2.5 Volts

The best known example of the electron-transfer-induced isomerization is dialkyl maleate/fumarate system. The addition of an electron to the LUMO produces a rapid isomerization in the radical anion.[55-57] Examples of kinetic effects were noted with tetraalkylhydrazines and dibromocyclohexanes,[54] where nitrogen inversion in the former or ring flips in the latter were noted. Several other examples of conformational changes and isomerizations were reviewed by Evans and O'Connell.

Nicholson and Shain used numerical parameters from cyclic voltammetry to characterize the reactions involved. Through graphic analysis, they were able to identify six types of reactions, each of which are recognized from its own unique set of curves.[58] Savéant and others, as an extension of the Nicholson-Shain examples, analyzed the peak potential (E_P) and the peak width ($E_{P/2}-E_P$) variations with the scan rate (v).[59] From these curves the nature of the mechanism, either concerted or sequential, can be deduced. Mathematical treatment produces bond strengths and relative LUMO energy for the homologs tested, showing that high LUMO energy with low bond strength promoted concerted reactions; the opposite resulted in stepwise reactions. Graphically, low α values together with steep slopes favor concerted reactions. Values of α closer to 0.5 with smaller slopes favor stepwise mechanisms with electron transfer followed by a chemical step. Comparing plots (Figure 16) of the data for Compound 5 curves in Table 3, the phenyl analog, to Savéant's criteria confirmed that we were dealing with an EC mechanism.
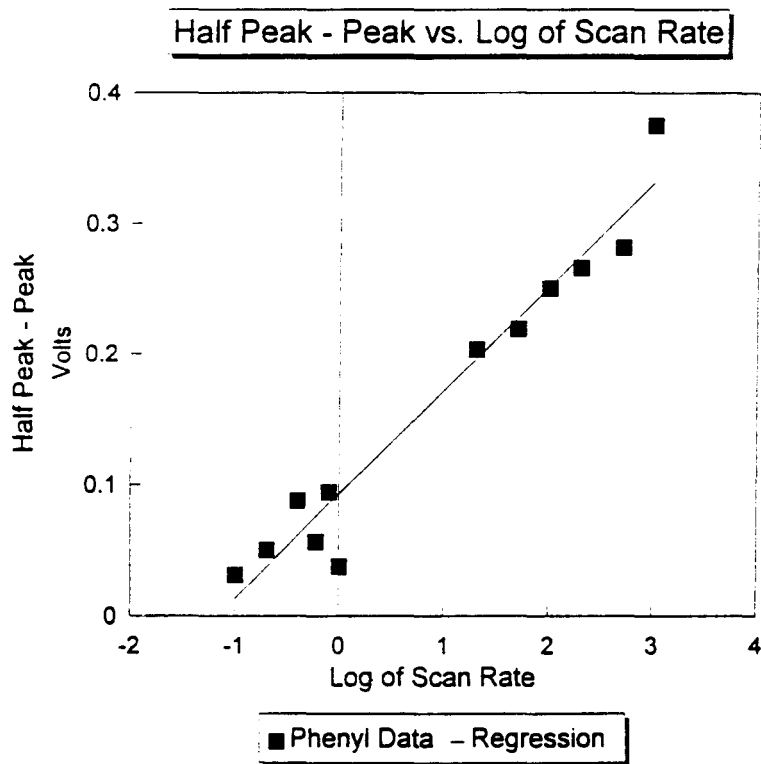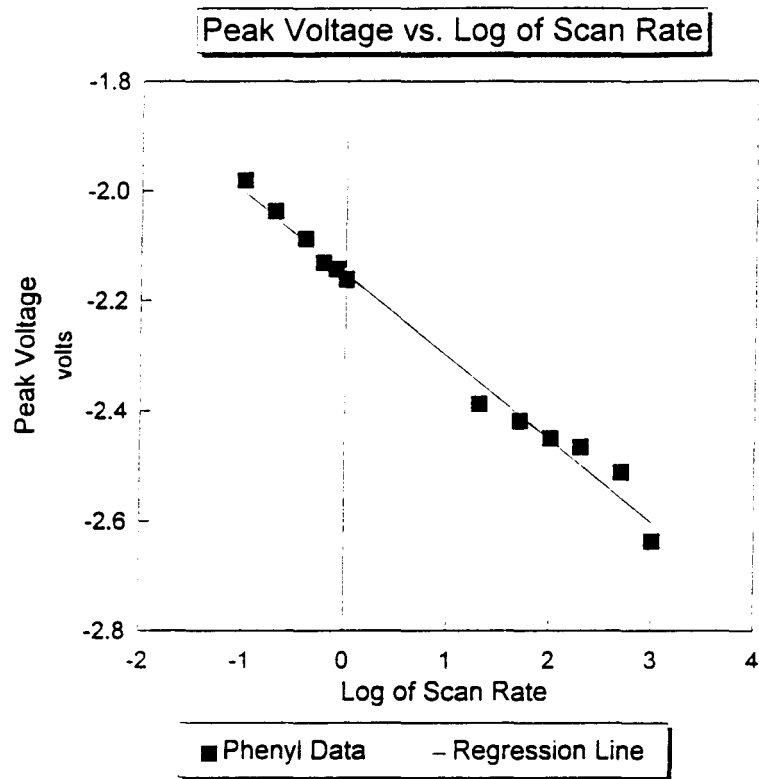
Figure 17   Savéant Analysis

Table 3
Data for Compound 5 Curves

Scan Rate in Volts	Peak Voltage in Inches	Half Peak in Inches	Peak Voltage in Volts	Half Peak - Peak in Volts	Log of Scan Rate	Peak Voltage Y=mX+B	Half Peak - Peak Y=mX+B
0.1	4.906	4.750	-1.981	0.031	-1.000	-2.002	0.013
0.2	5.188	4.938	-2.083	0.050	-0.699	-2.047	0.037
0.4	5.438	5.000	-2.088	0.088	-0.398	-2.092	0.061
0.6	5.656	5.375	-2.131	0.056	-0.222	-2.119	0.075
0.8	5.719	5.250	-2.144	0.094	-0.097	-2.138	0.085
1.0	5.813	5.625	-2.163	0.037	0.000	-2.152	0.092
20.0	1.375	0.969	-2.388	0.203	1.301	-2.348	0.196
50.0	1.438	1.000	-2.419	0.219	1.699	-2.407	0.227
100.0	1.500	1.000	-2.450	0.250	2.000	-2.453	0.251
200.0	1.531	1.000	-2.466	0.266	2.301	-2.498	0.275
500.0	1.625	1.063	-2.513	0.281	2.699	-2.558	0.307
1000.0	1.875	1.125	-2.638	0.375	3.000	-2.603	0.331

