ELECTROCHEMICAL REDUCTION OF SOME UNSATURATED ORGANIC COMPOUNDS

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Ph.D.

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To my parents

DECLARATION

I declare that this thesis is my own composition and describes my own work. Where the work of other authors is referred to, this is clearly indicated.

The thesis describes the results of research carried out in the Department of Chemistry, University of Edinburgh, under the supervision of Dr. A.J. Bellamy, and in the Chemical Institute, University of Aarhus, Denmark, under the supervision of Dr. P.E. Iversen, since the 1st October 1974, the date of my admission as a research student.

I attended the following courses and conferences during the three years of research:

One year at Laboratory 29 group seminars in Edinburgh University Chemistry Department; one year at electrochemical group seminars ("Tea Meetings") in the Chemical Institute, University of Aarhus (2 units);

Ten lectures by Professor L.L. Miller on "Ion Radicals in Organic Chemistry" (1 unit);

Ten lectures by Dr. C. Degrand on "Electrochemistry" (1 unit);

Five lectures by Dr. G. Tennant on "Molecular Rearrangements" (1 unit);

Five lectures by Dr. W.D. Cooper and Dr. A.J. Bellamy on "Electrode Reactions" (1 unit);

Five lectures by Dr. D. Leaver on "Organic Sulphur Compounds in General Synthesis" (1 unit);

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John B. Kerr.

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Abstract of Thesis

Three separate systems have been investigated.

Firstly, the electrochemical reduction of some cyclic immonium salts has been examined by means of polarography, cyclic voltammetry, coulometry and preparative electrolysis using aprotic solvents (CH_3CN and DMF) as the medium. The immonium salts were reduced to their two-electron reduction products but only one electron per mol was exchanged. The observation of the corresponding enamine among the products led to an investigation of the mechanism by linear sweep voltammetry and stereochemical analysis. This showed that the immonium cations were reduced to neutral radicals which underwent a radical-radical disproportionation reaction involving hydrogen-atom transfer. The effects of proton donors, ion-pairing and adsorption were also investigated.

The second study concerned the reduction of acetophenone and 3-methylcinnamonitrile in dry (ca. 100ppm H_2O) CH_3CN. Products resulting from attack of the conjugate base of the solvent upon the substrate, 3-hydroxy-3-phenylbutanenitrile and 3-methyl-3-phenylglutaronitrile among others, were observed in addition to the usual dimerization products. The residual water in the solvent has been shown to play a crucial role, the participation of OH^- ions being implicated in the formation of $^-CH_2CN$ ions which then form an adduct with the depolariser. It has been proposed that the residual water affects the stereochemistry of the dimers and that dimerization takes place in solution. Evidence for adsorption has been presented but this does involve the dimerization process.

The third study involved the reductive cleavage of the cyclopropyl ring in certain 1-cyclopropylalkylidenemalononitriles in aprotic solvents. Linear sweep voltammetry and stereochemical analysis have shown that the cleavage proceeds via a radical-ion and that the cleavage mechanism is radical in character. The cleavage reaction has been shown to

be reversible for 2,2-di-alkylsubstituted cyclopropyl rings and irreversible for less substituted rings.

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CHAPTER 1

GENERAL INTRODUCTION

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General Introduction

Since the primary act of any electrochemical process consists of the exchange of an electron between the electrode and the species under study, it is worthwhile to consider, first of all, the characteristics of electron transfer in organic electrochemistry. The study of electron transfer in organic electrochemistry has proven to be somewhat difficult due to the secondary chemical reactions which frequently occur between the electrochemically generated species and its environment. Nevertheless, systems do exist which are amenable to study from both the thermodynamic and kinetic points of view.[1]

The main conclusions of such studies are that, in general, electrochemical reactions proceed by successive electron transfer steps if more than one electron is involved and that such transfers are usually fast. This situation arises due to the relatively large size of organic molecules in comparison with small inorganic ions and a consequent small change in solvation energy involved upon electron transfer. Of course, the situation could change, if, for example, there was an internal electronic rearrangement resulting in a conformational change[2] or bond cleavage.[3]

Bi-electronic transfers are known[4] in organic electrochemistry but in many cases what appears to be a two electron transfer is actually two separate one-electron transfer steps interspersed with a chemical step. The product of the first electron transfer step reacts with its environment to form a species which is either more reducible or more oxidizable than the original substrate molecule. This species is rapidly reduced or oxidized giving the appearance of a two-electron transfer.[5] This kind of reaction, commonly called an ECE reaction (electrochemical, chemical, electrochemical) occurs frequently in organic electrochemistry and, indeed,

most electro-organic processes consist of a series of electron exchanges at the electrode interspersed with secondary chemical reactions either at the electrode surface or in the bulk of the solution.

The mechanistic implication of the studies on electron exchange is that the rate of electron transfer is generally so fast that the overall kinetics of the electrochemical process are controlled by the follow-up chemical reactions and mass transfer. In essence, this means that the electroactive species is reduced or oxidized as soon as it arrives at the electrode surface if the electrode potential is at a value such that mass transfer governs the overall rate of reaction. The resulting species is either carried out into the bulk of the solution where it reacts chemically or it may be reduced or oxidized further depending upon the electrode potential.

The intervening chemical reactions mentioned above may be of various types:

Acid-Base (or more generally, nucleophile-electrophile) These reactions occur between the product of the electron exchange and its medium, in particular the solvent which can act as an acid or a base.

Atom Exchange

In particular, hydrogen atom transfer reactions which can occur between an intermediate species and the solvent and also as a form of disproportionation reaction.

Electron Exchange in Solution

That is, redox reactions in solution between couples produced as a result of the exchange of electrons at the electrode. A notable example of this type of reaction is disproportionation.

Bond Cleavage

These cleavages can be either homolytic or heterolytic and may

involve a leaving group such as an ion or a neutral molecule. On the other hand, the cleavage could involve ring-opening as in the case of cyclopropyl groups.

Dimerization

There are three main types of dimerization reaction:- radical-radical, radical-substrate and ion-substrate.

Reactions on the Electrode Surface

These reactions include all the chemical reactions mentioned above and can take place after either the depolariser or an intermediate has interacted with the electrode surface. The extent of this interaction can vary from very weak physical adsorption to actual bond formation in the form of organometallic compounds.

The properties of the medium, and especially those of the solvent, play an important role in these chemical reactions, the effect being most marked in the case of acid-base type reactions. In general, reduction results in the production of a basic species while oxidation yields an acidic species. Consequently the acid-base properties of the solvent are important. In order to minimise proton transfer from or to the solvent, solvents of low proton donor or acceptor character such as acetonitrile, N, N-dimethylformamide (DMF) and liquid ammonia are commonly used. The main drawback with these solvents, apart from the question of their purity, is that one cannot buffer the medium very adequately which leads, in the case of reductions as will be seen in the present studies, to an ever-increasing basicity of the catholyte medium and an ever-increasing acidity of the anolyte medium as the reaction proceeds. This may mean that the conditions of electrolysis are markedly different at the end of the reaction from those at the beginning and, as a result, the mechanism of reaction may change during the course of a preparative

electrolysis leading to a complex and sometimes unexpected distribution of products.

The present work consists of three separate studies on different systems in aprotic media which involve, at one point or another, almost all the types of chemical reaction mentioned above. In the first study, that of reduction of the immonium cation, the interest lies in dimerization and disproportionation reactions. This system is particularly suitable for such a study since, as the product of the electron transfer is a neutral radical, acid-base reactions are avoided to a great extent. The second study, by contrast, involves acid-base type reactions to such an extent that electron transfer itself is interfered with and leads to unexpected products from the reduction of acetophenone. The third study differs from the first two in that interest lies in an internal reaction of the product of electron transfer in addition to reaction with the medium or another species. Such a study of the ring-cleavage of cyclopropyl groups sheds light upon the structure of the intermediate formed as a result of electron transfer and also illustrates the usefulness of electroanalytical methods for elucidating reaction mechanisms.

The role of the medium is important for all of these studies especially in the second case where it actually becomes involved chemically in the reaction mechanism. In addition to the acid-base properties of the solvent mentioned above, specific solvent effects can be of importance. For example, the well-known inability of DMF to efficiently solvate small localized negative charges[6] can be of importance in the considerations of the mechanisms. Ion-pairing between radical-anions and cations must also be considered and the presence of impurities, such as water, can have effects on the system in addition to their acid-base properties.

The techniques used to investigate the systems studied in this work parallel, at least in outline, the methods normally used to elucidate

reaction mechanisms in organic chemistry e.g. kinetic studies and product distribution. Polarography, cyclic voltammetry and coulometry were the tools with which the kinetics of the system were investigated and preparative electrolysis provided the products. From these products, especially the isomeric distribution of the products, information concerning the reaction intermediates could be inferred in exactly the same manner as in conventional organic chemistry.

CHAPTER 2

ELECTROCHEMICAL REDUCTION OF SOME CYCLIC IMMONIUM SALTS IN APROTIC MEDIA

CHAPTER 2

Electrochemical Reduction of Some Cyclic Immonium Salts In Aprotic Media

Introduction

Oxidative and reductive coupling is one of the most common reactions in organic electrochemistry and one of the most useful for synthetic purposes. A well known example of oxidative coupling is the Kolbe reaction[7] involving the oxidation of carboxylate ions which leads to decarboxylation and coupling of the resulting radicals. In recent years interest in reductive coupling has been kindled by the series of electroreductive coupling syntheses by Baizer and co-workers,[8] especially the commercially important synthesis of adiponitrile from acrylonitrile.[9]

Many groups of workers have investigated reductive dimerization reactions using several different approaches (for reviews, see references 8, 10, 11) and one of the most systematic approaches to the problem of reductive coupling has been that carried out by Saveant and his co-workers in their extensive study of electrodimerization. According to Beck[10], there are 11 different pathways leading to hydrodimers which need to be considered. A full kinetic analysis of the situation taking into account the relative speed of the constituent steps of the pathways has been carried out by Nadjo and Saveant[12] which shows that there are 32 different reaction schemes to be considered. Obviously, given such a complex situation as this, formulation of criteria with which to distinguish the possible mechanisms operating has not been easy and this has necessitated the introduction of certain simplifying assumptions in the initial approach to the problem.[13] Among the possible reaction steps, only three kinds of dimerization reaction and/or diffusion were considered by Saveant and co-workers to be rate determining. Hence (i) only one electron transfer at the surface of the electrode was taken into

account and it was considered as fast, (ii) electron transfers in solution were disregarded, (iii) adsorption of the reacting species at the electrode as well as surface reactions with the electrode material were ignored, (iv) atom-exchange reactions were disregarded and (v) acid-base reactions were completely disregarded.

Given such restrictive assumptions, it then proved possible to reduce the number of possible dimerization mechanisms to only 3. These were considered to be radical-radical coupling (DIM 1), radical-substrate coupling followed by reduction of the product of the coupling (DIM 2), and ion-substrate coupling (DIM 3); the radical was the result of a transfer of one electron from the electrode to the substrate and the ion was the result of a transfer of two electrons. Diagnostic criteria were then formulated to allow the distinction of these mechanisms by means of linear sweep voltammetry behaviour and these were as follows (for 25°C):

DIM 1 - the variation of the peak potential (E_p) as a function of sweep rate (ν) was found to be 19.7mV per decade in the cathodic direction, $(\partial E_p/\partial \log \nu) = -19.7$mV/decade. The variation of the peak potential as a function of the initial concentration (C_o) was found to be 19.7mV per decade in the anodic direction, $(\partial E_p/\partial \log C_o) = 19.7$mV/decade. The peak width (ΔE), that is, the difference between the peak potential and the potential where the current is half that of the peak current, was found to be 38.8mV.

DIM 2 - $\partial E_p/\partial \log \nu = -29.6$mV/decade; $\partial E_p/\partial \log C_o = 29.6$mV/decade; $\Delta E = 58.3$mV.

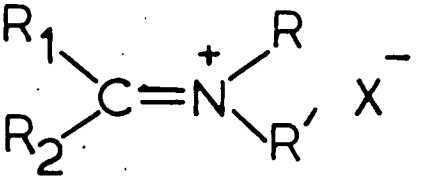
DIM 3 - $\partial E_p/\partial \log \nu = -14.8$mV/decade; $\partial E_p/\partial \log C_o = 14.8$mV/decade.

The obvious problem in applying these criteria lies in the simplifying assumptions which were made in deriving them. From the considerations mentioned previously in the General Introduction, the first assumption concerning the number of electrons transferred and the speed of

such transfers seems justified. However, the possibility of electron transfer in solution is very real and this has been considered in a later paper by Saveant and co-workers.[14] Adsorption phenomena are widespread in organic electrochemistry[15] although their effects can often be small or negligible. Atom-exchange reactions, although not negligible, can for the most part be regarded as an alternative pathway to a radical dimerization process[16] and, consequently should not seriously interfere with the above criteria.

Of all the assumptions, the most severely limiting as regards the applicability of the diagnostic criteria is that of disregarding acid-base reactions. Certainly as far as hydrodimerization is concerned, such criteria are inapplicable, as they are for most systems where the substrate is an uncharged organic molecule, since electron transfer would result in an unstable charged species. However, this assumption is, as mentioned above, a necessary step in simplifying the situation in reductive coupling and systems are known to which the diagnostic criteria are applicable. Such a system is the reduction of the immonium cation[17] in aprotic solvents which was chosen by Andrieux and Saveant as a model to test the diagnostic criteria for dimerization.

Twenty-two different salts of the form

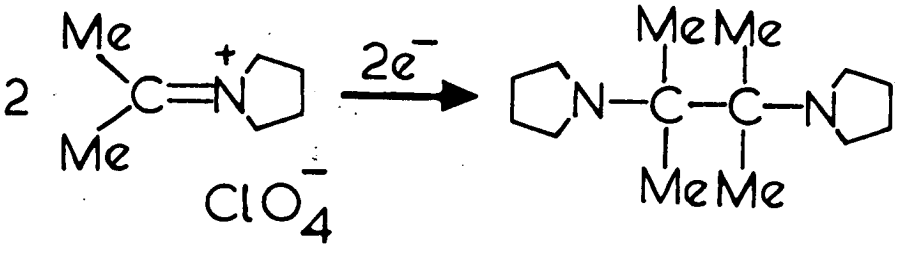


were studied in aprotic media, the main structural effect on the electrode process being by the R_1 and R_2 groups rather than by R and R′. In all but one case R_1 and R_2 were not joined together to form a ring; the one exception being the case where the R_1 R_2 group was derived from camphor. The main feature of the polarograms of the salts (2mM in

acetonitrile containing tetraethylammonium perchlorate as supporting electrolyte) was a one-electron wave at potentials much more anodic than the reduction potential of the parent carbonyl compounds. In some cases a second wave was observed at very negative potentials, the values of which were very dependent upon the presence of acidic impurities (e.g. phenol) in the solution. The first wave, by contrast, was reported to be unaffected by the presence of phenol (up to 6mM) in either potential or height.

Three classes of immonium cation were distinguished by means of their behaviour in cyclic voltammetry. In the first class were cations whose voltammetric pattern was completely irreversible whatever the potential sweep rate, in the second class were cations which exhibited complete reversibility and in the third class were cations whose behaviour was intermediate between the two, exhibiting irreversible behaviour at slow sweep rates but reversible behaviour on increasing the sweep rate. Since the irreversibility was ascribed to a dimerization reaction, preparative electrolyses with the potential fixed on the plateau of the first polarographic wave were undertaken on some salts of the first class and the products were isolated.

e.g.



No evidence for the formation of the monoamine, N-prop-2-ylpyrrolidine, was obtained.

Preparative reductions on salts which exhibited complete reversibility in their voltammetric patterns, produced stable free radicals. This behaviour was observed when R_1 and R_2 were both aromatic and the electron paramagnetic resonance (epr) spectra were recorded. By using a flow system,[18] the epr spectra of some of the less stable radicals were also recorded.

Having shown that radicals were produced on reducing the immonium cation electrolytically and that dimers were formed on electrolysis of the cations belonging to the first class, Andrieux and Saveant proceeded to study the mechanism of dimerization by means of the diagnostic criteria for linear sweep voltammetry. Their conclusion was that the mechanism of the dimerization process was a purely radical one for all the immonium cations studied. Experimental difficulties arose in some cases due to irregularities which were observed in the reduction peaks. These were ascribed to adsorption effects and were avoided by the use of benzonitrile as solvent in place of acetonitrile.

Finally, the rate constant of the dimerization process was measured for those salts which had exhibited partially reversible behaviour. This was accomplished by means of linear sweep voltammetry and triangular, asymmetrical sweep voltammetry,[19] and the accuracy of the two methods was compared.

Prior to the work described above, immonium cations had not been reduced electrolytically although several chemical reductions had been carried out.[20] On the other hand, the electroreduction of saturated ammonium salts had been extensively studied, the products formed on reduction at a mercury cathode being those derived from cleavage reactions.[21] The electroreduction of some heterocyclic enammonium salts in protic media has also been studied by Iversen and Madsen.[22]

In the latter work, the enammonium salts studied were prepared from cyclohexanone enamines and α-chloroacrylonitrile and had the general

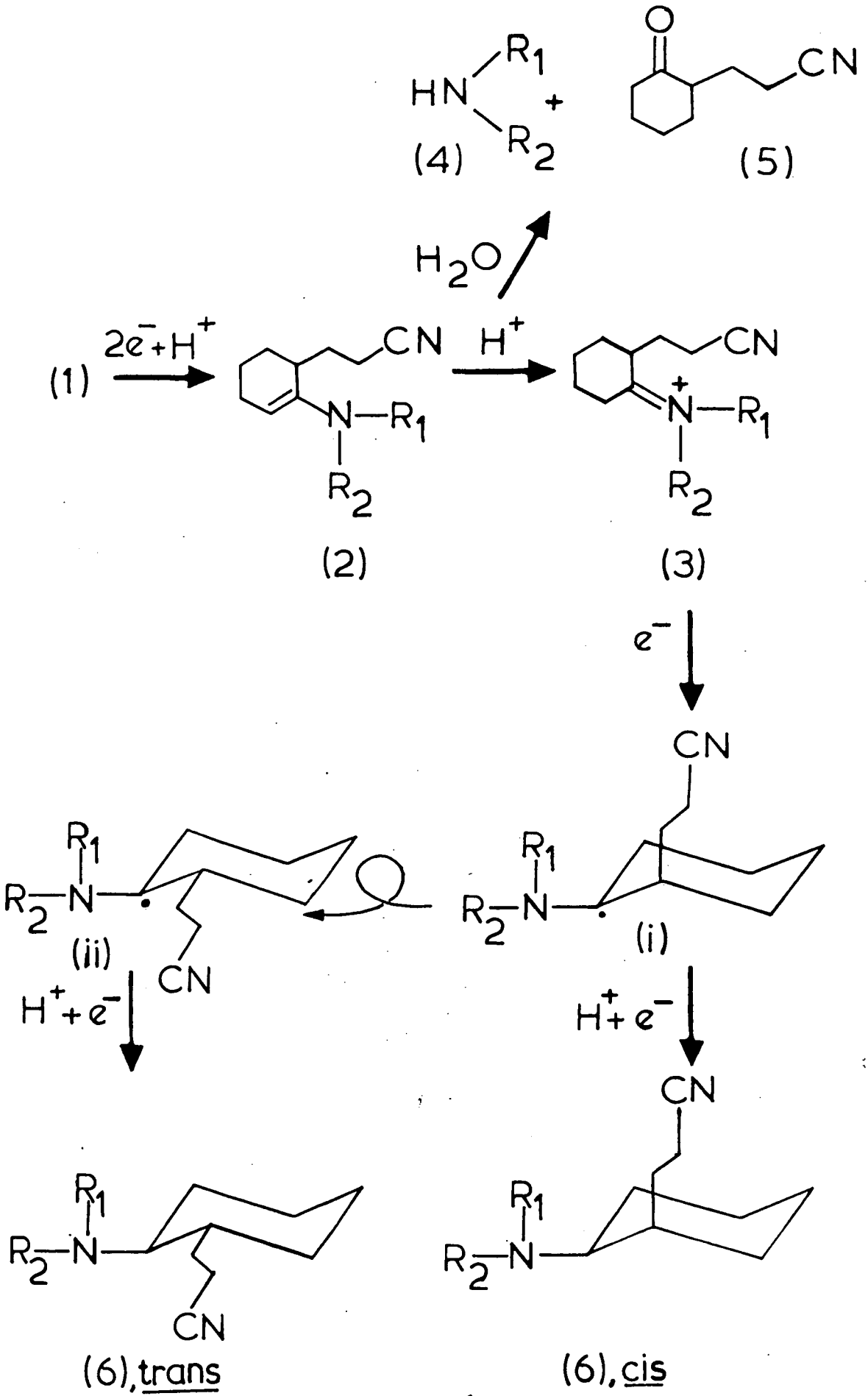
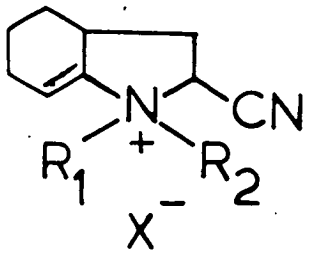

HN
R1
R2
(4)
+
O
CN
(5)
H2O
(1)
2e⁻+H⁺
CN
N—R1
R2
(2)
H⁺
CN
N—R1
R2
(3)
e⁻
CN
R1
R2—N
(i)
R1
R2—N
(ii)
CN
H⁺+e⁻
H⁺+e⁻
CN
R1
R2—N
CN
(6), trans
CN
R1
R2—N
(6), cis

Figure 1

structure:

(1)



1(a): $R_1 = R_2 = CH_3$, X = Cl

1(b): $R_1R_2 = -(CH_2)_4-$; X = ClO_4

1(c): $R_1R_2 = -(CH_2)_5-$; X = Cl

1(d): $R_1R_2 = -(CH_2)_2 - O - (CH_2)_2-$; X = Cl

These salts were reduced polarographically in various aqueous buffer solutions and it was observed that the $E_{\frac{1}{2}}$ of the reduction wave was independent of pH. Preparative reductions showed the uptake of more than $4Fmol^{-1}$ at pH 4.3 and about $3Fmol^{-1}$ at pH 9.4 and the resulting products, compounds (4) - (6) were suggested to be formed according to the scheme shown in Figure 1.