The phenyl analog was selected to carry out a comparison of solvents and electrolytes. The systems of DMF/TBAF, DMF/TEAP, AN/TBAF and AN/TEAP were compared in Figure 17. In this study, the potential range was restricted to -2.6 volts, and the scan rates were slower than in the AN/TEAP shown in Figure 13. Recall that for the AN/TEAP system, reversibility was found only at the highest scan rates. At the scan rate shown here, 200 mV/s, reversibility was obtained only in DMF/TBAF. This data suggested solvent or electrolyte electrophilic attack of the reduction product. This mechanism, electrochemical reduction followed by chemical attack is termed an EC. The lack of reversibility in AN was consistent
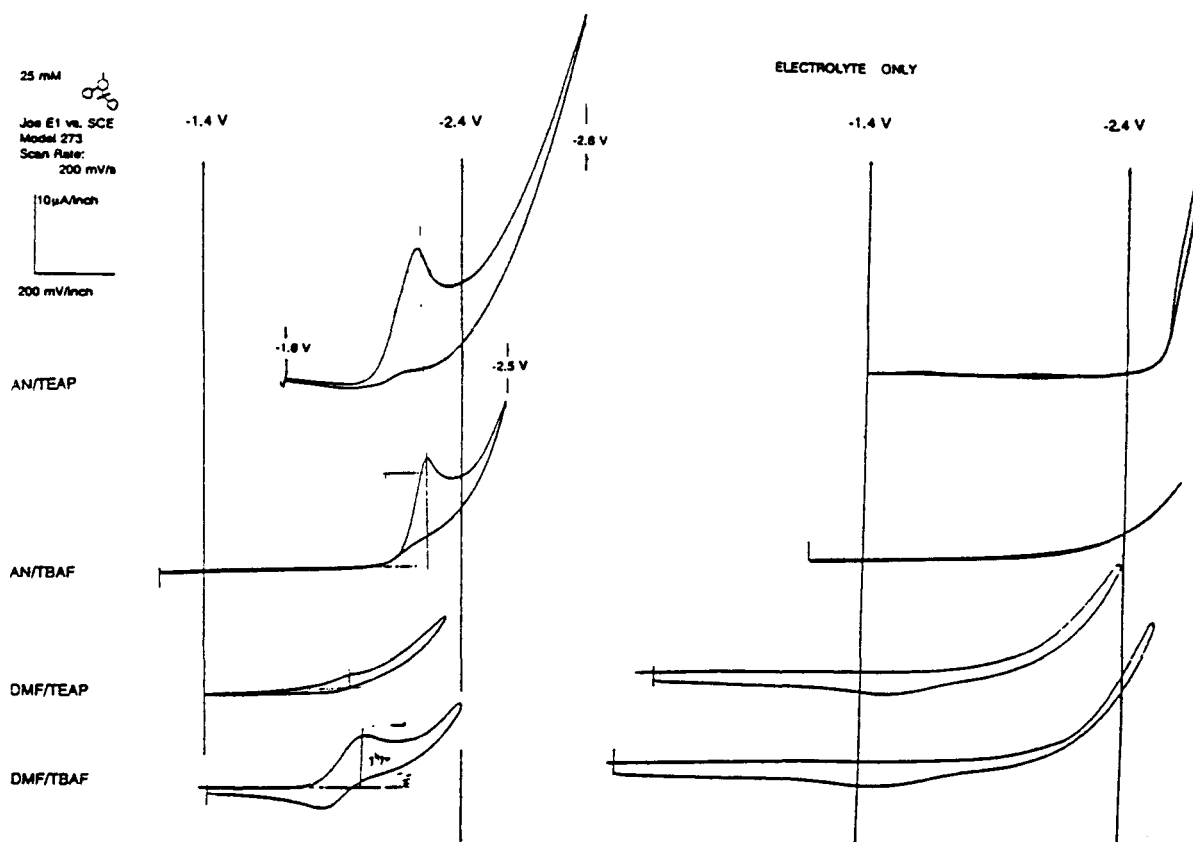
Figure 18   Comparison of Solvents and Electrolytes

with the greater acceptor number of AN (19.3) compared to DMF (16.0), where the acceptor number was a measure of the electrophilicity of the solvent.[60] A puzzling feature of the solvent/electrolyte comparison was the shift to negative potentials for the irreversible reductions in AN. Normally and EC mechanism produced a positive shift in potentials as the following chemical reaction facilitated the electrochemical step.

When AN with TBAF was used (Figure 18), no return peak could be observed, even at a scan rate of 1 V/s, a scan rate which allowed a return peak in AN when TEAP was used. Also of interest is the fact that the following chemical reaction was quite fast, as shown in Figure 19, when the scan rate is increased from 200 mV/s to 1 V/s. No evidence of a return peak was noted, even at 1 V/s. Consistent with the fast following chemical step, these peaks showed a linear dependence upon the square root of the scan rate (Table 4, Figure 19), suggesting that the rate limiting step was a diffusional controlled reduction.

Table 4
Test Solution 0.25mM Phenyl Phenyl Sulfone
0.1M TBAF in CH_3CN

Curve Number	Scan Rate	Cathode			
		Peak Current		Peak Voltage	
		Inches	Milliamps	Inches	Millivolts
305	100.0	1.688	84.38	4.906	-1981.25
306	200.0	2.125	106.25	5.188	-2037.50
307	400.0	2.531	126.56	5.438	-2087.50
308	600.0	3.125	156.25	5.656	-2131.25
309	800.0	3.500	175.00	5.719	-2143.75
310	1000.0	3.875	193.75	5.813	-2162.50