The cis-isomer of (6) was found to be the predominating isomer when the reduction was carried out at pH 4.3, and as the pH was raised (pH 6.7) the amount of the trans-isomer increased until, at pH 9.4, the trans-isomer was the major isomer. The total yield of (6) also decreased on raising the pH. These trends were explained by initial reductive cleavage of (1) to give the enamine (2). In an acidic medium (2) would be rapidly protonated to give the immonium salt (3) which would then be reduced at the electrode to give amine (6). The enamine (2) and the immonium salt (3) are both susceptible to hydrolysis in aqueous solution to give (5), (4) and the protonated form of (4). In neutral and basic solution, protonation of (2) would be expected to be less favoured than in acidic solution giving less opportunity for the formation of (6). This explanation was supported by carrying out reductions of (1b) and (2b) in DMF containing 1M HCl and also of the immonium salt (3b) in aprotic DMF. These reductions gave product distributions which were very similar to that found for the reduction of (1b) in acidic buffer solution.

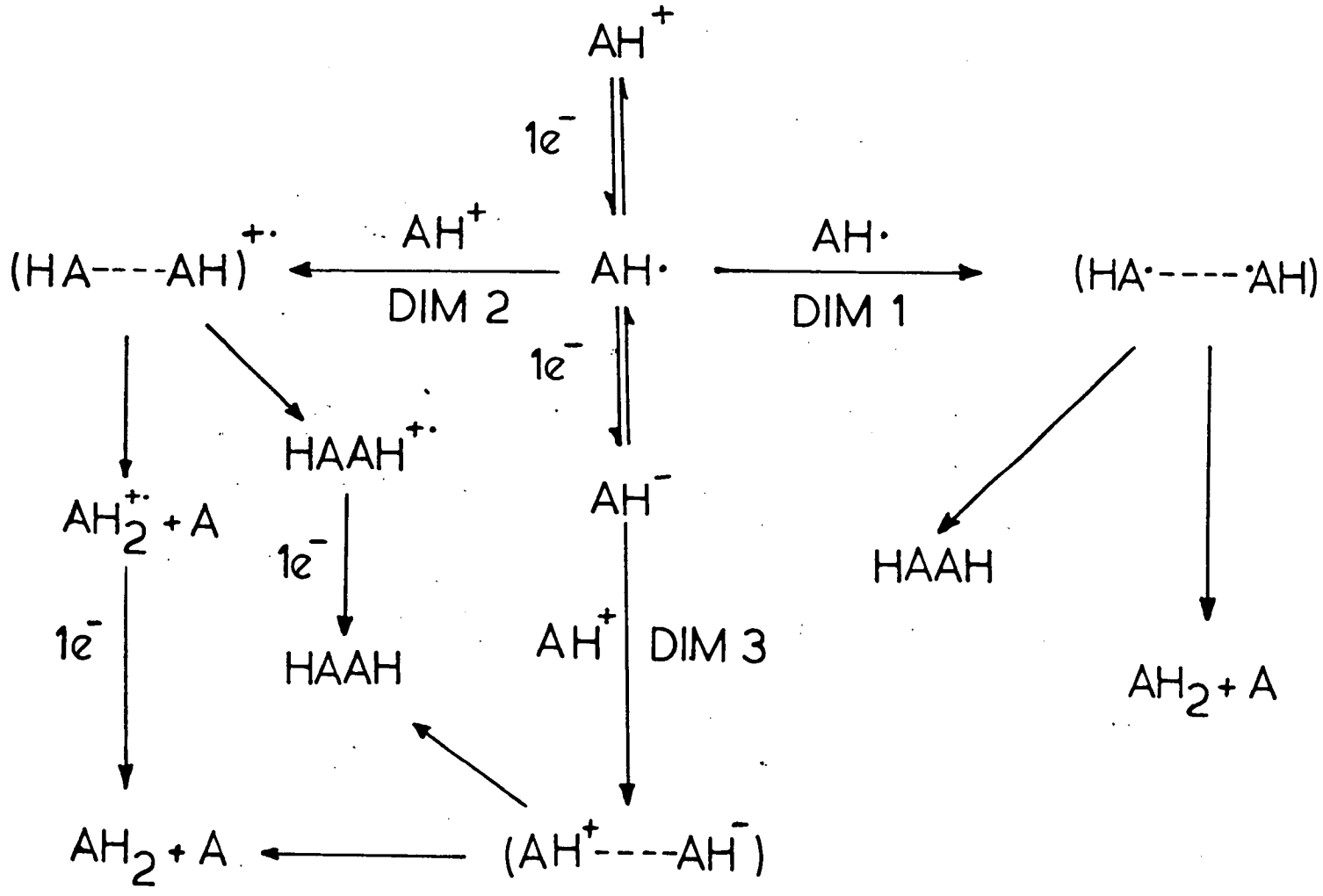

AH+
1e-
AH+
(HA----AH)+·
AH·
AH·
DIM 2
DIM 1
(HA·----·AH)
1e-
HAAH+·
AH-
AH2+·+A
1e-
HAAH
1e-
AH+
DIM 3
HAAH
AH2+A
AH2+A
(AH+----AH-)

Figure 2

The variation of the cis/trans isomer ratios of (6) were explained on the basis that addition of an electron to the immonium salt (3) leads to the neutral radical (i). It was proposed that the nitrogen atom of the radical was rapidly protonated in a low pH medium followed by reduction and proton rearrangement to give cis-(6). However, in a higher pH medium, it was proposed that radical (i) existed for long enough to permit isomerization to what was thought to be the thermodynamically more stable radical (ii) of trans-geometry, which on protonation and reduction gave trans-(6). In the case of the reduction of the immonium salt (3b) in aprotic DMF, it was proposed that the substrate cation acted as a proton donor, donating a proton to the neutral radical (i) which was then reduced to mainly cis-(6), while the immonium cation was transformed into enamine (2b). However, because of the work-up procedure, the enamine was not directly observed. No evidence for the formation of dimeric products similar to those found by Andrieux and Saveant[17] was obtained.

Apart from the obvious difference in the type of product formed, viz. monomerization versus dimerization, which one would expect on steric grounds, a further difference between the work of Iversen and Madsen on one hand and Andrieux and Saveant on the other lies in their respective mechanistic interpretations. This is illustrated by referring to Figure 2 where AH^+ represents the substrate immonium cation, A the corresponding enamine, AH_2 the monoamine such as (6) above and HAAH dimeric products such as those found by Andrieux and Saveant. The important point is the fate of the intermediate radical AH·. Andrieux and Saveant found that this radical meets and reacts with another radical AH· in aprotic solvent, whereas Iversen and Madsen have proposed that it meets and reacts with an immonium cation. The pathway followed after the reaction complex (the parts in parentheses in Figure 2) is formed is of no importance to the kinetics of the system since the kinetic terms are

the same whether monomerization or dimerization follows.[16] Consequently, although the findings of Iversen and Madsen were not unexpected as regards the absence of dimers, their mechanistic interpretation was not in accord with the results of Andrieux and Saveant. This question of whether post-electrochemical reactions proceed via a radical-radical mechanism or a radical-substrate mechanism has also arisen in studies of the electrohydrodimerization reactions of 1, 2-diactivated olefins by both Baizer and co-workers[23-27] and Bard and co-workers.[28,29]

The purpose of the present work in the electrochemical reduction of cyclic immonium salts in aprotic media was to extend the initial work of Iversen and Madsen, to confirm or otherwise the absence of dimers for this kind of immonium cation, to demonstrate the formation of enamine in the monomerization reaction and tc try to reconcile the apparently conflicting mechanistic interpretations.

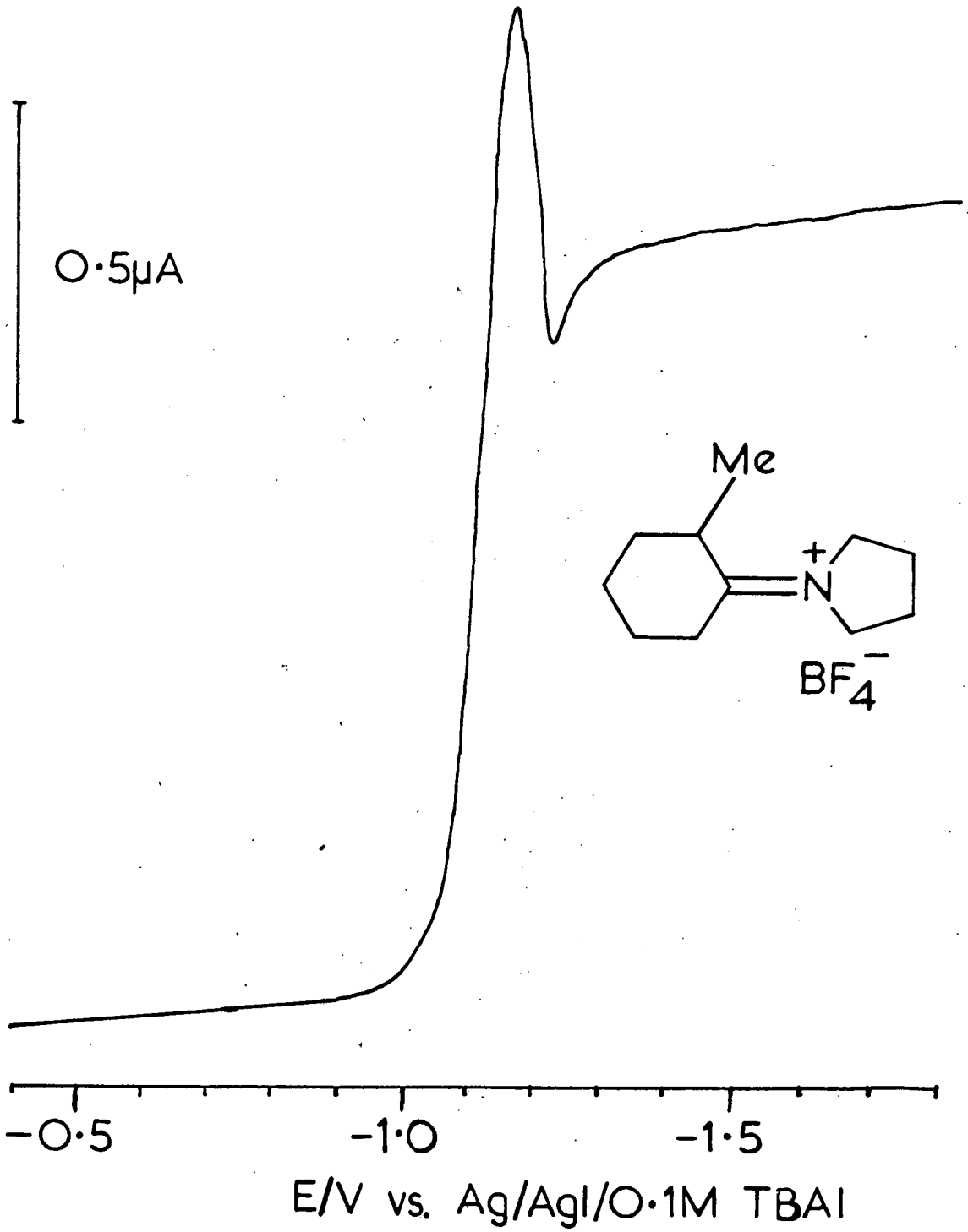


Figure 3. D.C. Polarogram of N-(2-methylcyclohexylidene)pyrrolidinium fluoroborate. conc^{n}. = 4.0 x 10^{-4}M in 0.1M $TBABF_4$-CH_3CN.

Discussion

The four immonium cations which were studied are listed in Table 1. All of the salts were prepared in good yield by the method of Leonard and Paukstelis[30] which involves the condensation of the relevant ketone with pyrrolidinium fluoborate or perchlorate. Attempts to prepare N-(2-methylcyclohexylidene)morpholinium fluoborate by the same method failed. The synthesis of this compound was therefore attempted through the preparation of N-(2-methylcyclohex-1-enyl)morpholine followed by protonation of this enamine by hydrogen chloride. The salt formed in this manner was very hygroscopic and decomposed on exposure to air. However, a more stable salt of this immonium cation was apparently obtained when the chloride anion was exchanged with a perchlorate anion. A non-hygroscopic white solid was isolated which exhibited an i.r. absorption (ν_{max} 1640cm^{-1}) which is characteristic of the immonium cation function. Unfortunately on attempted recrystallization from absolute ethanol, the salt decomposed to 2-methylcyclohexanone and morpholinium perchlorate and lack of time prevented further work upon this compound.

Voltammetry

The results from dc-polarographic measurements are given in the second and third columns of Table 1. The half-wave potentials ($E_{\frac{1}{2}}$) are a little uncertain due to a pronounced maximum which was observed in all cases; a typical polarogram is shown in Figure 3. The $E_{\frac{1}{2}}$- values of all four cations were very similar; this is not surprising considering their closely similar structures. The height of the wave for each salt corresponds to a one-electron reduction since the I_d-value for the first, reversible, one-electron reduction wave of benzophenone under similar conditions was found to be 3.04. This was confirmed by coulometry performed at potentials corresponding to the polarographic plateau current which showed that only one electron was exchanged.

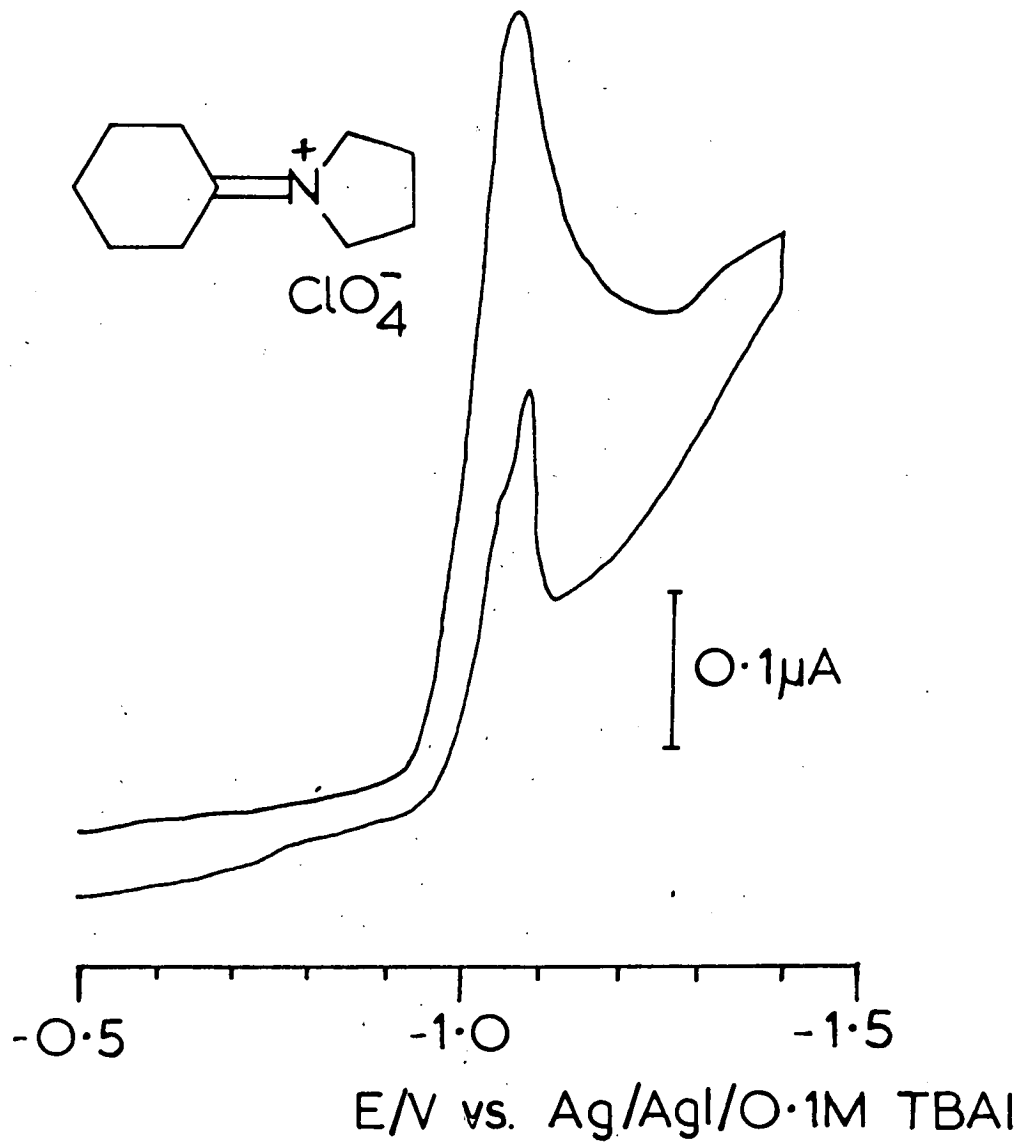


Figure 4. Cyclic Voltammogram of N-cyclohexylidenepyrrolidinium fluoroborate in 0.4M Et_4NClO_4 in CH_3CN.

Hanging Mercury Drop Electrode.

conc^n. = 0.46mM. Sweep Rate = 0.4Vs^{-1}.

The behaviour of the salts in cyclic voltammetry was completely irreversible. No sign of an anodic current was observed at even the highest sweep rates used ($500Vs^{-1}$). A typical cyclic voltammogram employing a hanging mercury drop electrode (hmde) is shown in Figure 4, illustrating the remarkable phenomenon of a cathodic peak during the anodic sweep. This effect was greatest at high concentrations of depolariser and at low sweep rates and it disappeared as the concentration was reduced or the sweep rate was increased. Similar observations have been noted by Andrieux and Saveant.[31] The phenomenon was not entirely reproducible in that it was dependent upon the state of the mercury used in the fabrication of the working electrode. When a long drop-time capillary electrode was employed for cyclic voltammetry, it was noted that twice-distilled mercury was more prone to exhibit the effect than triple-distilled mercury. Furthermore, on addition of the corresponding enamine to the solution, the effect disappeared.