25 mM

Joe E1
vs. SCE
Model 273
0.1M TBAF in
CH₃CN

5mA/inch

200 mV/inch

-1.0 to -2.5V vs SCE

1 69

2 13

4 90

2 53

3.13

3 5

3 88

5 19

5 44

5 66

5 72

5 81

100 mV/s

200 mV/s

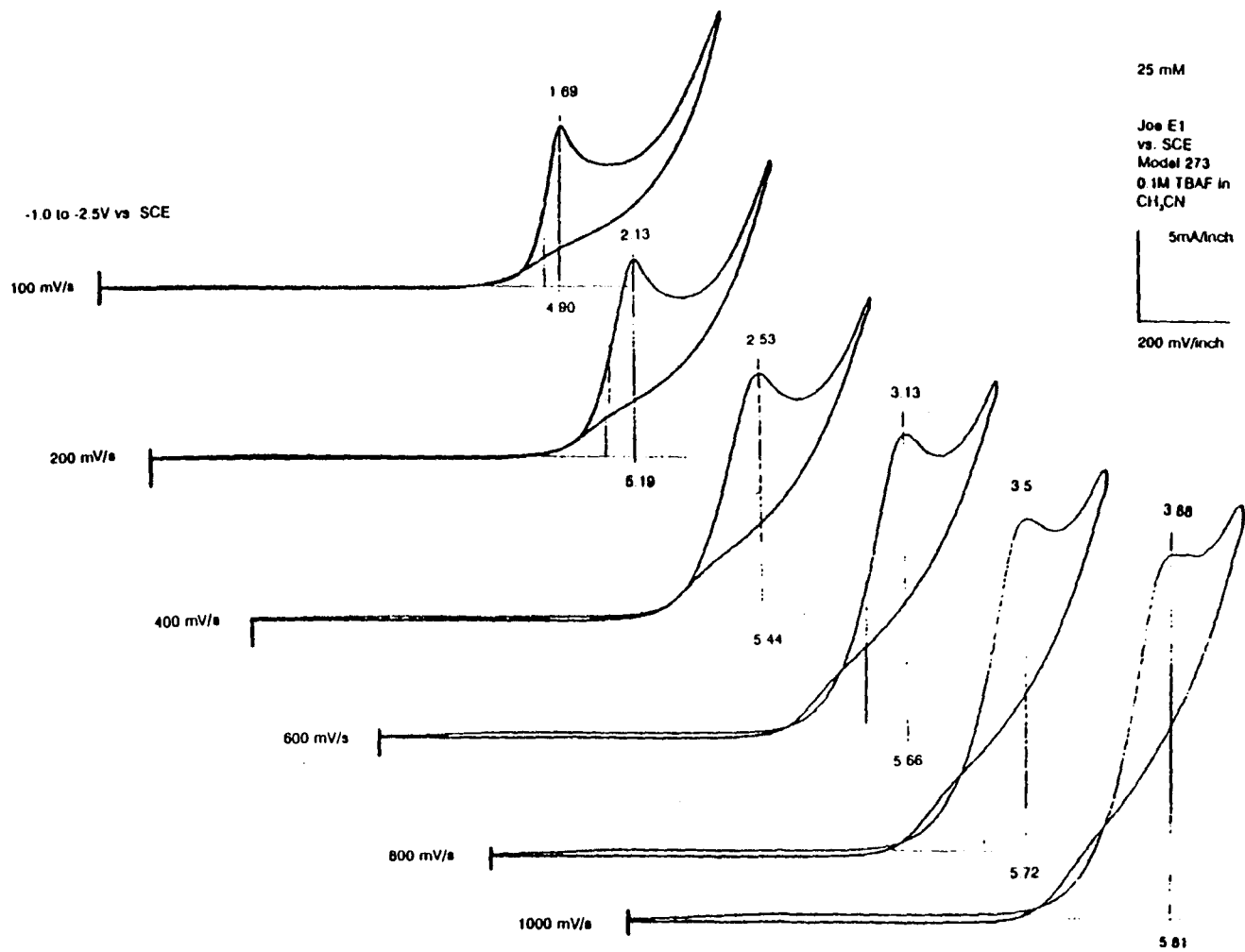400 mV/s

600 mV/s

800 mV/s

1000 mV/s

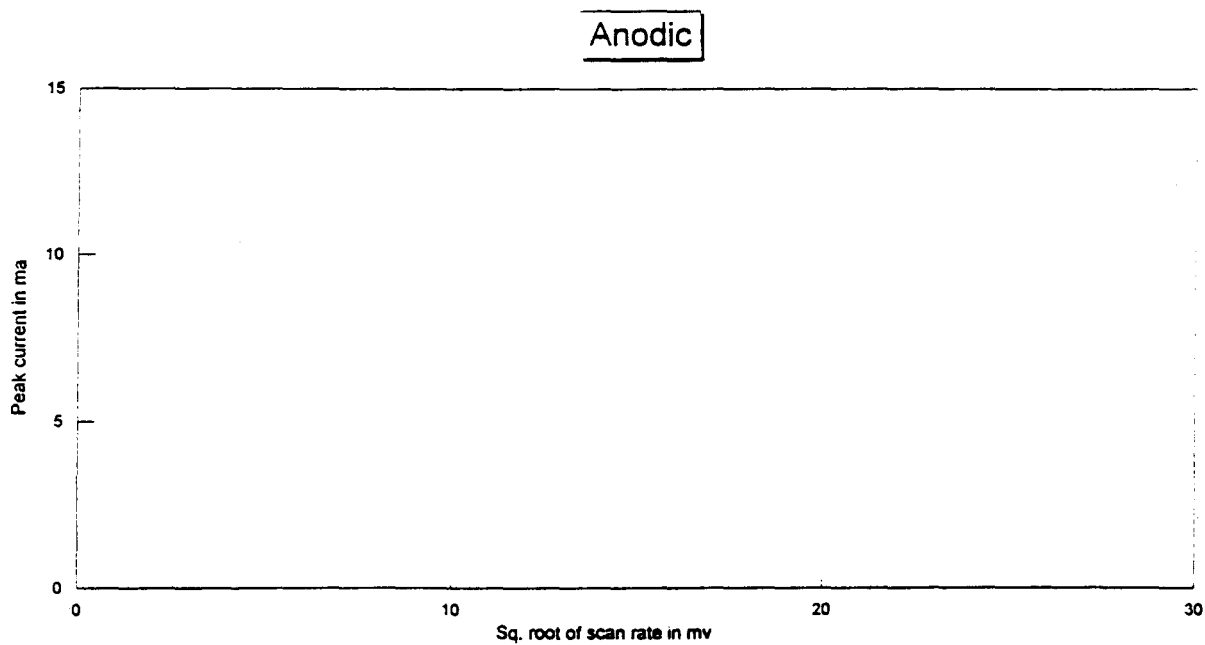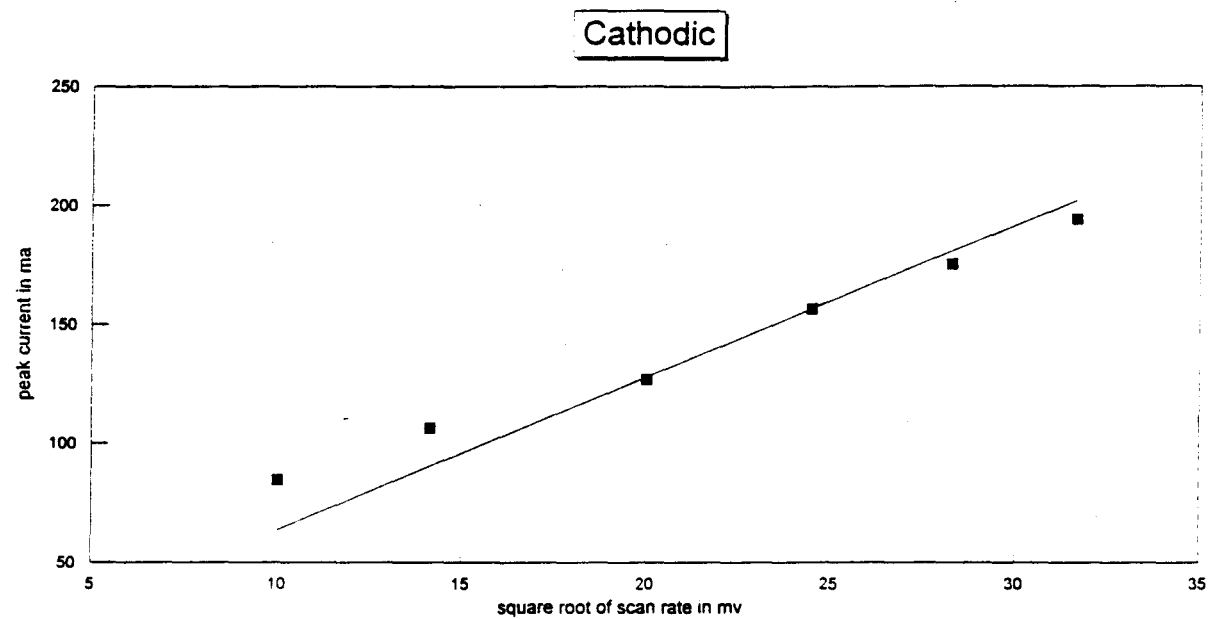Figure 19   Shift of Peak Current with Scan Rate

Figure 20   Analysis of Peak Current Shift

In the presence of DMF/TBAF reversible scans could be obtained up to 1 V/s (Figure 20 and Table 5, Figure 21). Note that the peaks obeyed a nice relationship with the square root of the scan rate.

Table 5
Test Solution 0.1mM Phenyl Phenyl Sulfone
0.1M TBAF in DMF

Model 273 Potentiostat			Plotter Settings				
Voltage:		vs. SCE in DIW	X Direction 1x200xmv				
E1, E3		-1.4	Y Direction 1x5xmA				
E2		-2.4					

Curve Number	Scan Rate	Cathode				Anode			
		Peak Current		Peak Voltage		Peak Current		Peak Voltage	
		Inches	Milliamps	Inches	Millivolts	Inches	Milliamps	Inches	Millivolts
222	100.0	0.344	3.44	2.750	-1950.00	0.188	1.88	2.375	-1875.00
223	200.0	0.438	4.38	2.438	-1887.50	0.188	1.88	2.375	-1875.00
224	400.0	0.594	5.94	2.906	-1981.25	0.375	3.75	2.344	-1868.75
225	600.0	0.656	6.56	2.938	-1987.50	0.406	4.06	2.344	-1868.75
226	800.0	0.750	7.50	2.906	-1981.25	0.438	4.38	2.344	-1868.75
227	1000.0	0.969	9.69	2.938	-1987.50	0.438	4.38	2.344	-1868.75

The products of a 2-electron bulk electrolysis of the phenyl specie (Compound 5) were analyzed by IR, TLC, UV, GC and HPLC. Analysis was complicated by the electrolyte which proved difficult to remove.
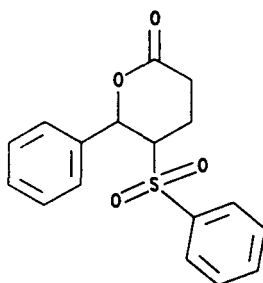
Compound 5
6-phenyl-5-(phenylsulfonyl)-
3,4,5,6-tetrhydropyran-2-one
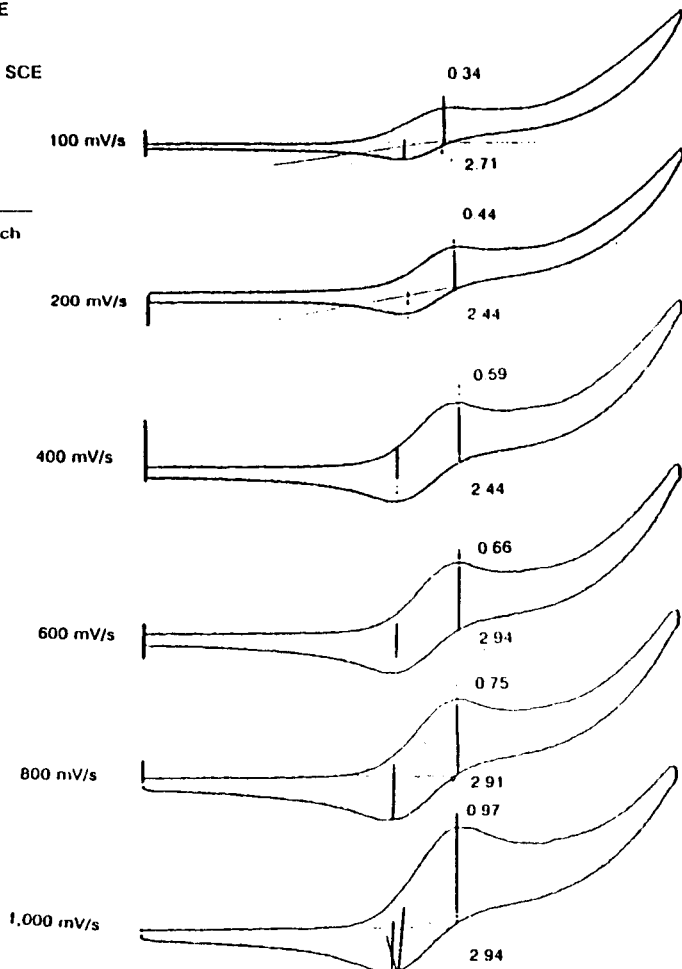mwt. 312.37
P(PSTHP)
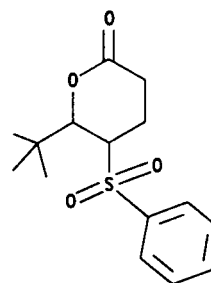
Compound 6
6-tetrabutyl-5-(phenylsulfonyl)-
3,4,5,6-tetrahydropyran-2-one
mwt 292.38
TB(PSTHP)