In addition to this phenomenon on the anodic sweep, what appeared to be a maximum was often observed on the initial cathodic sweep. This suggested that streaming of the solution was occurring due to movement of the mercury drop surface. In order to avoid this, solid electrodes such as platinum, vitreous carbon or gold were employed for cyclic voltammetry whereupon the irregularities in the cyclic voltammograms disappeared. Further evidence for ascribing these irregularities to movement of the electrode surface came from the polarograms which exhibited classical maxima of the first kind. A more detailed study of the polarographic situation was achieved by observing the i-f(t) curves which were recorded on growing drops of mercury at various potentials. These are illustrated for N-(2-methylcyclohexylidene)pyrrolidinium fluoroborate (9) in Figure 5. The current for a drop at the steeply rising part of the maximum is represented in Figure 5(a) showing a fairly normal curve except that the current is very much greater than that found with a drop

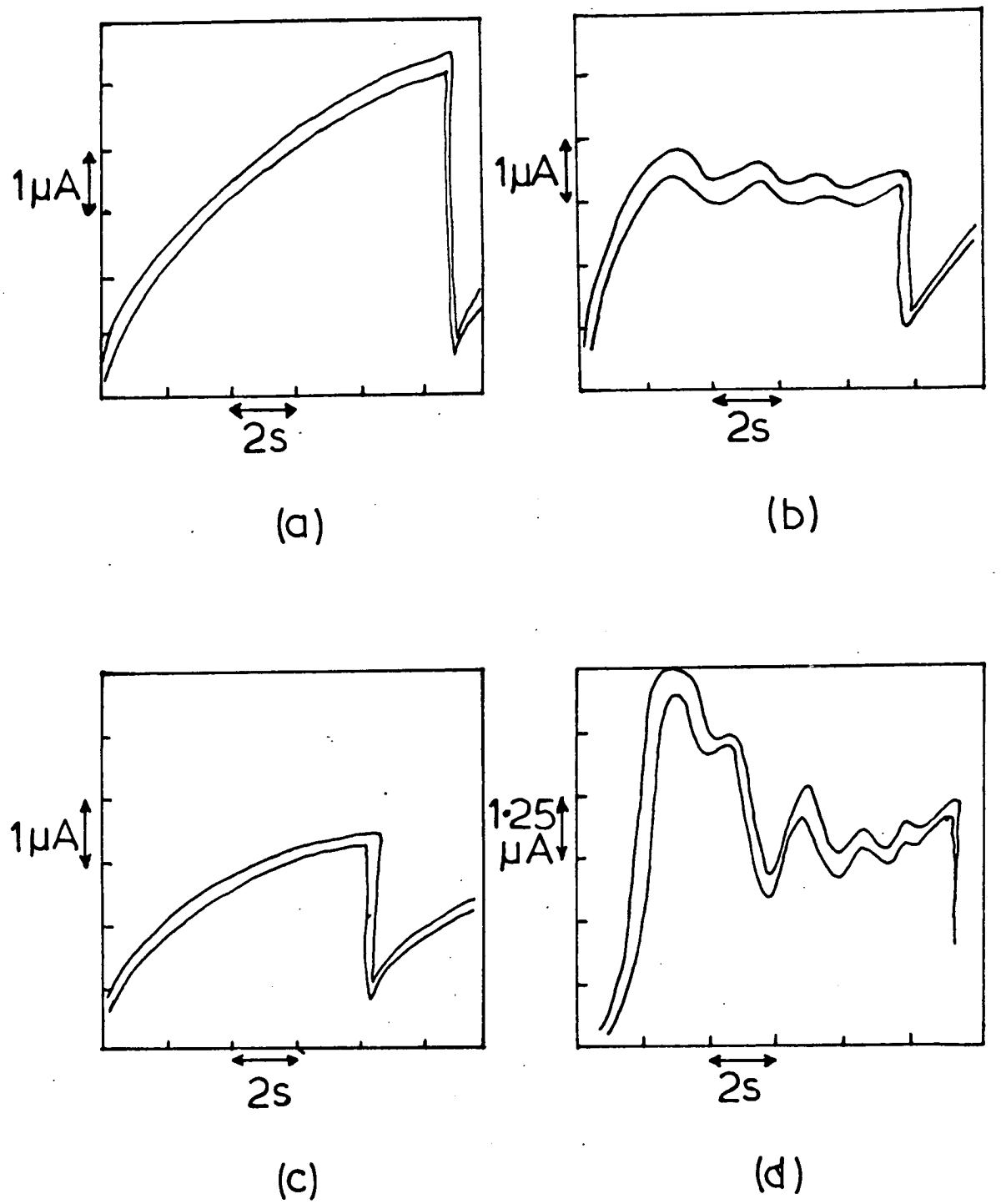


Figure 5. I-f(t) curves of N-(2-methylcyclohexylidene)pyrrolidinium fluoroborate in 0.1M $TBABF_4$-CH_3CN recorded on growing mercury drops. (a), (b) and (c), $conc^n.$ = 0.65mM; (d), $conc^n.$ = 1mM. Working potential vs. Ag/AgI/0.1M TBAI: (a), -1.155V: (b), -1.200V; (c), -1.300V; (d), -1.200V.

whose potential lies on the plateau of the polarographic wave (Figure 5(c)). The situation at the top or falling part of the maximum is illustrated in Figures 5(b) and 5(d) showing the oscillations in the current which are characteristic of a streaming maximum.[32]

The origins of polarographic maxima have been the object of much discussion and several explanations have been proposed (for a review see ref. 32). Different types of polarographic maxima have been identified. Adsorption of some species from the solution seems to be implicated to some extent and is thought to be the prime cause of maxima of the third kind.[33] Polarographic maxima of the first kind, however, are thought to be due mainly to shielding of the drop by the glass of the capillary which eventually leads to a non-uniform interfacial tension of the mercury surface.[34] This variation in surface tension causes the mercury to move from one part of the drop to another drawing surface layers of the solution with it and thus setting up convection current in the solution.

Santhanam and Bard[35] have reported that streaming takes place at a hanging mercury drop electrode during the anodic sweep of cyclic voltammetry carried out on 9, 10-diphenylanthracene in 0.1M TBAI/DMF solution. However, in this case the wave was completely reversible and streaming of the solution resulted in an increase of the anodic current. By contrast, the reduction waves for the immonium salts observed in this study were completely irreversible, indicating that a rapid follow-up chemical reaction was immediately removing the radicals which would be responsible for an anodic wave. It follows then, that any streaming of the solution which occurred would increase the supply of immonium cations to the electrode, resulting in an increase in the <u>cathodic</u> current.

Saveant and Binh[36] have described what appears to be the same effect in the cyclic voltammograms of ethyl- and methyl-triphenylphosphonium cations in acetonitrile which they ascribed to the adsorption of the depolariser and self-inhibition. Interestingly, they found that the

phenomenon was absent when a platinum electrode was used. Similarly, the irregularities observed by Andrieux and Saveant were also ascribed to adsorption and auto-inhibition.[17,31] The possibility of auto-inhibition in the present study on immonium salts appears unlikely from the evidence of the i-f(t) curves shown in Figure 5 which display little resemblance to the curves recorded by Laviron[37,15] for such an inhibiting film. However, the role of adsorption and inhibition obviously will be unclear if the surface of the mercury drop is in motion and adsorption of the depolariser may well be responsible to some extent for initiating streaming. The fact that the presence of the corresponding enamine in solution suppresses the irregularities in the cyclic voltammogram demonstrates the surface activity of this type of compound. Presumably, the enamine is adsorbed on to the surface of the mercury and thus prevents the inequalities of surface tension. Unfortunately, ac-polarographic studies of the capacitance current (tensammetry) were unable to shed any light on the situation.

Despite these difficulties, it proved possible to study the reduction peaks by linear sweep voltammetry. All of the salts 7, 8, 9 and 10 exhibited an anodic shift of peak potential with increasing substrate concentration and a cathodic shift with increasing sweep rate, while the peak widths (ΔE) were in the region of 40 to 45mV. Using a long drop-time capillary electrode and a low concentration of depolariser in order to minimise the effect of the uncompensated cell resistance, the peak potentials were measured for a range of sweep rates. After correcting for the residual uncompensated resistance by comparison with the behaviour of the one-electron, reversible wave of benzophenone under the same conditions (see Experimental), the peak potential values gave linear plots (correlation coefficients > 0.99) against the logarithm of the sweep rate (ν) and the slopes of the lines are given in the fourth column of Table 1.

N-Prop-2-ylidenepyrrolidinium perchlorate (10) had previously been studied by this method[17] using more accurate equipment and is included here as a test of the less sophisticated apparatus used in this study. The value of the slope obtained (22.1mV/decade) using a 1mM concentration is in reasonable agreement with that previously reported (18.1mV/decade). When a lower concentration (0.135mM) was used, the value was found to be 18.1mV/decade.

In agreement with Andrieux and Saveant, the addition of a proton donor such as phenol to the solution was observed to have no effect upon the value of the peak potential. However, for salts (7), (8) and (9) a marked increase in the peak current was observed, particularly in acetonitrile, the magnitude of the increase being dependent upon the proton donor concentration. The effect on the peak height of the N-prop-2-ylidenepyrrolidinium cation (10) was much smaller. The addition of phenol also tended to increase the occurrence of the maxima described above. Consequently, it was hoped that complete removal of acidic impurities by the addition of activated alumina to the solution[38] might decrease the occurrence of the streaming maxima. Unfortunately, this caused the peak to disappear completely, presumably due to strong adsorption of the substrate on to the alumina.

It proved very difficult to study the voltammetry of the salts in the presence of lithium cations due to the proximity of the reduction waves to the discharge potential of lithium. However, it appears that the peak potential is unaffected by the presence of lithium cations. The behaviour is very similar to that observed in the absence of lithium e.g. ΔE = ca.45mV, showing that the lithium cations had little effect upon the kinetics of the reaction.

The observed voltammetric patterns are very similar to that exhibited by the immonium cations studied by Andrieux and Saveant, e.g. ΔE, $\partial E_p / \partial \log \nu$ values. Thus some form of radical-radical reaction is indicated.

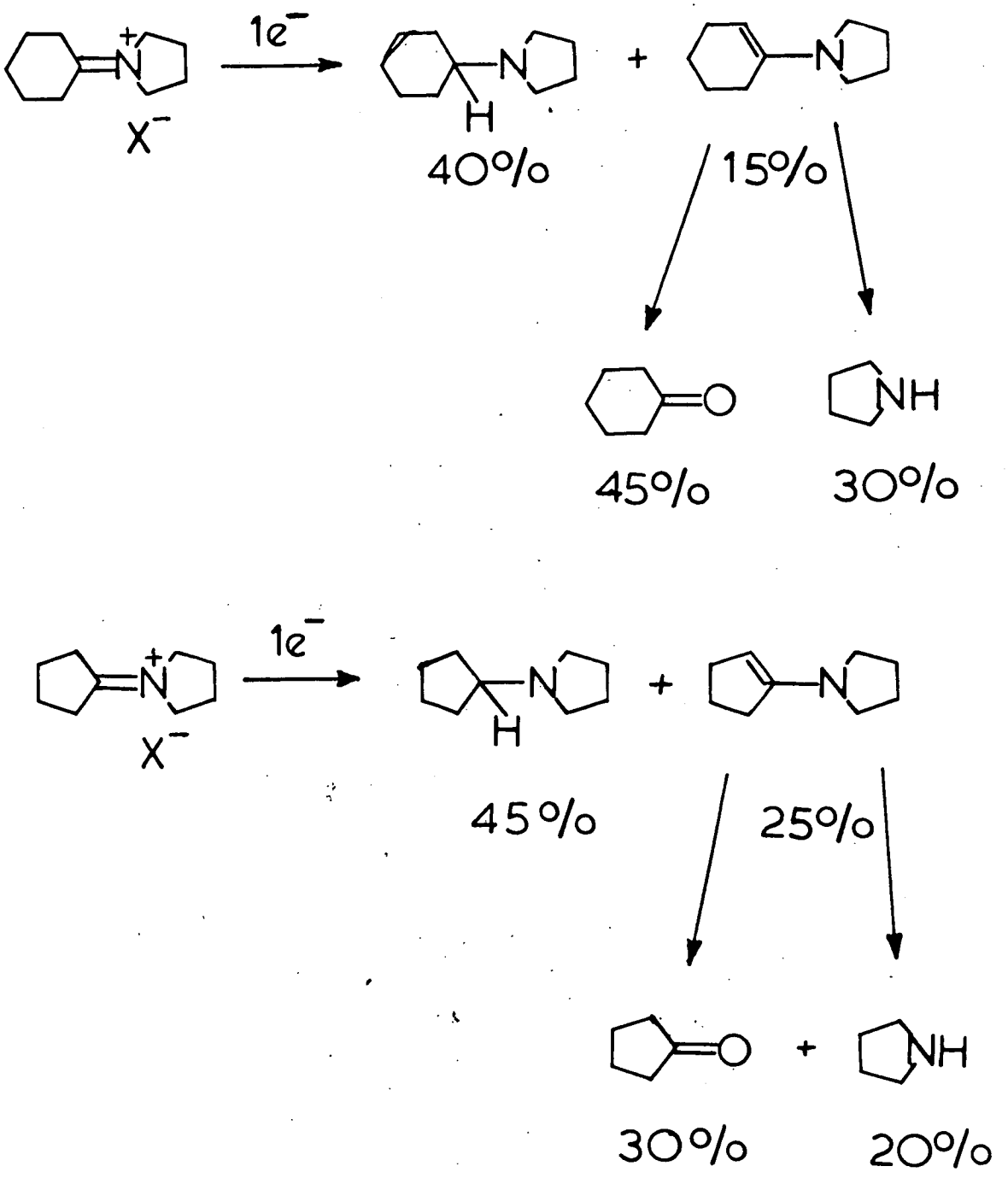


Figure 6. Preparative Electrolyses of Cyclic Immonium Salts.

X = BF_4^- or ClO_4^-; Electrodes: Hg, Pt or Graphite;

Solvents: DMF or CH_3CN; Electrolytes: $Bu_4N^+BF_4^-$ (or ClO_4^-),

$LiBF_4$, LiCl.

Preparative electrolyses

By contrast to the voltammetric results, the products of preparative electrolyses of N-cyclohexylidene- & N-cyclopentylidenepyrrolidinium cations are very much in line with the findings of Iversen and Madsen.[22] The product distributions observed using different conditions are listed in Table 2 and Table 3 and the situation is summarized in Figure 6. These results seem to confirm the absence of dimerization reactions for this type of cyclic immonium salt although the formation of dimers in trace amounts can not be entirely ruled out. Furthermore, the direct observation of the products by glc analysis of the reaction mixtures confirms the formation of enamines in these reactions.

Although the preparative results confirm the hypothesis concerning the production of enamines, it can be seen from Figure 2 that there are several different pathways which can lead to the observed products. In order to elucidate the mechanism, it is necessary to take into account the voltammetric evidence and also to attempt to obtain more information from the distribution of products, One such method is to study a cyclic immonium salt substituted in the 2-position such as the N-(2-methylcyclohexylidene)pyrrolidinium cation (9). The results of preparative reductions of this cation under many different conditions are listed in Table 4; the isomer ratios of the saturated amine, N-(2-methylcyclohexyl)-pyrrolidine, are included (cis/trans).

The mechanism of reduction of cyclic immonium cations

In any attempted rationalisation of the experimental findings, it is necessary to consider all reasonable pathways for the reduction of the immonium cations. It has already been shown in Figure 2 that several pathways are possible which could lead to the observed products. However, this illustration does not show all the possibilities, a more complete list of which is given in Table 5 together with the theoretical

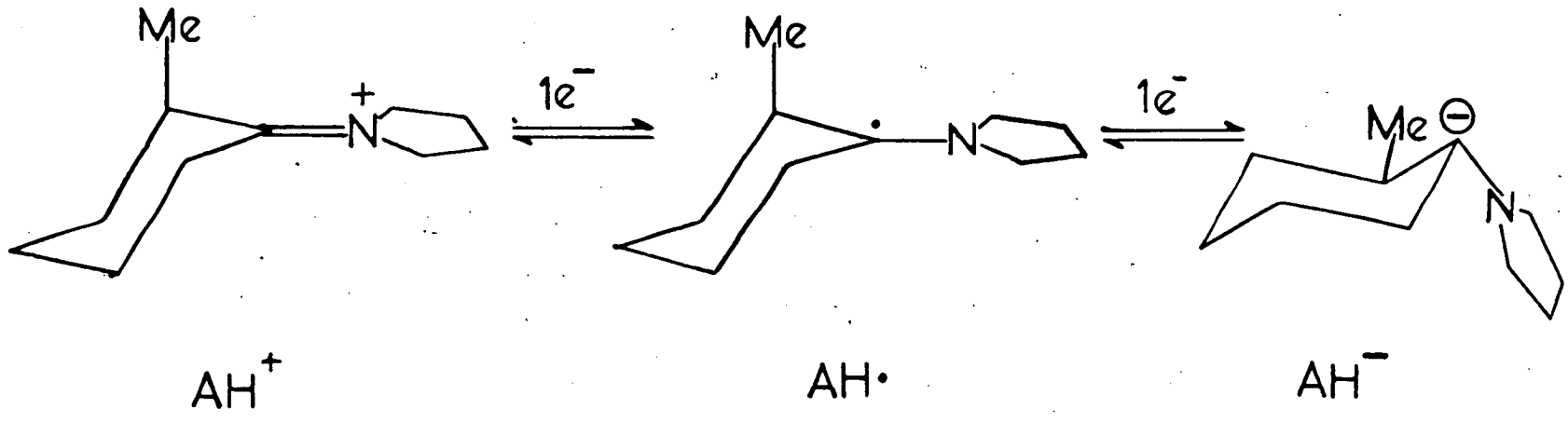


Figure 7. Shapes of molecules involved in the reduction of the N-(2-methyl-cyclohexylidene)pyrrolidine cation.

slopes of the E_p - log ν diagrams for each mechanism and the predicted stereoisomer of the resultant amine when the immonium cation is substituted in the 2-position of the carbon ring (compound (9)).

The slopes given for reaction types (ii), (iii) and (iv) are the results of calculations by Saveant and co-workers.[13] The values for the monomerization reactions can be inferred from these results since the kinetic terms are the same for dimerization and monomerization.[16] In other words, if a dimerization reaction whose rate determining step consists of the reaction of two radicals leads to a slope value of -19.7mV/decade, then so also will a monomerization reaction whose rate determining step involves the reaction of two radicals. Similar reasoning will hold for the radical-substrate and ion-substrate reactions. The slopes given for reaction types (viiia) and (viiib) can be inferred from the results found by Saveant and co-workers for dimerization reactions where homogeneous electron transfer plays a significant role.[14] The stereochemical reasoning given below which allows one to predict the preferred stereoisomer is, however, somewhat different from that previously proposed.[22]

In the first place, it is necessary to consider the likely molecular shapes of the species which are probably involved in the reaction; these are illustrated in Figure 7. The 2-methyl substituted cation, AH^+, is believed to exist with the 2-methyl substituent in the axial position in order to avoid steric interactions with the pyrrolidine ring which must lie in the same plane as the carbon-nitrogen double bond.[39,40]

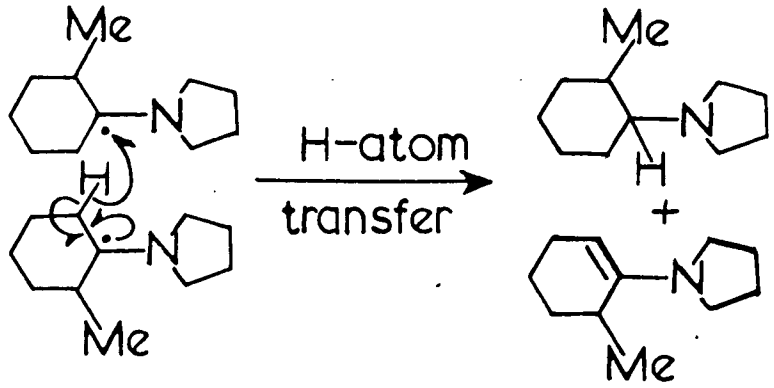
For the reduced species, it is necessary to consider the energies of the filled orbitals in the double bond in relation to the molecular shape. Since both the σ-bonding and the π-bonding orbitals are completely filled in the immonium cation, any further electrons will go into the π^*-antibonding orbital. Now, if only one electron is added, the net electronic effect is still bonding and π-character will be retained.

Therefore the radical species would prefer to remain planar, provided the π-stabilisation energy is greater than the destabilisation energy of the 1, 3-diaxial strain due to the axial position of the 2-substituent.

If this were not so, then the situation would be the same as for the case where two electrons are added to the cation and the π-character is completely lost. In this case, the species would change its shape and, consequently, the planarity about the carbon-nitrogen bond would be lost (Figure 7).

It may also be possible to deduce some information concerning the shape of the intermediate resulting from electron transfer by examining the voltammetric behaviour of the cations. The slope values $(\partial E_p/\partial \log \nu)$ listed in Table 1 indicate that the overall rate-determining step is the follow-up chemical reaction rather than electron transfer itself. Since the voltammetric pattern remains completely irreversible for all the sweep rates attainable, this then implies that electron transfer is fast and reversible as is usually the case for organic compounds. This, in turn, may mean that no large stereochemical change is occurring on addition of one electron to the substrate. Recently, some doubt has been thrown on the extent to which conformational change may contribute to a reduction of electron transfer rates[41] and the conformational change proposed in the case of the immonium reduction may be insignificant in this respect. Nevertheless, the fact that no charge transfer kinetic control[42,43] is observed tends to support the proposal that the intermediate radical remains planar and that the 2-substituent remains in the axial position as in the cation.

One must now consider the various types of reaction which determine the stereochemistry of the products (Table 5): (a) hydrogen atom transfer (v, ix), (b) proton transfer followed by electron transfer either at the electrode or in solution (vii, viii), (c) electron transfer either at the electrode or in solution followed by proton transfer (vi, x).



Stereochemistry

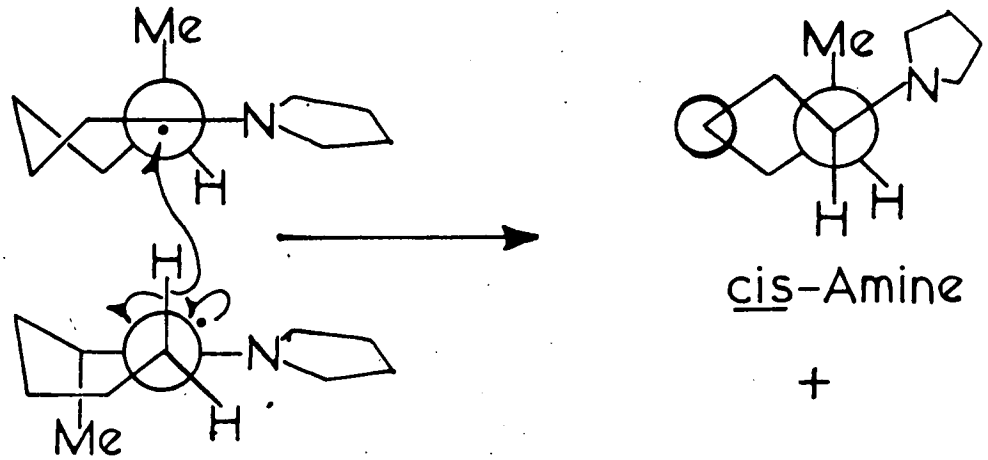
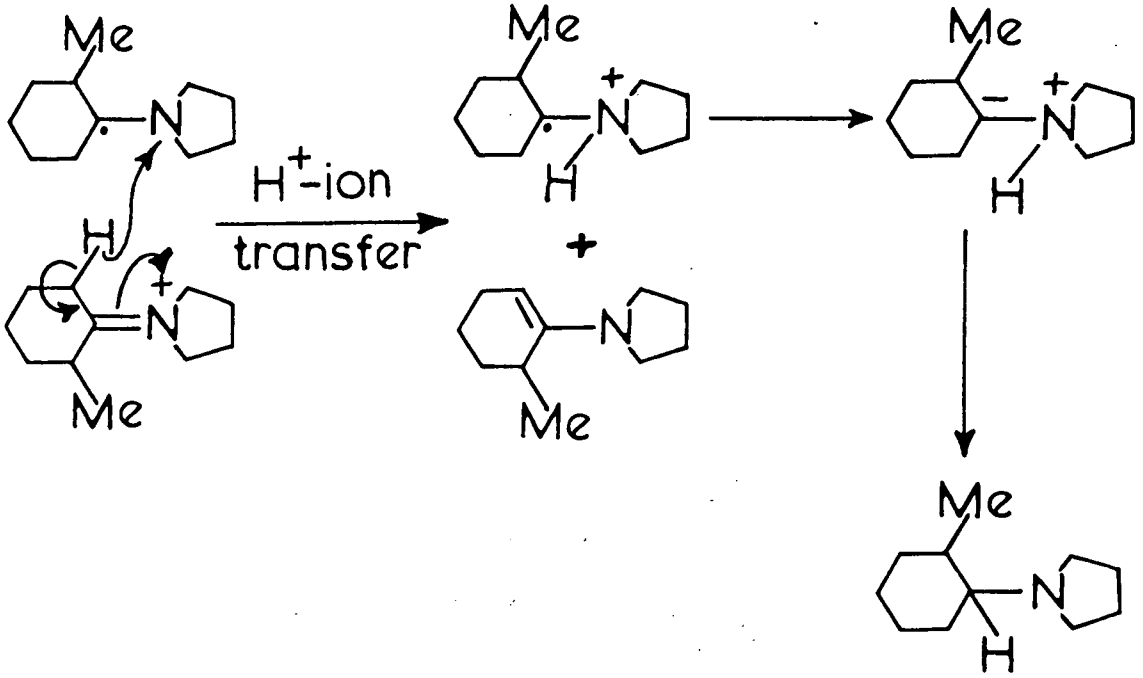
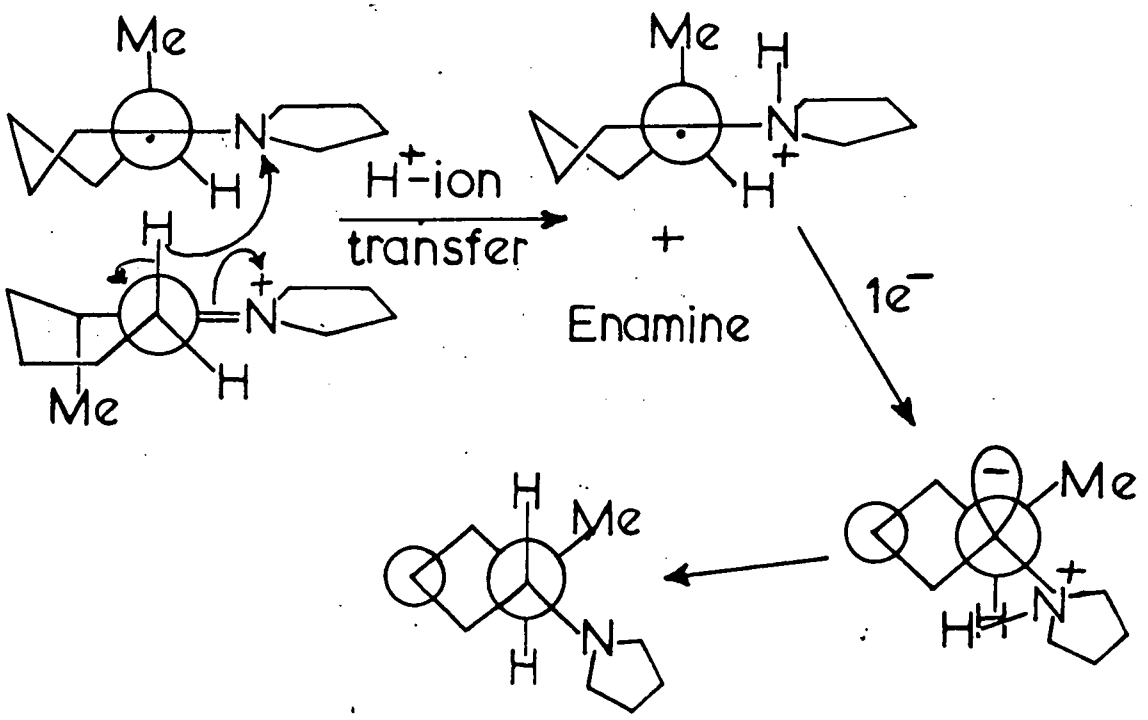


Figure 8



Stereochemistry



trans-Amine

Figure 9

Case (a) is outlined in Figure 8 for a radical-radical hydrogen atom transfer disproportionation. Inspection of a molecular model of the radical illustrates most clearly the steric hindrance that exists on one side of the molecule; this is indicated to some extent by the Newman projection shown in Figure 8. In consequence, any hydrogen atom donor will prefer to approach the less crowded side of the molecule and therefore the cis-form of the product amine ought to be preferred.

In Figure 8, hydrogen atom abstraction is shown as taking place with a secondary hydrogen rather than what might be regarded as the more likely tertiary hydrogen. However, it must be noted that, in the transition state of this step, the other hydrogen (secondary case) or the methyl substituent (tertiary case) in the embryonic enamine must be moved into a near-planar configuration. The steric interactions between the methyl and the pyrrolidine ring probably increase the transition state energy considerably and slow down the abstraction of the tertiary hydrogen. Obviously, the extent of this will depend on whether the transition state is product-like or reactant-like. It seems more likely that the abstraction will take place, as shown, from the secondary site in order to avoid any methyl-pyrrolidine non-bonded interactions.

In case (b), addition of a proton to the intermediate radical $AH^{\cdot}$ by the substrate AH^{+} is subject to the same stereochemical restraints as in case (a) (see Figure 9). However, the protonation would be expected to take place on the nitrogen of the radical, by analogy with the protonation of enamines[44], to give a protonated radical similar to an enammonium cation.[45] Rapid reduction of this protonated radical would follow leading to a change in the molecular shape as illustrated in Figure 9. Finally, rearrangement of the proton to give the product amine favours the trans-isomer, since the molecular geometry has already been determined by the second electron transfer.

For case (c), protonation of the anion, AH^{-}, also leads to the

predominance of the trans-isomer following similar reasoning as for case (b). The step which determines the resultant stereochemistry is the addition of a proton to the bent AH^- species.

In principle, there is also a possibility of a hydride ion transfer from the anion, AH^-, to the substrate, AH^+, in which the accepting species is flat and the hydride ion should be transferred directly to the carbon of the receiving molecule. This means that the stereochemical reasoning of case (a) would apply and, consequently, the cis-isomer of the amine should be favoured. Hydride ion transfer to an immonium cation is known in the case of the formic acid reduction of enamines[46] in which a reversible protonation[47] of the enamine takes place before hydride ion transfer. In the present case, however, the hydride ion transfer would be competing with the protonation of the anion and, since these immonium salts can act as proton donors, it seems reasonable to assume that such a route contributes very little to the reaction.

The results of preparative reductions of N-(2-methylcyclohexyl)-pyrrolidinium salts (9) at mercury, platinum or graphite in DMF or acetonitrile containing tetra-alkylammonium salts as supporting electrolyte (Expt. Nos. 1, 2, 3, 8-12, 14, 18 in Table 4) consistently demonstrate that the cis-isomer is the predominant form of the product amine. Taking into account the voltammetric behaviour of the salt, where the variation of the peak potential with the logarithm of the sweep rate was found to be ca.20mV/decade (Table 1), the remaining mechanistic possibilities of Table 5 (v or ix) can be distinguished. Mechanism v is the only pathway which fits the kinetic and stereochemical evidence. One can therefore conclude that the mechanism of the reduction of the N-(2-methylcyclohexylidene)pyrrolidinium cation in these conditions consists of a one-electron transfer followed by a rate-determining, radical-radical disproportionation reaction involving hydrogen atom transfer.

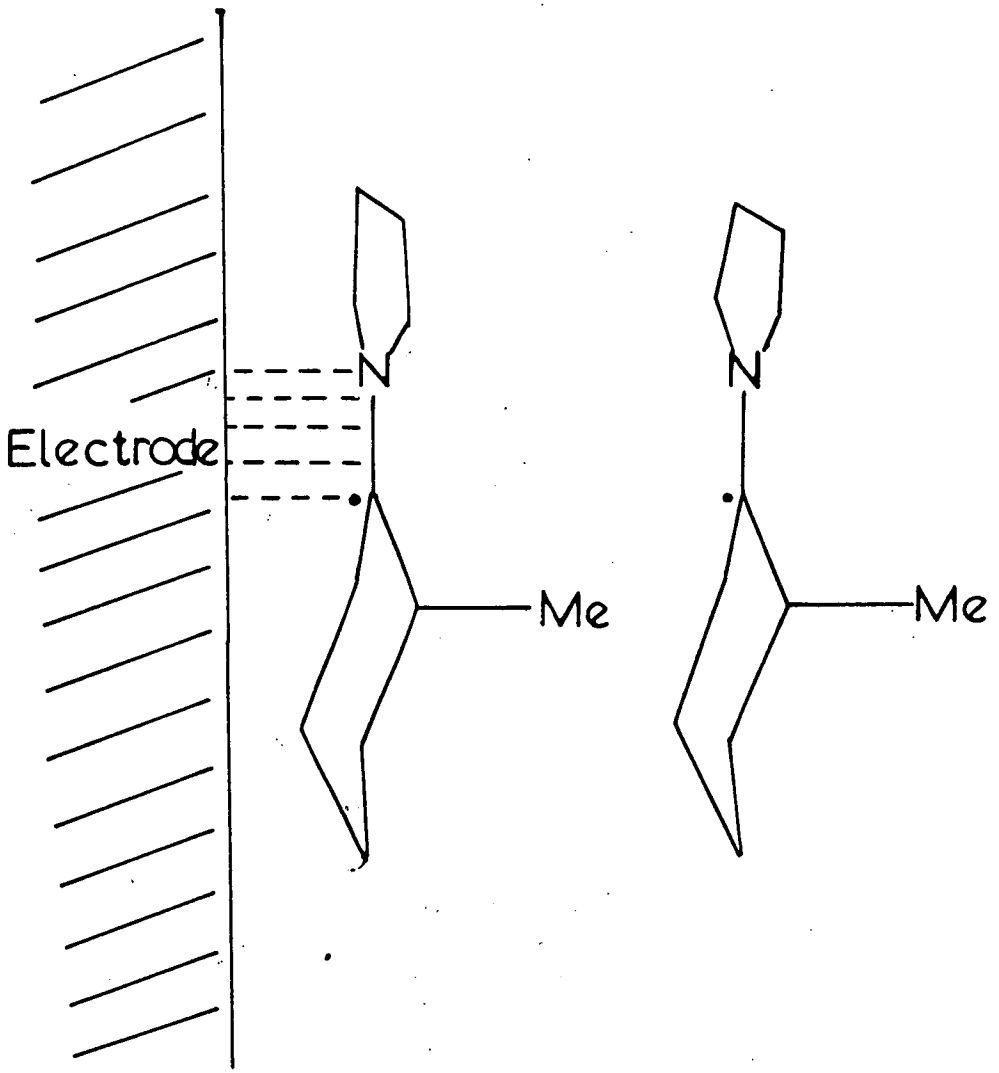


Figure 10. Possible orientation of the adsorbed radical intermediate on the electrode surface, illustrating the steric block to the approach of another radical.

It is of interest to compare the observed isomer ratios of the product amine with the ratio obtained in the case of the formic acid reduction[46] of the corresponding enamine (cis/trans = 5.5). This value is very similar to the ratios obtained in the reductions at mercury and carbon electrodes and since the formic acid reduction involved addition of a hydride ion to a planar immonium cation, the assumption concerning the planarity of the intermediate radical appears to be justified.

The role of the electrode surface

In all of the arguments outlined above, it was assumed that the follow-up chemical reaction took place away from the electrode surface. However, in view of the appreciable difference in the observed isomer ratios on reduction at platinum (Expt. Nos. 10, 11, 12, Table 4) as compared with those found at mercury and graphite, the nature of the surface appears to have some effect. It is possible that the intermediate radical is adsorbed on to the metal electrode such that the sterically free side of the molecule is blocked, thus preventing the normal reaction from taking place. It can be seen (Figure 10) that the approach of another radical will become much more difficult if the radical were to adopt this orientation and, possibly, electron transfer may become more favoured due to the increased interaction distance. The electron transfer may be from the electrode to the adsorbed molecule which would then desorb due to coulombic repulsion or perhaps an electron may be transferred from the adsorbed molecule to a free radical in solution. Such a scheme is obviously difficult to prove or disprove but the surface activity displayed at mercury by the cation and the enamine with respect to the streaming maxima in polarography and voltammetry indicates the existance of some surface interactions. However, it must be pointed out that the surface effects have no influence on the product distributions where mercury is used as the electrode, even when a low depolariser concentration

is used (Expt. No. 9, Table 4). This may well be due to the agitation of the mercury surface which, of course, is not possible with platinum.

The low isomer ratios obtained at platinum may, however, have nothing to do with adsorption initially, but may be due to different heterogeneous electron transfer rates at the different metals. In the previous discussion on mechanism, it was observed that the voltammetric evidence showed that the electron transfer rate was fast. This means, as pointed out in the General Introduction, that the cations are reduced as soon as they arrive at the electrode and, consequently, the concentration of cations at the electrode surface is zero, while that of the radicals is high. Since the follow-up chemical reaction is fast, then the reaction must take place close to the electrode where there are no cations present. Consequently, the chemical step is a radical-radical reaction. These voltammetric results were obtained on mercury and it may be possible that the electron transfer is slower at platinum. Such a situation has been found in the reduction of cyclooctatetraene.[41] The cyclic voltammograms of the immonium cations on platinum do not show any evidence for this, although it is difficult to be sure due to the much increased effects of the uncompensated cell resistance. Nevertheless, it may be that, during the course of an electrolysis, a film of adsorbed molecules may build up on the electrode surface and that this film may slow down the heterogeneous electron transfer rate. In such a situation, the cations will not be reduced immediately upon arriving at the electrode surface and they may remain there long enough to react with a radical or an anion. If this were to happen, then from Table 5, more trans-isomer would be expected to be formed (e.g. mechanism vii and viii). Once again, with mercury the agitation of the electrode surface would prevent such a film from building up.

The influence of proton donors and ion-pairing upon the mechanism

The presence of phenol or lithium cations in solution apparently has some influence upon the mechanism judging by their effects upon the product distributions (Table 4). Their presence has no effect upon the peak potentials in voltammetry although the height of the wave increases markedly for the cyclic cations on addition of phenol. This implies that the reaction kinetics remain the same and, consequently, rules out the possibility of pathways vii, viiia and x (Table 5) making significant contributions to the reaction, with phenol taking the place of AH^+ as the proton donor. Both of the remaining pathways, vi and viiib, would be consistent not only with the peak potential remaining constant, but also with the observation of an increase of peak current on addition of phenol to the solution.

Under the aprotic conditions used, electron transfer (vi) should be faster than hydrogen atom transfer (v). This is due to the difference in mass between an electron and a hydrogen atom which affects the kinetic situation. In the kinetic theory of reactions, a transition state energy barrier is envisaged over which the system has to pass. However, it has been shown that, due to the small mass of a proton, quantum mechanical tunnelling takes place in some proton transfer systems.[48] Since an electron possesses 1/2000 times the mass of a proton, electron transfer must be treated according to quantum mechanics. The system does not behave in a classical fashion and need not pass over the energy barrier. Furthermore, the electron will be able to tunnel through much wider barriers than those for a proton and, presumably, those for a hydrogen atom. For atom transfer, the atom is transferred between adjacent reactants and the distance travelled by the atom is ca.0.1nm.[49] An electron transfer, however, could take place over distances up to ten times as large as this[49] and this has an obvious application to the immonium radical

system under consideration where steric requirements force the electron or atom donor to remain a relatively long distance away. Consequently, it can be imagined that there exists a dynamic equilibrium involving electron transfer between two radicals to give a cation and an anion. However, this equilibrium is likely to be very much in favour of the reactants since, although a second reduction wave was not observed for the cations in this study, waves involving reduction of the radical to the anion were observed at much more negative potentials than the initial cation reduction wave by Andrieux and Saveant.[17]

The presence of a proton donor, e.g. phenol, in the solution will change the above situation. The anion, AH^-, cannot reduce phenol in the same way as it can rapidly reduce the cation, AH^+, and since phenol may be able to approach more closely than the only other proton donor in the solution, the immonium cation, some of the anions may be protonated by phenol. The equilibrium (vi, Table 5) will be displaced by removing the anion, AH^-, and the reaction will be pulled to the right.