Date: 2/26/91
0.1mm

0.1M TBAF in DMF
Joe E1 vs. SCE
No N₂ purge
Model 273
-1.4 to -2.4 vs. SCE

10µ/inch

200mV/inch
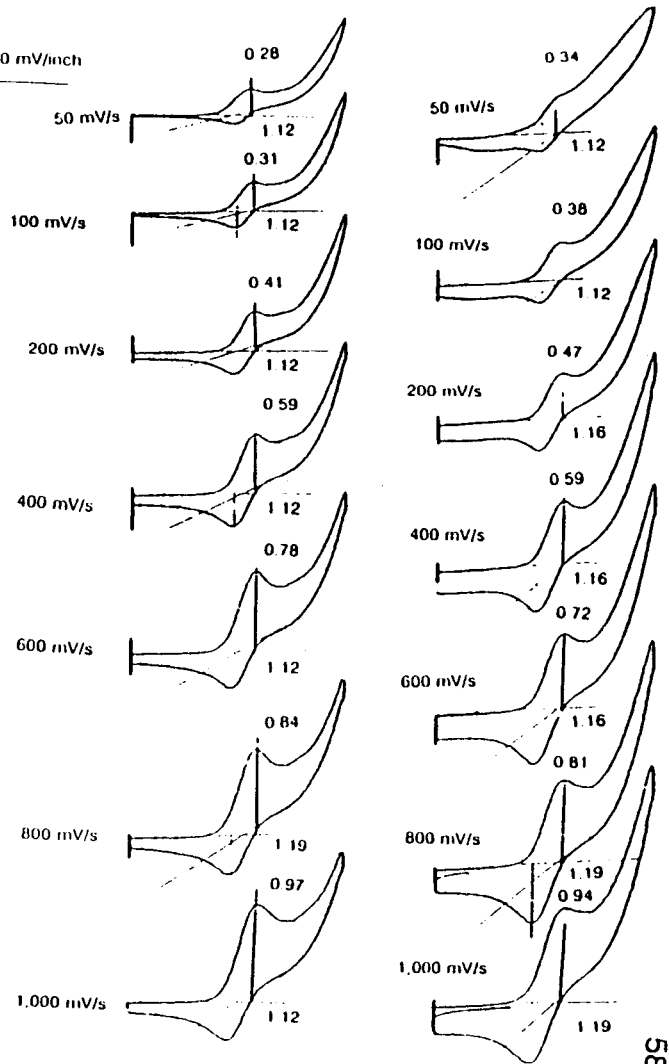
100 mV/s

200 mV/s

400 mV/s

600 mV/s

800 mV/s

1,000 mV/s
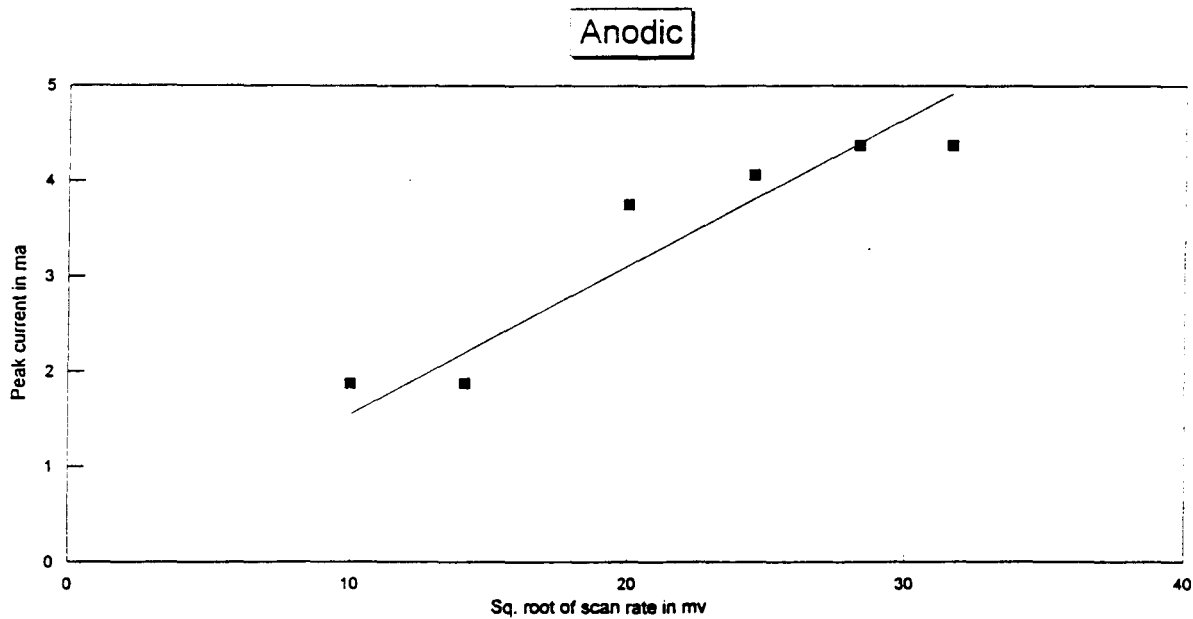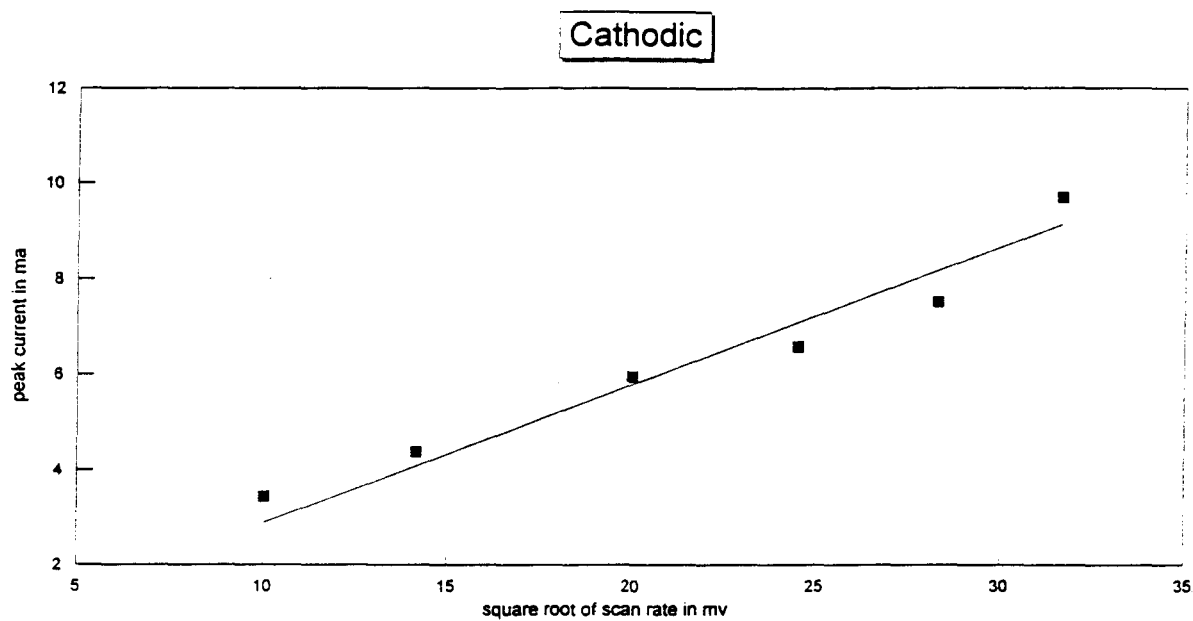
Figure 21   CV of Compound #5

Figure 22   Analysis of Compound #5

IR scans were made of Compound 5, electrolyte, solvent, and sodium phenylsulfite as reference. Unfortunately, the scan of the extracted crystals looked exactly like the reference scan of electrolyte. Several other extraction techniques were tried. Nothing facilitated the separation of product from the electrolyte. All resulting IR scans, while it appeared that the peaks were diminishing, looked like the control scan of the electrolyte.