Lithium cations could also affect the equilibrium by ion-pairing with the anion (AH^-/Li^+). Presumably, formation of this ion-pair slows down the reverse electron transfer long enough for a proton to be transferred from a cation, AH^+.

The operation of mechanism viiib (Table 5) can also explain the observed effects with phenol but it is difficult to see how the presence of lithium cations could favour this pathway. If viiib is operating in the presence of phenol, then it implies that the protonation step is fast and not rate-determining since, otherwise, addition of phenol would cause a shift in the peak potential. In order to try and distinguish between the possible occurrence of mechanisms vi and viiib in the presence of phenol, it is useful to consider the behaviour of N-prop-2-ylidenepyrrolidinium perchlorate (Table 6).

Contrary to the findings of Andrieux and Saveant, significant amounts of N-prop-2-ylpyrrolidine were found in aprotic conditions in addition to the dimer (see Experimental). Taking into account the voltammetric evidence ($\partial E/\partial \log \nu$ = ca. 20mV/decade), this can be explained by the operation of the hydrogen atom disproportionation mechanism described above (v) in parallel with the dimerization reaction. Such a result illustrates the duality of dimerization and atom transfer disproportionation reactions which has previously been remarked upon.[13,16] The presence of phenol in the solution should have no effect upon either of these reactions.

As discussed for the reduction of the 2-methyl-substituted cyclic cation (9), however, the presence of phenol may bring into play mechanisms vi and viiib. If the former mechanism were operating, then one would expect the presence of phenol to increase the amount of monoamine formed. The magnitude of this increase would depend upon the relative speed of the dimerization process and the extent to which the electron transfer equilibrium is displaced to the right. If mechanism viiib were operating, then the protonation of the radical, AH·, would be required to be faster than the homogeneous electron transfer and therefore should be faster than dimerization. It follows then, that the radicals would not have time to dimerize and that only monomer would be formed. Hence, one would expect a much greater increase in the yield of monoamine than that actually observed on addition of phenol, thus indicating that mechanism viiib is making no significant contribution to the reaction. This leaves mechanism vi, the homogeneous electron transfer followed by protonation, as the most likely possibility.

The arguments set out above concerning the speed of homogeneous electron transfer are of significance with respect to the effect of conformational change upon the rate of electron transfer, In the stereochemical arguments used in the mechanistic diagnosis for compound 2, it

was proposed that the formation of the anion, AH^-, or the reduction of the protonated radical, $AH_2^{+\cdot}$, resulted in a conformational change. Since the homogeneous electron transfer rate must be fast due to quantum mechanical tunnelling effects, then it appears that the conformational change does not appreciably slow down the transfer as was thought possible in the previous stereochemical argument. This tends to support the findings of Jensen and Parker[41] concerning the small effect of such conformational changes on heterogeneous electron transfer rates.

It is to be noted that the mechanistic conclusions of this study of cyclic immonium cations, although in harmony with those of Andrieux and Saveant, are somewhat different from the previous mechanistic proposals for the reduction of this type of salt.[22] The proposal that the reduction proceeds via pathway vii (Table 5) in aprotic media with the substrate salt acting as a proton donor now appears to be erroneous. However, the results of electrolyses of cation 9 where the current was low (ca. 40mA.) either due to poor experimental conditions or where the potential was deliberately adjusted (-1.1V) such that only a small current was flowing, are interesting in this respect (Expt. Nos. 19, 21, 25; Table 4). It appears that the substrate salt is acting as a proton donor but, in view of what was said above, it is more likely that it is protonating the anion produced via route vi rather than protonating the radical as in routes vii and viii. This is because, under these conditions, the rate of the heterogeneous electron transfer has been reduced, thus allowing the concentration of substrate to remain higher than normal in the region of the electrode for the major part of the reaction and, consequently, pulling equilibrium (vi) to the right by acting as a proton donor.

Conclusion

It must be stated that, although the stereochemical and mechanistic

considerations proposed here are capable of explaining all the results observed in this study, it is somewhat more difficult to rationalize in a simple manner all the results of the previous study by Iversen and Madsen.[22] In particular, the predominance of the trans-isomer of N-(2-cyanoethylcyclohexyl)morpholine and the variation of the isomer ratios with the pH of the solution have not been explained. However, the conditions prevailing in the experiments of Iversen and Madsen would be much more complicated due to the parallel cleavage, hydrolysis and acid-base type reactions whose effects are more difficult to define. Unfortunately, lack of time prevented a study of the N-(2-methylcyclohexylidene)morpholinium cation in aprotic media, but it may be speculated that the morpholine group has a considerable effect, particularly upon the homogeneous electron transfer reaction in the presence of a proton donor.

Table 1 Half-wave potentials ($E_{\frac{1}{2}}$), I_d values and variation of peak potentials vs. log of immonium salts (1mM) in acetonitrile containing 0.1M TEAP[a] or 0.4M $TEABF_4$[b]

Compound	$E_{\frac{1}{2}}$(V vs. SCE)[a]	I_d[a,c]	$\partial E_p/\partial \log \nu$ (mV/decade)[b]
N-Cyclohexylidenepyrrolidinium fluoroborate (7)	-1.67	2.85	-18.4± 4
N-Cyclopentylidenepyrrolidinium fluoroborate (8)	-1.79	2.45	-23.2 ± 4
N-(2-Methylcyclohexylidene) pyrrolidinium fluoroborate (9)	-1.73	1.88	-17.9 ± 4[d]
N-Prop-2-ylidenepyrrolidinium perchlorate (10)	-1.76	2.31	-22.1 ± 4[e]

c I_d = height of wave (mm) x sensitivity (mA/mm)/concn. (mM x $m^{\frac{2}{3}}t^{\frac{1}{6}}$); $m^{\frac{2}{3}}t^{\frac{1}{6}}$ = 1.21

d At C_o = 0.17mM, $\partial E/\partial \log \nu$ = -18.5mV/decade

e At C_o = 0.14mM, $\partial E/\partial \log \nu$ = -18.1mV/decade

Table 2 Results from preparative reductions of N-cyclohexylidene-pyrrolidinium fluoroborate (0.1M) in 0.1M $TBABF_4$/DMF. Products: 1, pyrrolidine; 2, cyclohexanone; 3, N-cyclohex-1-en-1-yl-pyrrolidine; 4, N-cyclohexylpyrrolidine. Mercury pool working electrode at -1.6V vs. Ag/AgI/0.1M TBAI.

$n(F\ mole^{-1})$	Yields (% by glc analysis)			
	1	2	3	4
0.98	29	32	12	34
0.84	43	37	19	36
0.98[a]	40	46	6	29
0.99[a]	31	38	8	35
0.94	36	52	5	47
1.00	36	31	20	41
0.87[b]	0	59	trace	16
1.01[c]	20	37	16	44
0.96[d]	25	30	20	35
0.89[a,d]	0	31	0	14
0.92[e]	54	56	11	30
0.95	34	39	21	52
0.99[c]	8	44	13	47
1.28[f]	41	43	21	38
0.96[g]	34	42	12	47
0 [h]	29	66	3	-

a, 0.1M LiCl as support; b, 0.015M substrate $conc^n$.; c, acetonitrile as solvent; d, 0.025M substrate $conc^n$.; e, platinum electrode; f, +0.1M phenol; g, graphite electrode; h, blank run - no current-injection after 120 min.

Table 3 Results from preparative reductions of N-cyclopentylidene-pyrrolidinium fluoroborate (0.1M) in 0.1M $TBABF_4$. Products: 1, pyrrolidine; 2, cyclopentanone; 3, N-cyclopent-1-en-1-ylpyrrolidine; 4, N-cyclopentylpyrrolidine. Mercury pool at -1.6V vs. Ag/AgI/0.1M TBAI.

Solvent	n ($F\ mol^{-1}$)	Yields (% by glc analysis)			
		1	2	3	4
DMF	0.79	19	28	24	43
ACN	1.03	14	23	25	51
ACN	1.12	16	31	11	50
ACN[a]	2.29	15	27	13	58
ACN[b]	1.09	23	35	31	39
ACN[c]	0.97	18	26	27	46
DMF[a,d]	1.00	3	3	8	44

a, electrolyte 0.1M $LiBF_4$;

b, platinum electrode;

c, graphite electrode;

d, substrate conc^n. 0.06M.

Table 4 Results of preparative reductions of N-(2-methylcyclohexylidene) pyrrolidinium fluoroborate or perchlorate (0.1M) in 0.1M $TBABF_4$ (A) or TBAP (B). Products: 1, pyrrolidine; 2, 2-methylcyclohexanone; 3, N-(2-methylcyclohex-1-en-1-yl)pyrrolidine; 4, N-(2-methylcyclohexyl)-pyrrolidine. Mercury pool electrode at -1.6V vs. Ag/AgI/0.1M TBAI unless otherwise stated.

Expt. No.	Solvent	Electrolyte	Initial Current(mA)	n ($F\ mol^{-1}$)	Yields (% by glc analysis) 1	2	3	4	cis/trans
1	ACN	A	320	0.95	16	18	34	47	5.7
2	ACN	A	200	0.98	14	20	31	46	5.2
3	ACN	A	300	0.97	15	23	28	46	5.2
4	ACN[a]	$LiBF_4$	10	0.98	2	52	4	18	1.1
5	ACN	$LiBF_4$	300	2	16	41	7	40	4.6
6	ACN	$LiBF_4$	200[b]	0.99	6	35	4	33	2.9
7	ACN	$LiBF_4$	200	2	7	30	5	18	4.6
8	DMF	A	200	0.98	61	-	6	28	5.8
9	ACN	A	250[c]	1.08	18	50	6	30	5.9
10	ACN[a]	B	180	0.99	15	13	39	43	2.1
11	ACN[a]	B	230	1.01	12	16	39	42	2.0
12	ACN[a]	B	180	1.05	15	15	37	39	2.0
13	ACN	B	430[b]	1.02	23	32	25	45	5.1
14	ACN[d]	B	160	1.07	23	30	26	36	5.3
15	ACN	B	340[b]	1.02	13	23	30	40	5.2
16	ACN	B[e]	260[b]	1.00	29	35	9	54	4.2
17	ACN	B[e]	140[b]	1.08	28	36	7	55	3.3
18	ACN[d]	B	130	1.03	14	32	24	42	5.3
19	ACN	B[e]	40[b,f]	0.95	25	37	7	45	2.0
20	ACN	$LiClO_4$	180[b]	0.97	19	40	3	51	3.7
21	ACN	$LiClO_4$	40[b,f]	0.98	10	45	1	37	1.9

Table 4 (contd.)

Expt. No.	Solvent	Electrolyte	Initial Current(mA)	n ($F\ mol^{-1}$)	Yields (% by glc analysis) 1	2	3	4	cis/trans
22	ACN	B[g]	300	2.06	3	33	17	62	2.4
23	ACN	B[h]	140	2.43	1.4	19	8	73	2.1
24	ACN	B[i]	380[b]	0.97	3	51	0	41	2.8
25	ACN	B	40[k]	0.91	1	45	0	52	2.7
26	DMF	B	250	1.01	2	-	6	43	5.1
27	DMF	B	40[f]	0.90	7	-	0	38	2.8
28	DMF	B	100[f]	1.05	3	-	0	38	3.7
29	DMF	B	240	1.02	0	-	3	46	5.6
30	DMF	B[e]	250[b]	0.98	7	-	0	39	3.7
31	DMF	B[g]	260	1.21	5	34	3	39	5.2
32	DMF	B[l]	250	1.24	0	27	4	38	3.7
33	DMF	$LiClO_4$	170[b]	1.100	0	32	0	22	2.0

a, platinum electrode; b, -1.2V; c, substrate conc^{n}. 0.01M; d, carbon electrode; e, +0.1M $LiClO_4$; f, unusually low current due (probably) to poor cell connections; g, +0.1M phenol: h, +1.0M phenol; i, +0.1M $LiClO_4$; k, -1.1V; l, +0.2M phenol.

Table 5 Possible reaction pathways for reduction of immonium cations

Reaction Type	Reaction Scheme	$\partial E_p - \partial \log \nu$ (mV/decade)	Isomer Preferred
(i) electron transfer at electrode	$AH^+ + e^- \rightleftharpoons AH\cdot$	-	-
(ii) radical-radical dimerization	$AH\cdot + AH\cdot \longrightarrow HAAH$	-19.7	-
(iii) radical-substrate dimerization	$AH\cdot + AH^+ \rightleftharpoons HAAH^{+\cdot}$ $HAAH^{+\cdot} + e^- \longrightarrow HAAH$	-29.6	-
(iv) ion-substrate dimerization	$AH\cdot + e^- \rightleftharpoons AH^-$ $AH^- + AH^+ \longrightarrow HAAH$	-14.8	-
(v) radical-radical H-atom transfer	$AH\cdot + AH\cdot \longrightarrow AH_2 + A$	-19.7	CIS
(vi) radical-radical electron transfer	$AH\cdot + AH\cdot \rightleftharpoons AH^+ + AH^-$ $AH^+ + AH^- \longrightarrow AH_2 + A$	-19.7	TRANS
(vii) radical-substrate proton transfer	$AH\cdot + AH^+ \rightleftharpoons AH_2^{+\cdot} + A$ $AH_2^{+\cdot} + e^- \longrightarrow AH_2$	-29.6	TRANS
(viii) radical-substrate proton transfer	$AH\cdot + AH^+ \rightleftharpoons AH_2^{+\cdot} + A$ $AH_2^{+\cdot} + AH\cdot \longrightarrow AH_2 + AH^+$	-29.6(a) † -19.7(b)	TRANS
(ix) radical-substrate H-atom transfer	$AH\cdot + AH^+ \longrightarrow AH_2 + A^{+\cdot}$ $A^+ + e^- \longrightarrow A$	-29.6	CIS
(x) ion-substrate proton substrate	$AH\cdot + e^- \rightleftharpoons AH^-$ $AH^- + AH^+ \longrightarrow AH_2 + A$	-14.8	TRANS

† a) protonation rate-determining

b) protonation fast and electron transfer is rate-determining

Table 6 Results from preparative reductions of N-prop-2-ylidene-pyrrolidinium perchlorate (0.1M) on mercury in 0.1M TBAP. Reference electrode: Ag/AgI/0.1M TBAI.

Solvent	Working Potential (V)	n ($F\ mol^{-1}$)	% N-prop-2-yl-pyrrolidine
ACN	-1.2	0.99	21
ACN	-2.0	0.99	21
ACN[a]	-1.6	1.99	39
DMF	-1.6	0.99	21

a, +0.2M phenol

CHAPTER 3

ELECTROCHEMICAL HYDRODIMERIZATION IN DRY ACETONITRILE

CHAPTER 3

Electrochemical Hydrodimerization in Dry Acetonitrile

Introduction

Of all the restrictive assumptions that were listed in the introduction to the last chapter, only two were essentially justified for the reduction of the immonium cations. These were (i) the number and speed of electron transfers and (v) the neglect of acid-base type reactions. As was shown in the study of the cyclic immonium salts, atom and electron transfers in solution and adsorption (assumptions (ii), (iii) and (iv)) could not be ignored. It was evident that even for a "simple" system like the reduction of the immonium cation, the process is complex. Turning to a more common system where acid-base reactions can not be ignored, the degree of complexity of the process will obviously increase.

A more common process in organic electrochemistry is that of hydrodimerization which involves a coupling process similar to that described for the immonium cations plus the addition of protons. Like the immonium cations, steric considerations control the products of the reaction and, similarly, the possibility of atom and electron transfers in solution must be considered. This leads, once again, to a competition between dimerization and monomerization reactions, and a thorough understanding of the factors which control this competition is not only useful in a synthetic sense, but is also of benefit in the elucidation of radical-ion behaviour.

Many compounds have been cathodically dimerized and these have been reviewed by Beck.[10] Among the compounds which have been extensively studied are activated olefins,[50] α,β-unsaturated carbonyl compounds,[51] saturated carbonyl compounds[52,53] and nitro- and nitroso-compounds[54], all of which can undergo, to some extent, hydrodimerization reactions.

The most extensively studied electrohydrodimerization reaction,

largely due to its commercial significance, was, initially, that of the almost quantitative conversion of acrylonitrile to adiponitrile achieved by Baizer and co-workers.[9] Unfortunately, it appears that this reaction is one of the more difficult to study from a mechanistic point of view. Tafel line analysis[55,56] showed that the rate-determining step is the transfer of the first electron and of a proton. No kinetic analysis of the dimerization step could therefore be derived from this result.

The study of α,β-unsaturated carbonyl compounds and 1,2-diactivated olefins has proved to be more fruitful as a means of elucidating the mechanism of electrohydrodimerization. Baizer himself has studied the reduction of 1,2-diactivated olefins in DMF using linear sweep voltammetry and concluded that the coupling step was a radical-substrate process.[23] In support of this mechanism, preparative experiments involving the production of mixed dimers were carried out by Baizer.[25,27] Bard and his co-workers have studied the electrohydrodimerization reaction using cyclic voltammetry, double-step potentiostatic chronoamperometry and chronocoulometry together with studies using the ring-disc electrode.[28,29,57-59] Their conclusion was that the coupling step in aprotic conditions was a radical-radical reaction involving radical-anions.

Saveant and co-workers, in continuation of their work on electrodimerization, have studied a varied group of 1,2-diactivated olefins and α,β-unsaturated ketones in aprotic media by means of linear sweep voltammetry.[11,60] They concluded that, for all the cases studied, the mechanism of dimerization was by means of the coupling of radical-anions. Evans and co-workers[51] found similar results from a study of the cyclic voltammetry of some α,β-ethylenic ketones in DMSO. In a recent study by Nadjo, Saveant and Tessier,[61] using the more sophisticated electroanalytical technique of convolution potential sweep voltammetry,[62] the dimerization step was unequivocally found to involve the coupling of two radical-anions on reduction of p-methylbenzylidenemalononitrile in

acetonitrile.

It is to be noted that all of these analytical studies were carried out using conditions which were somewhat different from those used in the commercial synthesis of adiponitrile, in which water is used as solvent together with a high concentration of acrylonitrile and tetra-alkylammonium salts. Most of the compounds which were used in the mechanistic studies mentioned above form monomers on reduction in protic media. For example, Zuman has studied the electrochemical hydrogenation of benzylidenemalononitrile at mercury in aqueous solutions containing 50% methanol;[63] no dimerization was observed. Similarly, α,β-unsaturated ketones form monomers in protic conditions[64] as does acrylonitrile itself.[65] However, the presence of the tetra-alkylammonium cations in solution and their specific adsorption on to the electrode[66] creates a water-poor zone in the region of the cathode surface. It has been shown[67] that DMF with 5% added water is roughly equivalent to the conditions used in the commercial synthesis, so that the commercial situation can be fruitfully paralleled to the reduction in aprotic solvents.

The other major difference between the analytical studies and the preparative situation lies in the concentration of the depolariser. For the analytical studies, the concentrations are in the range of 0.1 to 5mM while in the preparative reductions, concentrations can be 1000 times greater. Recently, Nadjo and Saveant[68] have studied the coupling mechanism of p-methylbenzylidenemalononitrile at preparative concentrations (up to 0.1M) in wet (10% H_2O) and in dry DMF, using chronopotentiometry; the coupling step was found to involve the coupling of radical-anions under these conditions also.

Apart from these electroanalytical techniques, it is possible, as was demonstrated in the previous chapter, to gain much useful mechanistic information from a study of the distribution of isomeric products of a preparative scale reduction. Indeed, since the reaction conditions may change on moving from the analytical to the preparative scale, it is perhaps

advisable to carry out such a study where possible. Furthermore, since the study of the stereochemistry of organic reactions remains one of the most widely used tools available to the organic chemist in his study of reaction mechanisms, it may be that such a study may be more impressive to an organic chemist who may be somewhat dubious about the benefits of electroanalytical techniques. In addition, such studies may bring to light stereoselectivity which would be of obvious synthetic value.