The product of electrolysis was observed as two spots with TLC, which were unique compared to the salt. The sample preparation procedure is shown in Figure 21, and the resulting TLC plates are shown in Figure 22. Sample 1, the starting material in AN/TEAP, showed two long trails which could have been due to the diastereomers of the starting material as further exemplified in the GC workup below. Sample 6, the AN/TEAP control, showed no spots as expected since the electrolyte and solvent are not UV active. Sample 3, the unelectrolyzed starting material after workup, and sample 5, the electrolyzed material after workup, showed two long trailing spots with crowns. The acid wash may have been hydrolyzing some of the reaction components to carboxylic acid (Scheme 25).
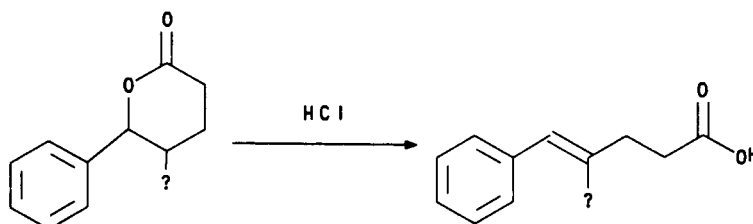
Scheme 25 Acid Wash Reaction

Sample 4, the electrolyzed sample before washing, showed a single long spot. This at least showed that some reaction took place.
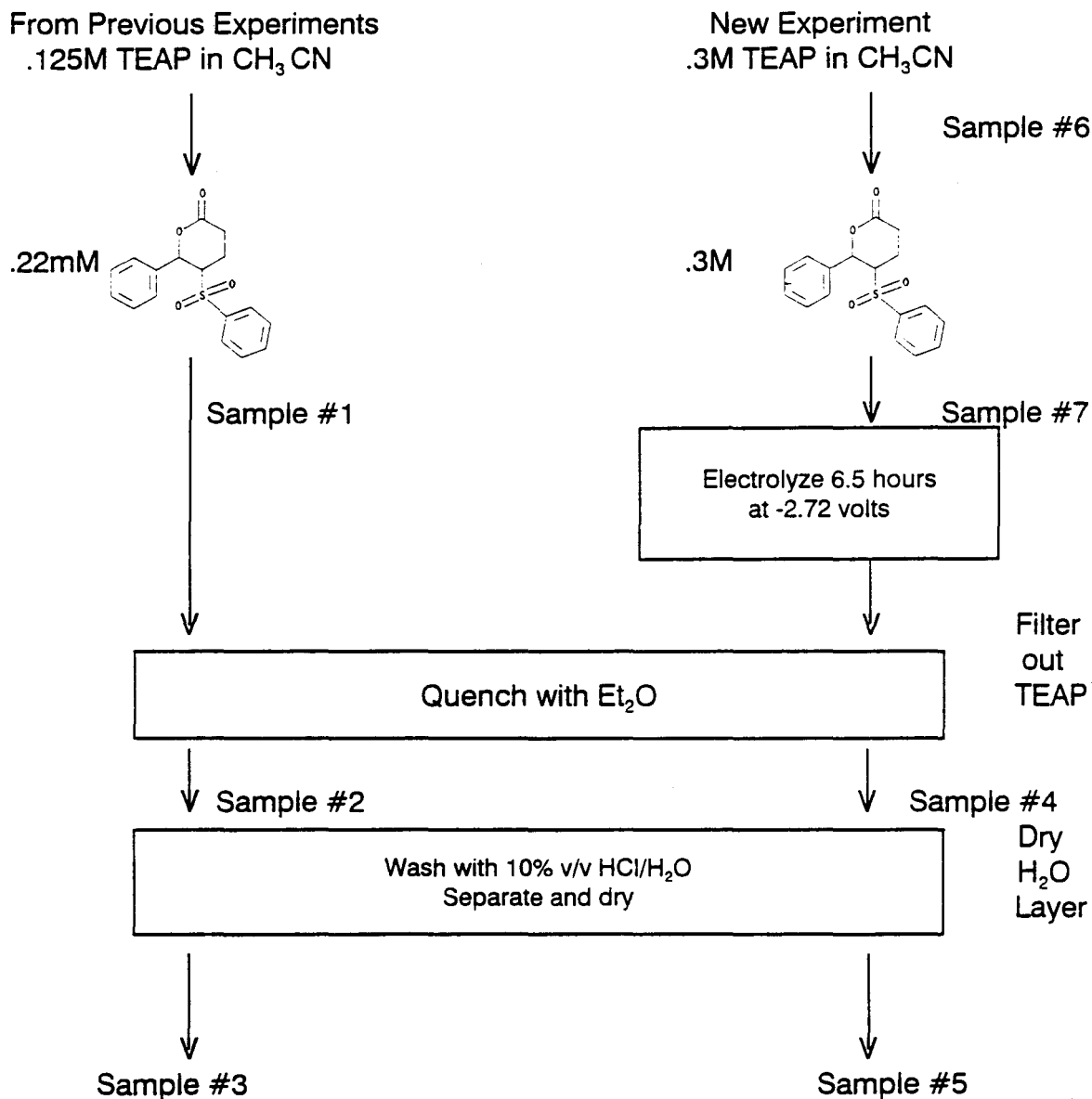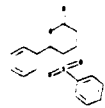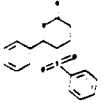
LOCATION OF SAMPLING POINTS