Compounds which have received much attention in connection with the stereochemistry of dimerization, are aromatic ketones and aldehydes. Such compounds have been the subject of extensive polarographic studies by Zuman and his co-workers.[69] In the most acidic media, two polarographic waves were observed, the first one corresponding to the formation of dimers while the second one corresponded to reduction to the alcohol. This was rationalized according to the scheme:

$$ArCOR + H^+ \rightleftharpoons ArCOHR^+$$

$$ArCOHR^+ + e^- \rightleftharpoons Ar\dot{C}OHR \ (E_1)$$

$$2Ar\dot{C}OHR \longrightarrow \text{dimers}$$

$$Ar\dot{C}OHR + Hg \longrightarrow \text{organomercury compounds}$$

$$Ar\dot{C}OHR + \text{solvent} \longrightarrow \text{products}$$

$$Ar\dot{C}OHR + e^- \rightleftharpoons Ar\bar{C}OHR \ (E_2)$$

$$Ar\bar{C}OHR + H^+ \rightleftharpoons ArCHOHR$$

On raising the pH, the half-wave potential of the first wave (E_1) shifts cathodically until the two waves merge into one two-electron wave which corresponds to reduction to the alcohol:

$$ArCOR + e^- \rightleftharpoons Ar\dot{\bar{C}}OR \ (E_3)$$

$$Ar\dot{\bar{C}}OR + H^+ \rightleftharpoons Ar\dot{C}OHR$$

$$Ar\dot{C}OHR + e^- \rightleftharpoons Ar\bar{C}OHR \ (E_2)$$

$$Ar\bar{C}OHR + H^+ \rightleftharpoons ArCHOHR$$

As the pH is increased further, the two-electron wave splits into two waves, the height of the second wave (E_4) increasing with pH at the

expense of the first wave (E_3) until two one-electron waves are observed:

$$ArCOR + e^- \rightleftharpoons Ar\dot{C}O\bar{R}\ (E_3)$$
$$Ar\dot{C}O\bar{R} + H^+ \rightleftharpoons Ar\dot{C}OHR$$
$$Ar\dot{C}OHR + e^- \rightleftharpoons Ar\bar{C}OHR\ (E_2)$$
$$Ar\bar{C}OHR + H^+ \rightleftharpoons ArCHOHR$$
$$Ar\dot{C}O\bar{R} + e^- \rightleftharpoons Ar\bar{C}O\bar{R}\ (E_4)$$
$$ArC\bar{O}R + 2H^+ \rightleftharpoons ArCHOHR$$
$$2Ar\dot{C}OR \longrightarrow ArR\bar{C}O\bar{C}ORAr$$
$$ArR\bar{C}O\bar{C}ORAr + 2H^+ \rightleftharpoons ArRC(OH)C(OH)RAr$$

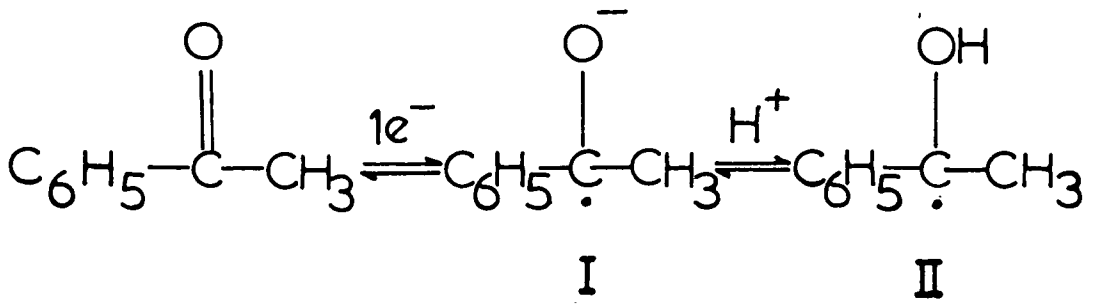
The formation of organometallic compounds and hydrocarbons has also been studied.[70] The pathway which is followed depends upon the structure of the ketone and upon the condition of reduction.

In Zuman's analysis, all of the electron transfers were assumed to take place at the electrode and possible solution electron transfers were not considered. This possibility has been investigated by Nadjo and Saveant[71] who have studied, by means of linear sweep voltammetry and coulometry, the reduction of several aromatic ketones in buffered alkaline media. The behaviour varied according to the structure of the ketone. Benzaldehyde, for example, was found to dimerize at all the pH values employed; acetophenone dimerized in the most alkaline buffer but was hydrogenated in the more acidic buffers, while benzophenone was hydrogenated at all the pH values studied. A study of the kinetics of reduction showed that the mechanism of dimerization in the alkaline buffers involved the coupling of a neutral ketyl radical with a ketyl radical-anion. Hydrogenation of acetophenone was found to involve a disproportionation reaction involving electron transfer from a ketyl radical-anion to a neutral ketyl radical at all the pH values, while for benzophenone this was found to be the case in only the most alkaline solution. First order kinetics, which may involve electron transfer either at the

electrode or in solution, were observed in the most acidic buffers, indicating that protonation of the ketyl radical-anion was the rate-determining step. It was also observed that, in the most acidic buffer solutions, the protonation reaction could be accelerated so that electron transfer itself became rate-determining.[43] In the case of benzaldehyde in the most acidic buffer, the dimerization reaction was accelerated, implying that the coupling was taking place between two neutral ketyl radicals.

Extensive studies on the stereochemistry of pinacolization of aryl alkyl ketones have been carried out by Stocker and his co-workers.[52,53,72] Acetophenone, in particular, has been studied because the stereochemical identity of the individual diastereoisomeric pinacols have been unequivocally determined[73] and synthetic routes to the pure diastereoisomers have been reported.[74] The ratios of the racemic dl-diastereoisomer to the meso-form of the pinacol formed electrochemically[52,53] and photochemically[75,53] using various media were compared. It was found that, in acid or neutral (pH 7) 80% ethanolic solutions, the dl/meso ratio was approximately 1:1 while in alkaline ethanolic solutions the dl/meso ratio was in the region of 3:1. The pH of the alkaline solution varied in the electrochemical reaction since the solution became more basic as the reaction proceeded, increasing from about pH 8 to about pH 12.

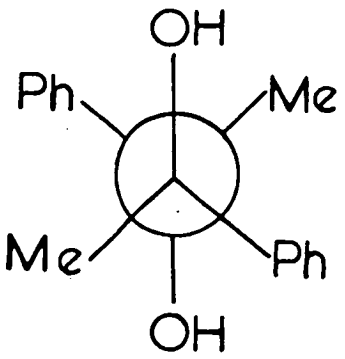
The pinacol isomer ratios found in the electrochemical reaction were explained by considering the stereochemistry of the coupling complex. The species taking part in the coupling process were thought to be either neutral ketyl radicals (II) or radical-anions (I):



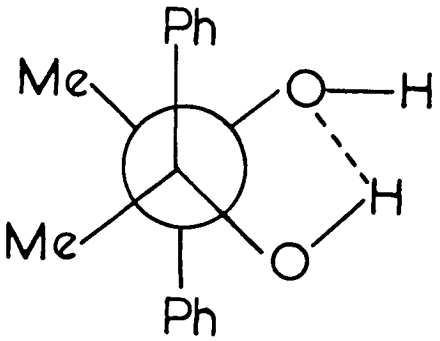
I II

The combination of two radical-anions (I) was thought to be unlikely due to coulombic repulsion and only the combinations of I with II and II with II were considered. For acid or neutral media, it was assumed that the radical-anion was protonated and that the dimerization involved two neutral radicals, while in an alkaline medium, the coupling was thought to involve a neutral radical and a radical-anion. Since the pK_a of the benzophenone ketyl radical was determined by Porter and Wilkinson[76] to be 9.2 in a water-propan-2-ol mixture, these assumptions seem reasonable.

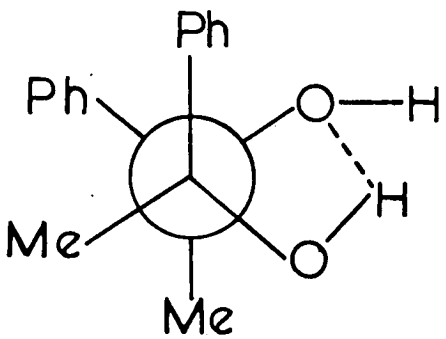
On steric grounds alone, one would expect that the meso-pinacol would be the predominant form since it minimises the non-bonded interactions (A):



A,meso

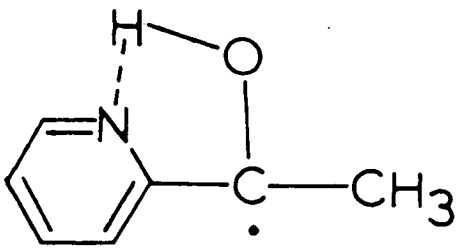


B,dl



C,meso

However, hydrogen bonding between the hydroxyl groups was suggested to play a role in the orientation of the radical species involved in the dimerization step and this effect was predicted to favour the dl-form. This is represented in the structures B and C above and accounts for the slight preference for the dl-form in acidic media. This argument was strengthened by the increased preference for the dl-form found in alkaline media where one of the hydroxyl groups is ionized, thus increasing the strength of the hydrogen bonding. This proposal for the role of hydrogen bonding was further reinforced by the study of 2-acetylpyridine[77] where hydrogen bonding could take place intramolecularly:



Consequently the hydrogen would be less available for intermolecular hydrogen bonding. As predicted, the meso-form of the pinacol predominates for this compound.

The fact that the isomer ratios of the acetophenone pinacol were independent of the electrode material and also were the same as those produced photochemically,[77] persuaded Stocker and his co-workers that the coupling process took place in solution and that adsorption did not play a significant role. However, Puglisi et al.[78] have found that the presence of adsorbable ions, such as tetra-alkylammonium cations, greatly reduces the dl/meso ratio in the reduction of benzaldehyde in aqueous acidic solutions. These authors deduced from this that the dimerization takes place in the interface, at least in the presence of adsorbable ions, where they considered that it was possible that the high fields of the double layer could interfere with the hydrogen bonding mechanism proposed by Stocker and co-workers. Evidence for the strong adsorption of p-bromoacetophenone as a complex with tetra-alkylammonium ions on to a mercury electrode has been presented by van Tilborg[79] using tensammetric methods.

Many studies of this aspect of adsorption have been carried out in

order to elucidate the mechanism of asymmetric induction in the reduction of ketones, such as acetophenone, to alcohols in the presence of chiral, adsorbable alkaloids.[80,81] It is, however, to be stressed that no asymmetric induction of the pinacols formed concurrently was observed under such conditions. This leads to the conclusion that the formation of alcohol is a surface reaction while the formation of pinacol is a homogeneous reaction.[82] In accordance with this idea, the formation of the optically active dl-form of acetophenone pinacol was observed when a chiral solvent was used.[83]

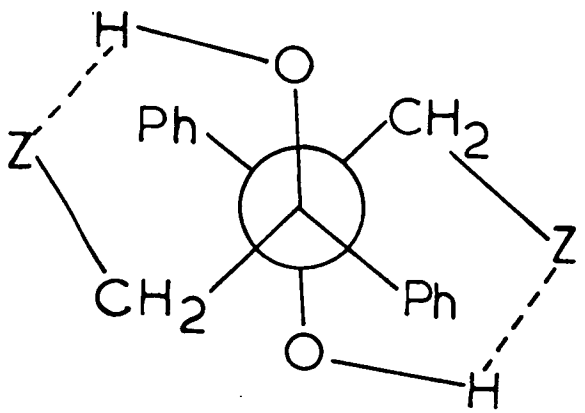
Conway et al.[84] have presented evidence for the adsorption of acetophenone and its pinacol on to mercury from water-methanol solutions. This evidence and that presented by Puglisi et al. cited above, has induced Bewick and co-workers[85,86] to make a study of the stereochemical factors in the cathodic pinacolization of acetophenone in aprotic DMF solutions. Stocker and Jenevein[72] had previously published a study of this reaction using acetonitrile as the solvent and tetraethylammonium bromide as the supporting electrolyte; in acetonitrile, they found an increased preference for the dl-form (dl/meso = 7) over that found previously in protic conditions. This was rationalized by invoking protonation of one of the coupling radical-anions by residual water in the solvent (0.2%); the possibility of dimerization of neutral ketyls was considered to be negligible, unlike the situation in protic media, and this was held to explain the results. Bewick and co-workers[85.86] found similar results but also investigated the effects of residual water and ion-pairing. With very dry solvent, these authors found that the dl/meso ratio was lower (4.1:1) than in wet solution (7:1) and that the presence of lithium ions considerably increased the preference for the dl-isomer (12.5:1).

In an attempt to rationalize these results, Bewick and co-workers proposed that dimerization takes place at the surface and involves two

radical-anions in aprotic conditions. Since such a coupling would lead to the predominance of the meso-isomer, they proposed that a tetra-alkylammonium cation was involved by means of ion-pairing with the radical-anions in a similar manner to the interspecies hydrogen bonding proposed by Stocker. The effect of lithium cations on the isomer ratios seemed to support this proposal. The addition of water to the solution was thought to cause protonation of one of the radical-anions so that the coupling will take place in a similar manner to that proposed by Stocker except that adsorption is involved in the process.

In addition to the kinetic studies by Nadjo and Saveant[71] on the dimerization reaction of carbonyl compounds in protic media, the conclusions of which are in agreement with the stereochemical proposals of Stocker as regards the species involved in the coupling step, Saveant and Tessier[87] have also studied the pinacolization of acetophenone in acetonitrile using convolution potential sweep voltammetry. These authors have found that the dimerization step in acetonitrile containing 0.3%, 1.3% and 5.3% water involved the coupling of two radical-anions. The addition of water to the solution was found to increase the rate of dimerization but did not change the mechanism, which is contrary to the proposals of Bewick and Stocker. Furthermore, they found no evidence for the adsorption which Bewick and Brown[86] have found in some voltammetric measurements.

The electron paramagnetic resonance spectrum of the acetophenone radical anion in DMF has been recorded by Andrieux and Saveant[88] as part of a study of the pinacolization of α-substituted carbonyl compounds.[88,89] In this study, the pinacols formed were examined in a similar manner to that described by Stocker and co-workers for 2-acetylpyridine, since the α-substituted acetophenones were capable of intramolecular hydrogen bonding:



(e.g. Z= —N O)

However, it was not possible to decide conclusively which pinacol isomer was formed, although it was thought that the meso-isomer predominated.

During the course of the preparative electrolyses which used acetonitrile as the solvent in the above study, it was noted that the solution progressively turned dark brown, became very alkaline and the yields of pinacols were very low (ca. 10%). This problem was largely avoided by adding perchloric acid to the solution while the electrolysis proceeded. Similar problems arose in the study of the electrochemistry of substituted benzophenones and fluorenones[90] in acetonitrile and some unidentified products were observed. This was ascribed to the formation of cyanomethyl anions by proton abstraction from the solvent and was also avoided by the addition of perchloric acid. van Tilborg et al.,[91] in a closely related study of p-bromoacetophenone, have reported the formation of a 3-hydroxynitrile in acetonitrile containing less than 5% water:

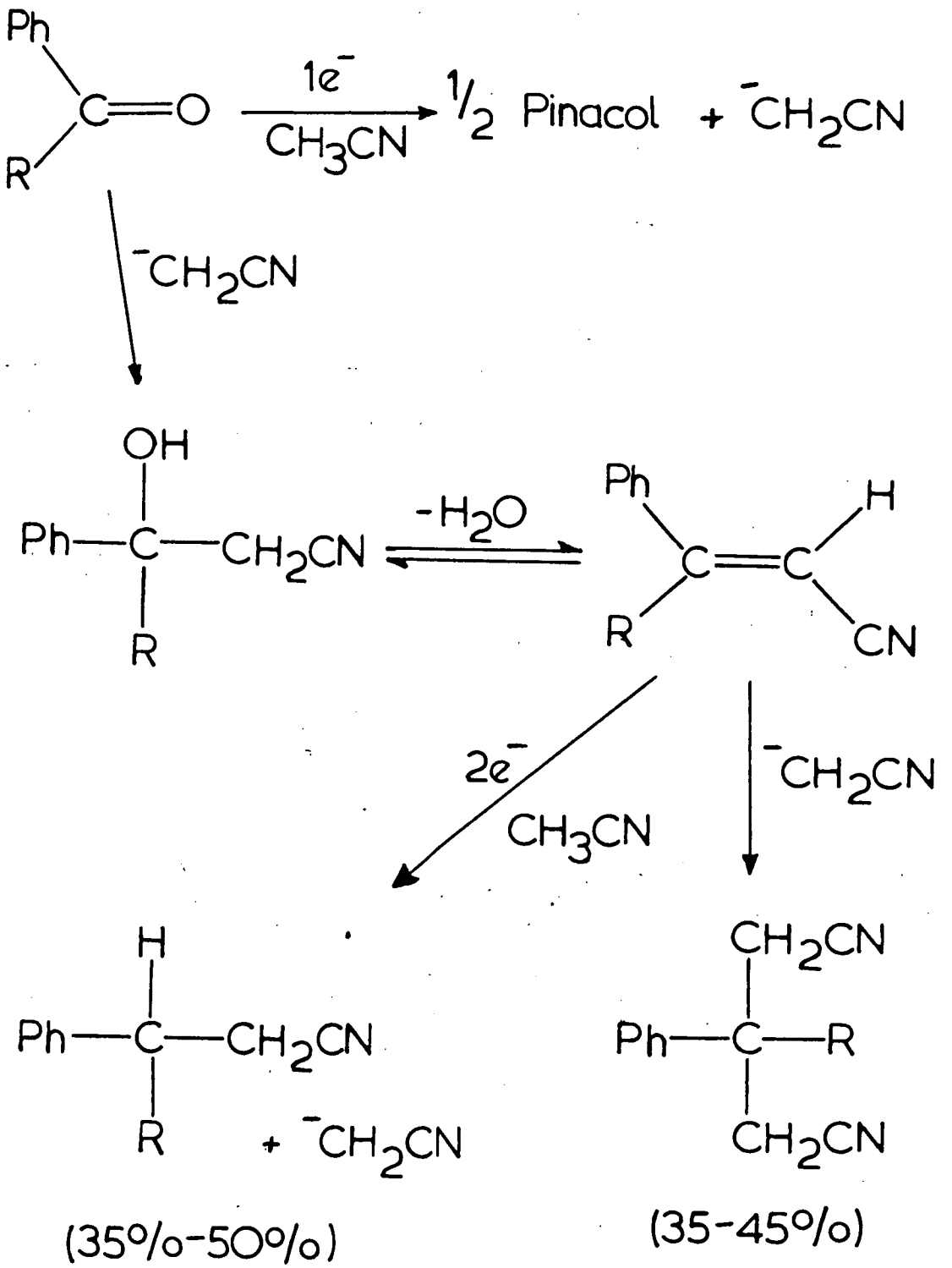
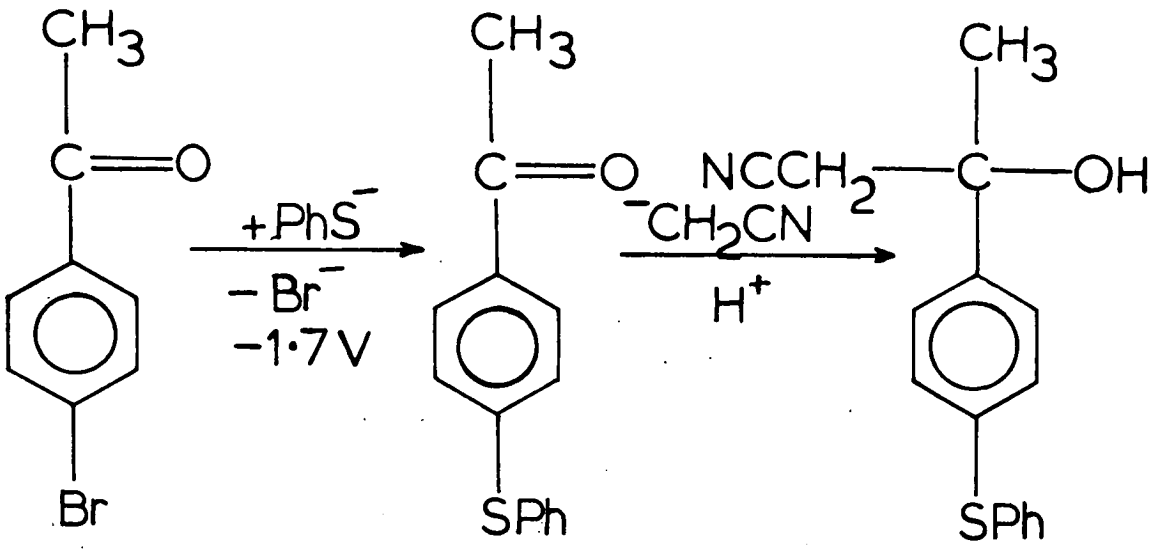

Ph
C=O
R
1e⁻
CH3CN
1/2 Pinacol + ⁻CH2CN
⁻CH2CN
OH
Ph—C—CH2CN
R
-H2O
Ph
H
C=C
R
CN
2e⁻
CH3CN
⁻CH2CN
H
Ph—C—CH2CN
R
+ ⁻CH2CN
CH2CN
Ph—C—R
CH2CN
(35%-50%)
(35-45%)

Figure 11



These authors found that addition of 5% water prevented the formation of the cyanomethyl-anion adduct. A similar kind of attack on the solvent may have been observed by Wawzonek and Gundersen[92] who reported the formation of tars and oils, which they were unable to analyse, on reduction of some aromatic ketones and aldehydes in DMF.

Similar findings to the above concerning the attack on the solvent have been observed in this laboratory.[93] On reduction of acetophenone at -3.0V vs. Ag/0.1M Ag^+ at mercury in dry acetonitrile (ca. 100ppm H_2O) containing 0.1M tetraethylammonium fluoroborate, large amounts of 3-phenylbutyronitrile and 3-methyl-3-phenylglutaronitrile were found. This was rationalized according to the scheme presented in Figure 11 which was supported by the presence of small amounts of 3-methylcinnamonitrile among the products. Similar products were obtained with benzaldehyde and benzophenone.

It was the purpose of the present investigation to study this system in more detail for acetophenone and, by means of a more detailed analysis of the products, to try to discover the factors favouring such

reactions. It was hoped that, by the correct combination of these factors, e.g. electrode material, supporting electrolyte and co-solvents, one of the nitrile products could be made to predominate, thereby providing a useful synthetic route to such compounds. In order to do this, it was necessary to confirm or disprove the scheme given in Figure 11 and to investigate the effects of the residual water on the reaction. Since the reduction of acetophenone has been much studied with respect to mechanism and stereochemistry, it was also hoped to gain additional information on the stereochemistry of pinacolization and the behaviour of radical-anions in very dry solutions, and thereby to resolve the mass of conflicting evidence and theories summarized above into some sort of reasonable harmony.

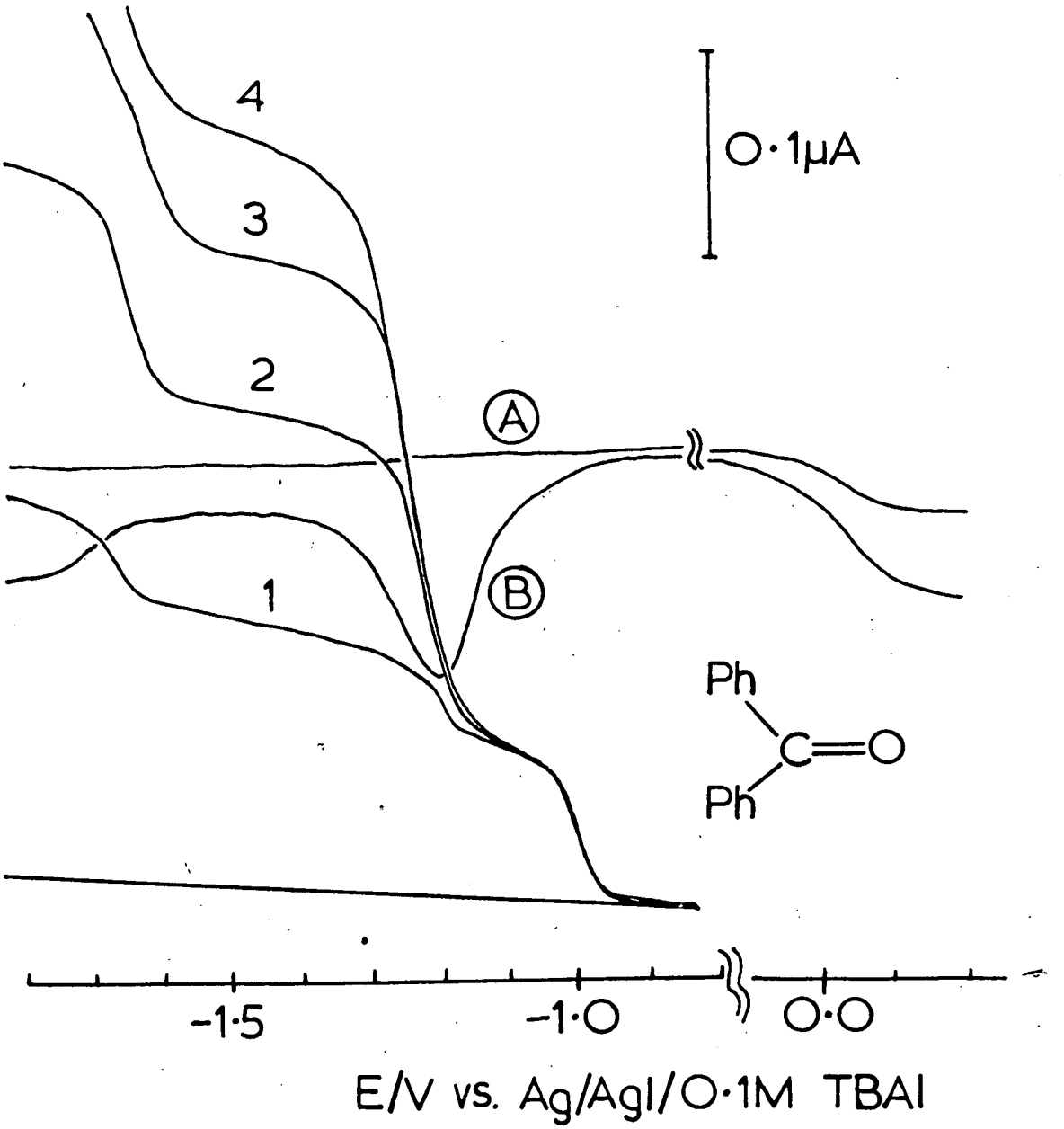


Figure 12. Polarographic and Tensammetric traces of benzophenone in 0.1M TBAP-DMF.

1, c_o = 0.26mM; 2, c_o = 0.50mM; 3, c_o = 0.71mM; 4, c_o = 0.91mM. A is the tensammetric trace of the blank solution. B is the tensammetric trace of 4.

Discussion

Voltammetry

In addition to acetophenone, 3-methylcinnamonitrile, benzophenone and fluorenone have been examined by means of polarography and cyclic voltammetry; details are listed in Table 7. All of the compounds exhibit two polarographic waves in acetonitrile containing tetraethylammonium salts as supporting electrolyte. When tetrabutylammonium perchlorate was used as the supporting electrolyte, acetophenone exhibited only one wave while two waves were still visible for the other compounds. The height of the first waves ($i_d(1)$) corresponds to a one-electron reduction step while only with fluorenone and 3-methylcinnamonitrile does the height of the second wave ($i_d(2)$) correspond to a one-electron step. The reduction in wave-height for the second wave observed with acetophenone and benzophenone may, in part, be due to a shorter drop-time at the negative potentials of the second wave but this cannot entirely explain the small wave-height. It was also noted that, as the initial concentration of the depolariser was increased, the relative height of the second wave decreased.

When DMF was used as the solvent, clear adsorption prewaves were observed for all the ketones and this phenomenon is illustrated for the case of benzophenone in Figure 12. Tensammetric curves were also recorded showing clear evidence for an adsorption process of some description since such curves show the capacitance current required for the charging of the double layer. For a more detailed description of this technique, the reader is referred to the monograph of Breyer and Bauer.[94]

Acetophenone, benzophenone and fluorenone also exhibit prepeaks when reduction takes place in DMF at a stationary mercury electrode during cyclic voltammetry experiments. These prepeaks are not present when acetonitrile is used as the solvent and are very small or absent in DMF if

more than one cycle is carried out. Furthermore, if one cycle is carried out followed by a second shortly after, then no prepeak or a much smaller prepeak is observed providing that no stirring of the solution with nitrogen is carried out during the waiting period. If, however, the solution is stirred with nitrogen during this interval, then the prepeak is observed once more. This indicates that a film is formed on the electrode surface after one cycle which inhibits the adsorption process and that this film can be destroyed with nitrogen. It was also noted that no corresponding anodic adsorption peak was observed, indicating complete irreversibility. Fluorenone, however, does exhibit anodic stirring similar to that described by Bard and Santhanam.[35]

In the absence of the adsorption peaks, all the ketones and 3-methylcinnamonitrile exhibit two reduction peaks in acetonitrile or DMF when tetraethylammonium salts are used as supporting electrolyte and only acetophenone does not exhibit two reduction peaks in the presence of tetrabutylammonium salts. The first peaks of benzophenone, fluorenone and 3-methylcinnamonitrile are almost completely reversible (i_{pa}/i_{pc} = ca. 1, E_{pc} is independent of C_o and ν) while that of acetophenone is considerably less than reversible (i_{pa}/i_{pc} = 0.52, τ = 1.1s, ν = 200mVs^{-1}). The second reduction peaks are all completely irreversible except for fluorenone which shows some sign of an anodic current. The second peak potentials vary with the initial concentration, sweep rate and the presence of residual proton donors. The heights of the second peaks are all smaller than those of the first peak, especially in the case of acetophenone.

The addition of proton donors, e.g. water or phenol, to the solution caused the suppression of the second reduction peaks and all the oxidation peaks, and caused an increase in the height of the first reduction peak. The effect of proton donor on the height of the first peak of acetophenone was small while the first peaks of benzophenone and

fluorenone more than doubled in height. This is consistent with a dimerization process for acetophenone and a hydrogenation process for the other two ketones. The first peak of 3-methylcinnamonitrile increases much more than that of acetophenone but less than that of the other ketones. In all cases, the peak potentials of the first wave shift to less negative potentials upon the addition of a proton donor.

The peak potentials varied with the sweep rate (ν) for all of the compounds in the presence of proton donors. Attempts to measure this variation in the case of 3-methylcinnamonitrile met with limited success. At a phenol concentration of 6mM in 0.4M $TEABF_4$-CH_3CN, a variation of 23.1mV/decade with log ν ($r = 0.988$) was found, while at a phenol concentration of 44mM, a variation of 28.7mV/decade ($r = 0.970$) was found. Some doubt about the validity of these values must be acknowledged due to the rather poor correlation coefficients (r), but they do point to the occurrence of a second order reaction at low concentrations of proton donor and a first order process at higher concentrations.

When the peak potential of acetophenone in dry acetonitrile was studied by means of linear sweep voltammetry, a potential shift was observed at low sweep rates while at higher sweep rates, the peak potential was found to be invariant. The value of the sweep rate at which reversibility was obtained depended upon the solvent. In acetonitrile which had been freshly dried and distilled, complete reversibility was obtained at less than $1Vs^{-1}$ whereas, in acetonitrile which had been stored for some time and consequently contained more water, complete reversibility was not attained until values of around $4Vs^{-1}$ were used, On addition of water, reversibility was only attained above $10Vs^{-1}$.

These observations are in accord with the findings of Saveant and Tessier[87] who reported that the radical-anions initially formed dimerized and that the rate of dimerization was accelerated by the addition of

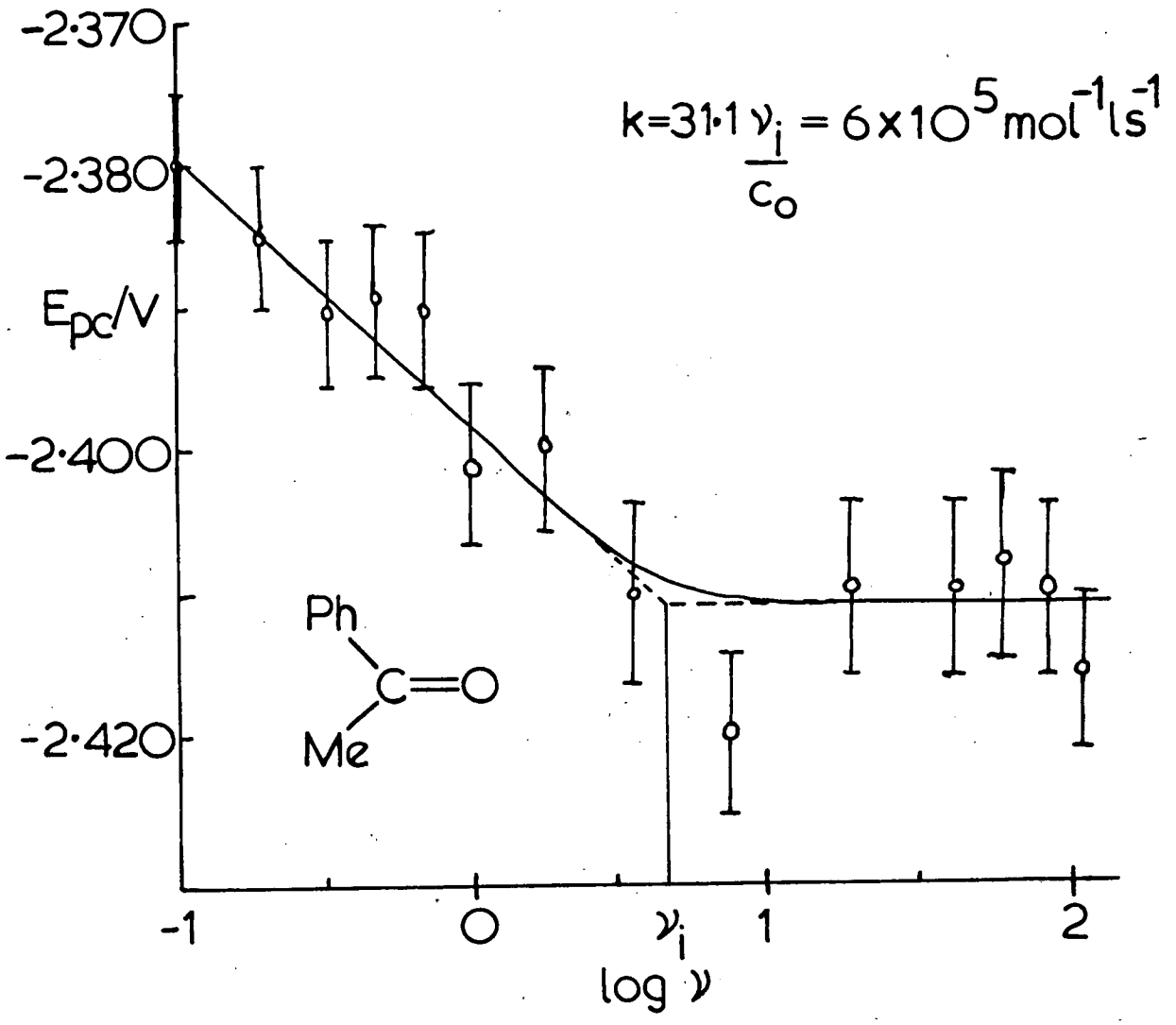


Figure 13. Peak potential behaviour of acetophenone (2.54×10^{-4}M) in 0.4M $TEABF_4$-CH_3CN + 1% H_2O. A long drop-time capillary electrode was used as the working electrode and an Ag/0.1M $AgNO_3$ electrode as the reference.

water to the solution. These authors found that, in acetonitrile containing 0.3% water, the rate constant of dimerization (k) is ca. 3 to 6 x $10^4 mol^{-1}ls^{-1}$, at 1.3% water, k = 4 x $10^5 mol^{-1}ls^{-1}$ and at 5.3% water, k = 1.3 x $10^6 mol^{-1}ls^{-1}$.

Since reversibility was attainable in the experiments carried out in this study, it was possible to estimate the rate constant of dimerization by the use of linear sweep voltammetry[14] and asymmetric triangular sweep voltammetry.[13,17,19] The procedure for these methods are outlined in the experimental section and the peak potential diagram for acetophenone in acetonitrile containing 1% water is illustrated in Figure 13. It can be seen that the slope of the oblique part of the line is about 20mV/decade which is consistent with a radical-radical dimerization process. The rate constant was calculated from the value of ν_i and was found to be 6 x $10^5 mol^{-1}ls^{-1}$ for these conditions. In the drier conditions, the estimation of the rate constant was much more difficult by this method because the oblique part of the line is much shorter, thus making it difficult to find the value of ν_i. However, using this method, the rate constant was found to be 7 x $10^3 mol^{-1}ls^{-1}$ for the freshly distilled acetonitrile (ca. 0.01% H_2O present) and 1 x $10^5 mol^{-1}ls^{-1}$ for acetonitrile which had been stored for some time. The rate constant was also measured by asymmetric triangular sweep voltammetry for the driest solution and was found to be 1 x $10^3 mol^{-1}ls^{-1}$. Although the accuracy of these values are ±60% at best, the order of magnitude of the rate constants are in accord with those measured by Saveant and Tessier.[87]

Preparative electrolyses

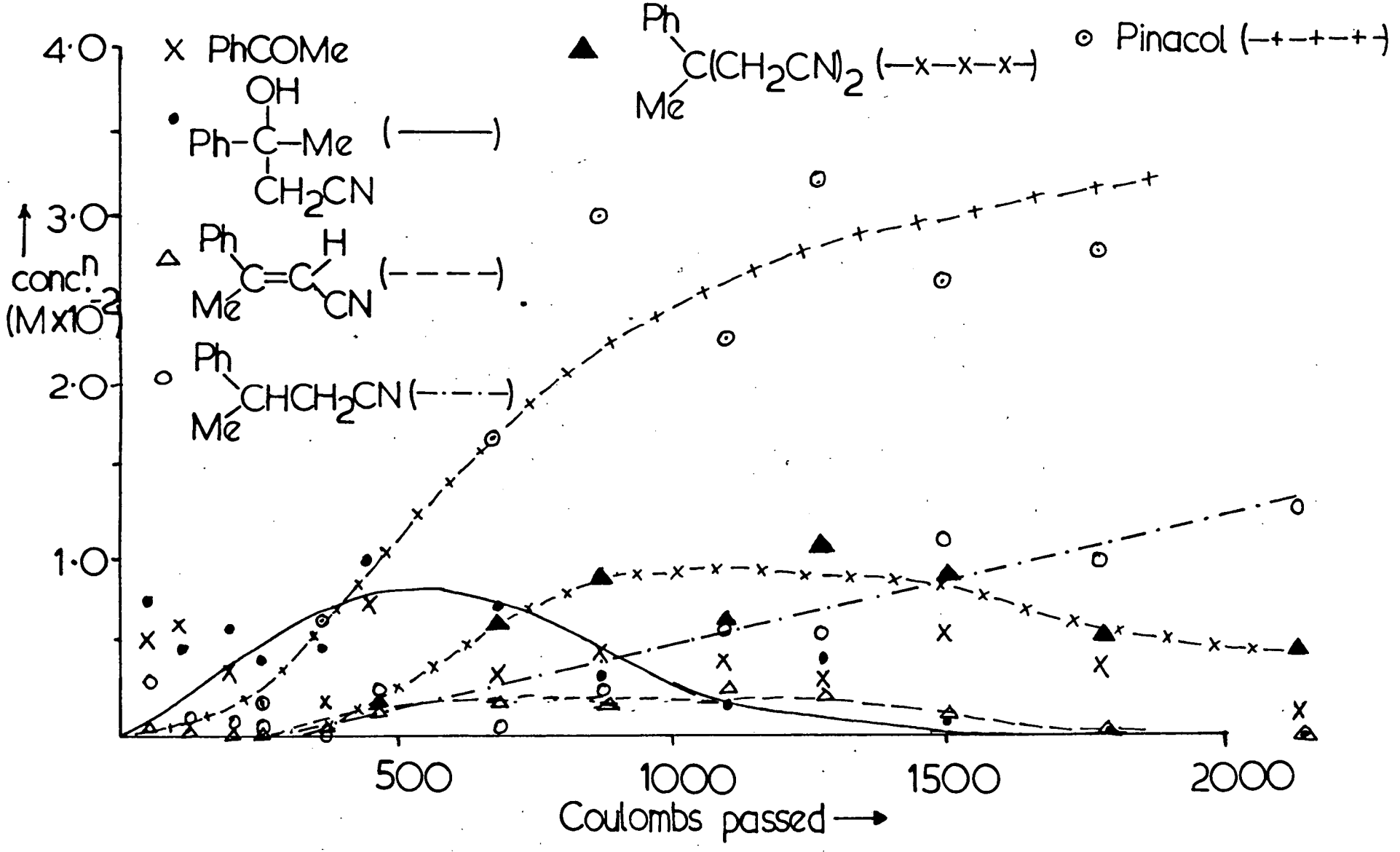
The product distributions of the initial series of reductions of acetophenone at mercury in dry acetonitrile were estimated by glc analysis and the results are listed in Table 8. The electrolyses listed were carried out with the same batch of purified solvent so that the solvent

used in the runs at the foot of the table had been stored for some time. In this series the acetonitrile had not been treated with sodium hydride. It is immediately obvious that the yield of nitrile compounds was considerably lower than that found previously (35% of 2 and 35-45% of 4, Table 8)[93] although it is noticable that the first four runs, which were carried out with more recently dried solvent, gave higher yields of nitrile compounds than later runs carried out with acetonitrile which had been stored for a longer period.