Figure 23   Location of Sampling Points

1. .22mM ⟨structure⟩ .125 mM TEAP in CH₃CN

2. #1 above extracted with Et₂O

3. #1 above extracted with Et₂O, washed with 10% HCl

4. .3M ⟨structure⟩ .3M TEAP in CH₃CN electrolyzed 6 hours and Et₂O extracted.
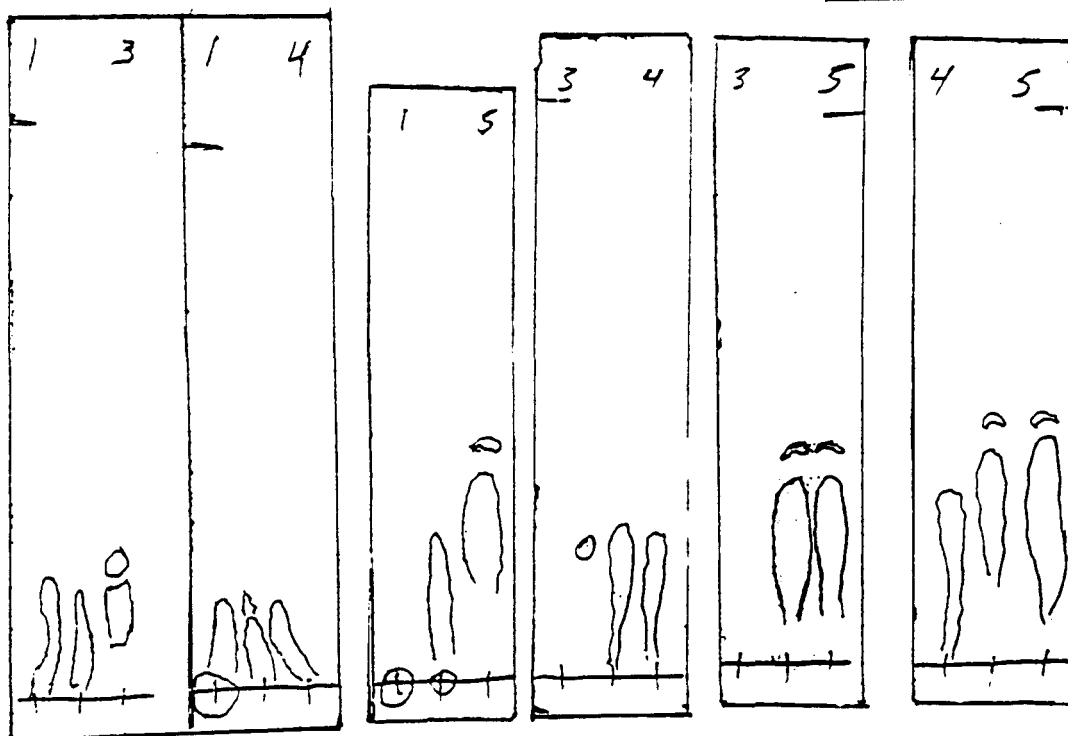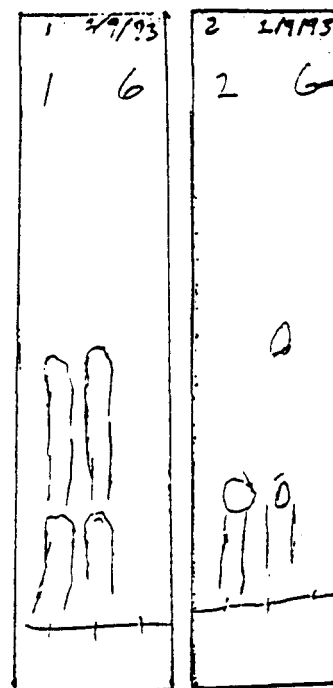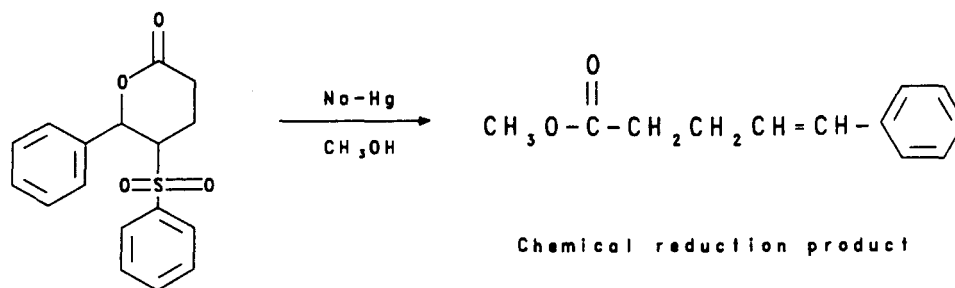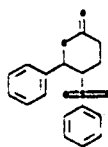
5. #4 above washed with 10% HCl

Figure 24   TLC Plates
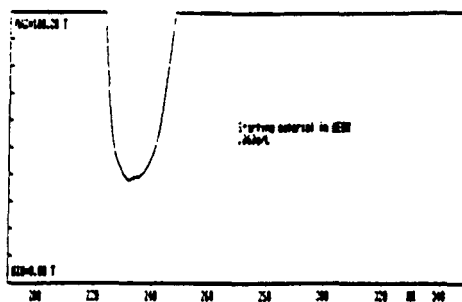
Scheme 26 Chemical Reduction Product

UV scans of the starting material showed a λ max at about 240 nm. The electrolyzed material showed an additional peak at 280/290 nm (Figure 23). The product of chemical reduction (Scheme 26) showed a λ max of 249 nm and no peak around 280/290 nm. This is supporting evidence that the product(s) of electrolysis is not the same as the product of chemical reduction.

GC of the unwashed, electrolyzed sample 4 showed a large number of products (Figure 24). This was not surprising since it was expected that the electrolyte would be carried into the organic layer and decompose into many products upon contact with the high column temperature. The washed, electrolyzed sample 5 showed three or four major peaks. Washing removed some electrolyte (Figure 26, Sample 4, Run 33). The washed sample (Figure 27, Sample 5, Run 22) showed three to four major peaks, a dramatic improvement over the unwashed sample. From this, seven or eight peaks could be assigned to the electrolyte which was removed by the washing. The startup material, run under the same conditions, showed two major peaks at T_R=16.5 and T_R=17.5 which could be assigned to the two diastereomers (Figure 26, starting material, in acetone).
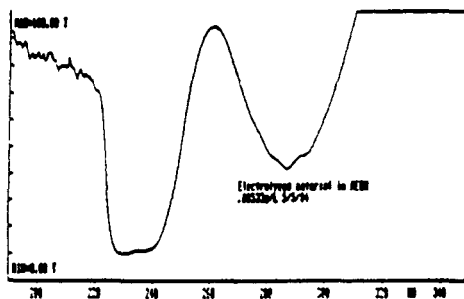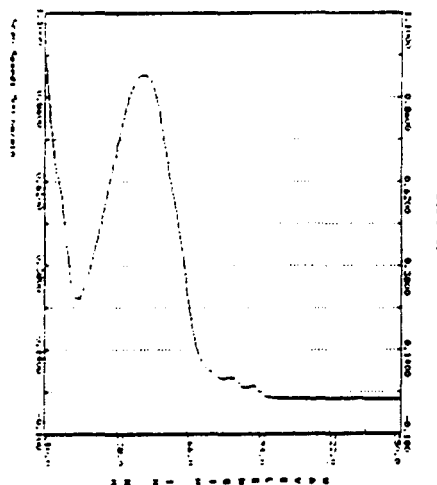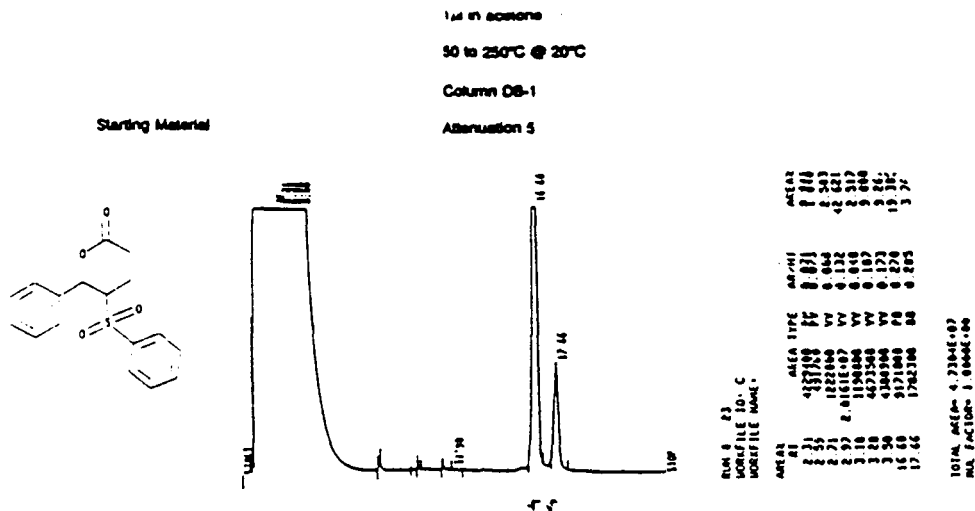
Figure 25   UV Scans

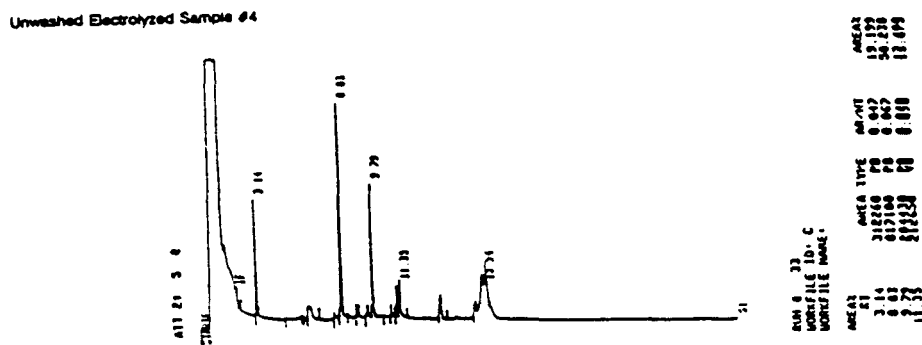Figure 26   GC of Original Unelectrolyzed Unknown

Figure 27   GC of Extracted Electrolyzed Unknown
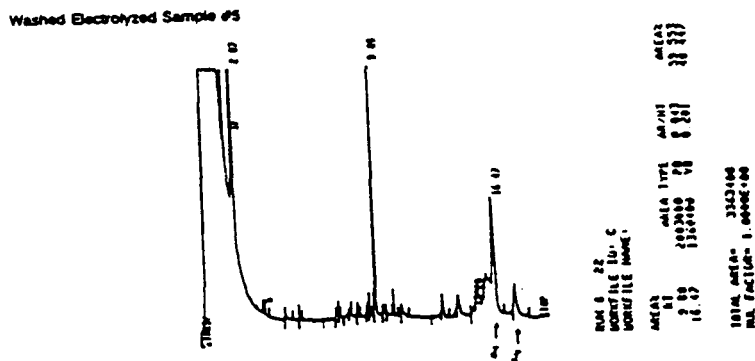
Figure 28   GC of Electrolyzed Washed Unknown

Comparison of the traces showed that two peaks (one major at T_R=9.80 and one minor at T_R=8.06 nm) were unidentified in both the washed and unwashed electrolyzed samples. These should have been the products of interest. After preliminary experiments, all three samples were repeated to ensure identical experimental conditions. Analyses of the GC's indicated that the peak at 9.88 minutes represented the electrolyzed product(s).

HPLC of a recrystallized sample of starting material showed only one major peak at 1.26 minutes (Figure 28). The electrolyzed, washed sample showed at least two, and maybe as many as four peaks eluting by 1.26 minutes.

In summary, while the product of electrolysis had not been obtained in a pure enough and large enough amount to be definitely identified, it had been shown that the two electron electrolysis product did not produce the ring opened species.

Figure 29   HPLC Scans

Two questions were asked initially. The first was whether electrochemical cleavage of a sulfone group, leaving the lactone ring intact was feasible. The second was what the effect of the substituent group was on the cleavage. We found that an electrochemical reduction was observed in the right potential range to be associated with a sulfone cleavage and that the product of that electrolysis differed from the product of chemical (ring opening) cleavage.

We further found that the mechanism of the reduction involved first the production of a stable anion radical, followed by insertion of a second electron with formation of irreversible products. The ease of reduction was affected by the nature of the substituent group, being significantly more difficult (more negative potentials) to achieve for the tert-butyl analog.

CHAPTER IV

FUTURE RESEARCH

Further analysis will attempt to increase the separation of HPLC peaks by adding water in increments, hoping that the hydrophilic components, if any, will elute faster. My colleague hinted at a couple of other techniques that would enhance separation, such as columns that are more or less hydrophilic or other blends of solvents, depending on the results of the added water tests. Again, results look promising, but no definite conclusions yet. We fully believe that separation will be achieved. Once the peaks can be isolated, the preparatory HPLC can then be used to collect pure samples. Pure samples prepared in this way would then give definitive carbon and proton NMR to identify our products.

Joseph E. Lohr, Jr.
1385 Michael Court
Hoffman Estates, IL 60195-1603

May 24, 1995

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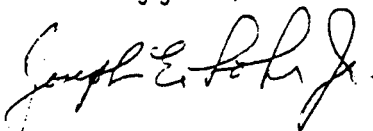
Organic Electrochemistry
Edited by Manuel M. Baizer and Henning. Lund, 1983
Page #1003
Scheme 1 - The electrochemical reactivity of sulphones and sulphoxides.

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I joined Stepan Company in 1969 as a laboratory technician while I completed my education at night school. I completed my Bachelor of Science degree from Elmhurst College in 1972 with co-majors in chemistry and physics. My first fifteen years at Stepan were in the agriculture lab, and I was promoted through the ranks to group leader in 1980. My responsibilities were to utilize Stepan surfactants to emulsify pesticides in water and liquid fertilizer.

During that time, I worked on the American Standards and Test Methods committee for the Standard Emulsion Test.; designed and patented the laboratory agricultural sprayer for testing pesticide emulsions, dispersions and spray compatibility; wrote a paper on spray compatibility which was presented to the ASTM by Norm Smith in 1983; presented a paper on analysis of emulsion optimization by experimental design to ASTM in 1985.

My synthesis activities included developing a Pestilizer line of phosphate esters and sulfo succinate emulsifiers; improving Ninate 401 (Ca dodecylbenzene sulfonate) to current 70% active level; and designing alkoxylated nonionic emulsifiers.

I was promoted to manager of Polyurethanes department in 1985 where I was responsible for project management, budgeting, recruiting for twelve positions in the urethane division. It was at that time that the ozone issue began receiving considerable public attention. I worked on the Society of Plastics Industries

committee on CFCs and co-authored a white paper on Polyurethane insulation properties to educate the Environmental Protection Agency on the extent and requirements of the polyurethane industry to utilize CFCs. I also worked on SPI committees to study and report to the EPA on the impact of CFC legislation and alternative techniques for insulation. During this time, we developed a line of modified isocyanurates for insulation applications to withstand temperatures over 250°F for insulating steam pipes. We installed and debugged Fluidyne computer-optimized models for analysis of polyurethane systems and utilized a video camera for quality control of spray foams. I also helped install several instruments to computers through A to D converters.

I was promoted to Administrator Product Development in 1990. My duties involved budgets, recruiting, project management and operating procedures of the product development laboratory consisting of thirty-four people working in fifteen business areas.

Most currently I have been involved in computer database design and application for data capture and information retrieval. I have completed the training to be certified as both a Crosby facilitator and an Statistical Process Control trainer.

Currently I am employed by Calgene Chemical to develop genetically engineered vegetable oils and derive surfactants and applications for the soap, detergent, lubrication and cosmetic industries.

APPROVAL SHEET

The thesis submitted by Joseph E. Lohr, Jr. has been read and approved by the following committee:

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The final copies have been examined by the director of the thesis, and the signature which appears below verifies the fact that any necessary changes have been incorporated and that the thesis is now given final approval by the Committee with reference to content and form.

This thesis is therefore accepted in partial fulfillment of the requirements for the degree of Master of Chemistry.

_4/4/96_

Date

Alanah Fitch

Director's Signature