The observation of 3-methylcinnammonitrile among the products prompted a search for the possible presence of the hydrodimer of this compound among the products. Analysis of one of the product mixtures by high pressure liquid chromatography showed the presence of 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcyclopent-1-ene in 21% yield. Avaca and Utley[95] have also found a very similar compound upon reduction of 2-cyano-3-phenylbut-2-enenitrile under similar conditions. Nevertheless, judging from Table 8 and even taking into account the formation of this hydrodimer, a large amount of material remains unaccounted for. Fortunately, it proved possible to analyse for acetophenone pinacol by means of hplc despite its low ultraviolet absorption and full analyses of different series of reductions are given in Tables 9, 10 and 11.

As in Table 8, each Table lists a series of reactions carried out with the same batch of solvent and, once again, the period of solvent storage increases down the Table. The solvent used in Table 9 had not been treated with sodium hydride whereas that used in Tables 10 and 11 had been so treated. The estimates for the hydrodimers (7 and 8) listed in Table 9 are likely to be high due to the preferential loss of the standard for liquid chromatography but this has been corrected for in the reductions listed in Tables 10 and 11 (see Experimental). However, this would have no effect upon the isomer ratios of the hydrodimers (dl/meso and dl/dl) which are listed in parentheses after the yields. No attempt

Figure 14


4·0
3·0
2·0
1·0
conc.n
(M x 10⁻²)
X PhCOMe
OH
Ph–C–Me
CH2CN
(———)
Ph
H
C=C
Me
CN
(– – – –)
Ph
CHCH2CN (–·–·–)
Me
Ph
C(CH2CN)2 (–x–x–x–)
Me
⊙ Pinacol (–+–+–+–)
500
1000
1500
2000
Coulombs passed →

has been made to normalise the yields since two different analytical methods were used, viz. glc and hplc.

Mechanism of nitrile formation

In Table 9 are listed the yields of 3-hydroxy-3-phenylbutanenitrile (4) which was only detected in this series of reactions. It is possible that, in the other series, the hydroxynitrile peak is merged with that of 3-methylcinnamonitrile since different glc columns were used. The production of this compound was confirmed by its isolation by means of dry column chromatography. The spectral data and the glc retention time of the isolated compound were identical to those of an authentic sample.

The isolation and identification of the hydroxynitrile strongly supports the scheme (Figure 11) which has previously been proposed to account for the observed products.[93] In order to investigate this pathway further, the course of the reaction was followed by means of sampling the electrolysis solution during an electrolysis and analysing these samples. The results of this procedure are listed in Table 12 and the concentrations of the various compounds which are formed were plotted against the number of coulombs passed (Figure 14). Although the yields of nitrile compounds involved are relatively small, it can be quite clearly seen that 3-hydroxy-3-phenylbutanenitrile and 3-methylcinnamonitrile are intermediates in the reaction.

The formation of these compounds is thought to be due to the production of the cyanomethyl anion, $^{-}CH_2CN$, which nucleophilically attacks acetophenone to form the hydroxynitrile. This then proceeds to lose water to form 3-methylcinnamonitrile which is electro-active whereas the hydroxynitrile is not. The products found then follow (see Figure 11). As further evidence for the formation of $^{-}CH_2CN$, 3-aminocrotononitrile and 4-amino-2,6-dimethylpyrimidine, base catalysed products of acetonitrile, were also detected by glc analysis. When the normal work-up

procedure was employed, involving the addition of ammonium chloride to the basic catholyte solution, then these compounds were seldom observed. However, if the ammonium chloride was not added, these compounds were formed in large amounts, indicating the occurrence of dimerization and trimerization of acetonitrile via $^{-}CH_2CN$ upon work-up. If a proton donor is added, then the anion is protonated and no further reaction occurs.

The formation of the adduct which results from the attack of the cyanomethyl anion upon acetophenone has been detected by means of cyclic voltammetry,[96,97] using the reduction peak of acetophenone in dry acetonitrile. After adding an equimolar amount of azobenzene to the acetophenone solution, the cyclic voltammogram was recorded and the properties of the acetophenone peak were compared with those in the absence of azobenzene. The peak current was found to be considerably less (55 - 75% decrease) and the system was found to become almost reversible in the presence of azobenzene, whereas it was initially only partially reversible. These observations were explained on the basis that the azobenzene was first reduced to its dianion which abstracted a proton from the solvent to yield the cyanomethyl anion. This anion then added to acetophenone to give an electro-inactive adduct, leaving less acetophenone available for reduction. Consequently, there was a decrease in the peak current. The increased reversibility of the acetophenone system was explained by the scavenging of proton donors and residual water by the azobenzene dianion. In the region of the electrode, the concentration of water must be seriously depleted and therefore, the rate of dimerization of the radical-anions will be decreased since the preferential solvation of these radical-anions by water accelerates the reaction.[87] Similar results concerning the peak height were found with benzophenone.

In order to confirm this interpretation of the voltammetric results, preparative co-electrolyses of azobenzene with acetophenone were carried

out. Two runs were performed at a potential of -2.2V and -2.1V vs. Ag/ 0.1M $AgNO_3$ respectively. Unfortunately, it appears that these potentials were too negative because, although the acetophenone pinacol could not be analysed for, the absence of acetophenone among the products indicates that the ketone is being reduced at these potentials. Furthermore, the yields of nitrile compounds are low which supports this explanation. When the co-electrolysis was carried out at -2.0V, however, acetophenone (20%) was recovered and a significant amount of 3-methylcinnamonitrile (39%) was detected among the products. Finally, azobenzene was reduced on its own in acetonitrile, followed by the addition of acetophenone, and the solution was then stirred with no current flowing for 16 h. Most of the recovered product was found to be acetophenone (60%) but small amounts of 3-methylcinnamonitrile (3%) and 3-hydroxy-3-phenylbutanenitrile (2%) were observed.

The results of these preparative co-electrolyses are in accord with the interpretation of the voltammetric results. However, in a recent report by Hallcher and Baizer,[98] evidence has been presented which implies that the azobenzene dianion is not as strong a base as was previously thought. These authors have been able to observe complete reversibility of the azobenzene radical-anion/dianion couple (1mM) in DMF which had been rigorously dried. Addition of acetonitrile (10mM) to the solution apparently had no effect upon the voltammetric pattern. They have found, however, that acetonitrile is deprotonated when used as the solvent in preparative experiments.[99]

The series of reactions listed in Table 9 confirm the initial findings of those listed in Table 8 which showed that the yields of nitrile products were lower than those observed in the previous work.[93] Table 9 shows that the variation of temperature or electrode material can make some difference. However, these low yields imply that either the previously reported yields of nitriles were over-estimates or that there was

some significant difference in the experimental conditions. A possible difference lies in the electrolysis cell geometry.

In the original report, the cell used was an H-type cell with a single glass frit separating the two compartments and the working and counter electrodes were well separated, thus leading to a fairly high cell resistance. A more serious flaw in the design lay in the positioning of the reference electrode which could not be placed close to the working electrode. This would mean that, because of the uncompensated cell resistance, the actual electrode potential would deviate from that set on the potentiostat. Harrar and Shain[100] have investigated the effect of the electrode geometry upon the potential distribution across the working electrode surface and have found that the potential could vary above and below the set potential. In the present case, this could mean that the electrode potential might sometimes deviate to a potential negative enough to reduce acetonitrile. The acetonitrile radical-anion could then produce the cyanomethyl anion according to the scheme:

$$CH_3CN + 1e^- \longrightarrow \dot{C}H_2CN$$

$$\dot{C}H_2CN \longrightarrow \cdot CH_3 + CN^-$$

$$\cdot CH_3 + CH_3CN \longrightarrow CH_4 + \cdot CH_2CN$$

$$\cdot CH_2CN + 1e^- \longrightarrow \bar{C}H_2CN$$

A similar kind of mechanism has been proposed to account for the action of sodium on acetonitrile[101] and experiments carried out in this laboratory have shown the production of methane and cyanide ions upon the addition of sodium to acetonitrile.[102]

In order to test this possible mechanism, an electrolysis was carried out using a potential of -3.2V vs. Ag/0.1M $AgNO_3$ (see Table 10) but the product distribution showed no significant change from that observed using a potential of -2.95V. Indeed, when the working potential was measured during the course of the electrolysis, it was observed that soon

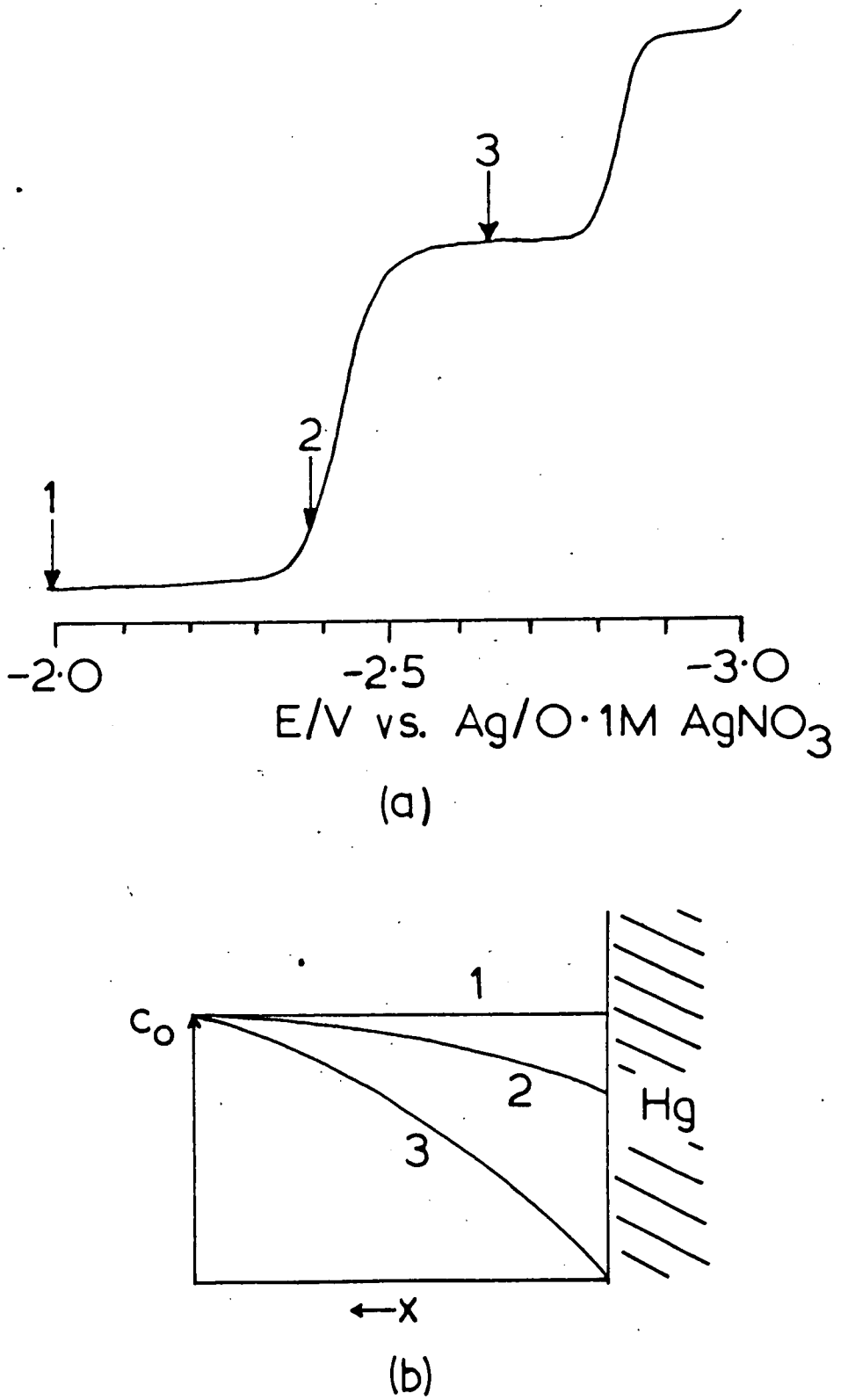


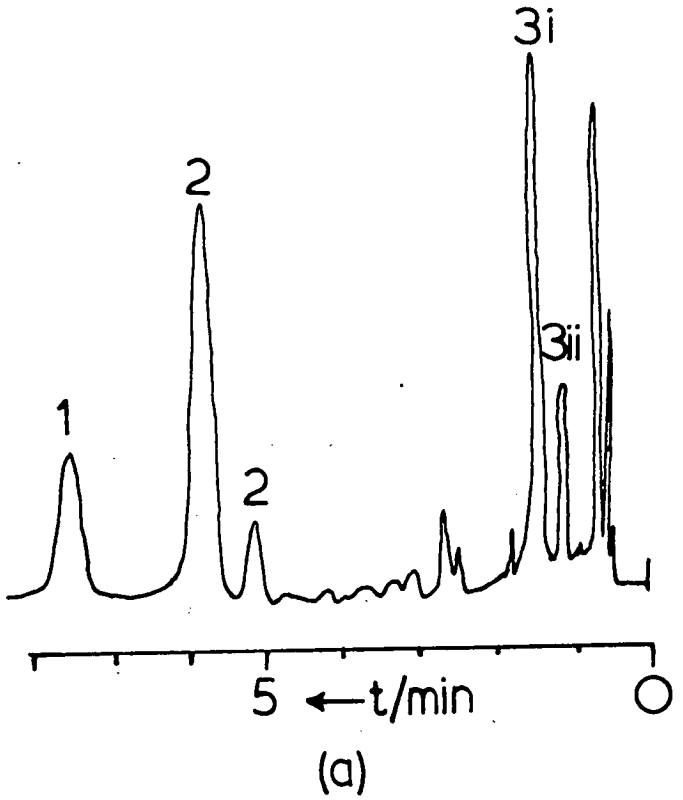
Figure 15. (a) Polarogram of acetophenone in acetonitrile ($0.1M\ TEABF_4$).

(b) conc^n. (c_o) profiles of acetophenone for the various potentials indicated in (a); x is the distance from the electrode surface.

after the commencement of the electrolysis, the potentiostat was unable to maintain this potential and the measured value was in the region of the half-wave potential of the first wave of acetophenone (-2.40V). Given this situation, it is most unlikely that the scheme proposed above could operate experimentally.

The inability of the potentiostat to maintain its set potential was noted in several experiments and this would be expected to occur even more with a cell where working, counter and reference electrodes are all widely separated as was the case in the original work. Consequently, it seems reasonable to propose that the actual working electrode potential did not correspond to the plateau of the polarographic wave, but somewhere on the rising portion of the wave. This would mean that the acetophenone molecules were not all being reduced immediately upon arrival at the electrode surface and that the concentration of ketone in the region of the electrode would remain high. By contrast, if the potential value lies on the plateau of the wave then the rate of transfer of electrons is diffusion controlled and the concentration of ketone at the surface is zero. The two situations are illustrated in Figure 15.

The production of the cyanomethyl anion is a consequence of the electrochemical reaction and, therefore, the concentration of the anion should be highest in the region of the electrode. Although addition to the ketone could well take place in the bulk of the solution, it seems reasonable that this reaction would be more favoured by the high concentrations of anion. However, the chemical reaction would have to compete with the electrochemical reaction which would deplete the concentration of ketone. Therefore, the most favourable situation for the formation of the adduct should be that corresponding to potential 1 (Figure 15), with the cyanomethyl anion being produced by some method not involving the reduction of the ketone, e.g. reduction of azobenzene. However, since the anion is produced via ketone reduction, the best situation



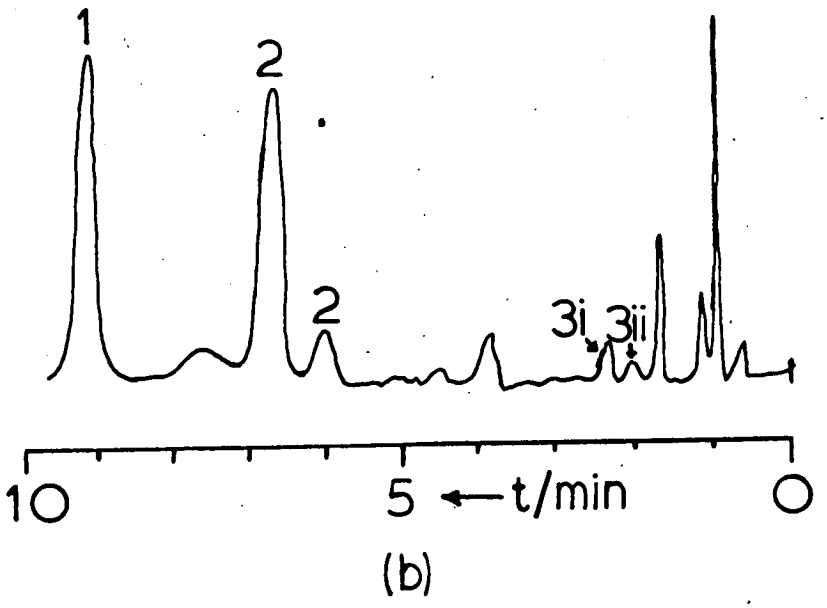


Figure 16. Liquid chromatograms of product mixtures. (a), E = -2.95V, i_o = 200mA; (b), E = -2.20V, i_o = 25mA. 1 = marker; 2 = hydrodimer of 3-methylcinnamonitrile, 2dl-isomers: 3 = acetophenone pinacol, i = dl and ii = meso.

would then be that shown for potential 2 which could correspond to the situation in the original work.

In order to test this hypothesis, an electrolysis was carried out at potentials such that the current remained in the region of 25mA and the product analysis showed a greatly reduced yield of pinacol and an increase in nitrile formation (cf. the first three electrolyses listed in Table 10). The change is illustrated even more strikingly by comparison of the liquid chromatograms shown in Figure 16 which demonstrates the dramatic fall in the yield of pinacol. This bears out the trend discernable in Tables 8 and 9 where low initial currents lead to higher nitrile yields.

It must be noted, however, that this procedure is ineffective if the solution is wet, as in later electrolyses (Table 10) where either water is added or the solvent had been stored for some considerable time. Furthermore, the yields of nitriles listed in Table 10 are considerably higher than those listed in Table 9 for situations where the potential lies at the top of the current plateau and the current is high. This must mean that, in the reactions listed in Table 10, either the nucleophilic addition is faster or that considerable reaction takes place in the bulk of the solutions. Either way, the change must be due to some difference in the solvent, probably as a consequence of the different purification procedures used.

So far, no mention has been made of how the cyanomethyl anion is produced by reduction of the ketone. From the work of Saveant and Tessier,[87] it seems that the ketyl radical-anion is not responsible and the monomer dianion does not appear to be involved since, except for cases where the electrolysis was carried out at reflux temperature, no alcohol was formed. Therefore, the dimer dianion appears to be the most likely origin.

From the voltammetric evidence, it has been shown that the residual water in the solvent plays a role in the formation of the dimer dianion and, from this, it can be inferred that the dianion is preferentially solvated by the residual water. A similar situation will hold with the azobenzene dianion which would also be expected to be preferentially solvated by water. These dianions can either act as bases or nucleophiles as exemplified by the work of Baizer and Troll with azobenzene.[103] As shown by voltammetric experiments on azobenzene and benzophenone in DMF,[96,97] it appears that the azobenzene dianion does not act as a nucleophile in the present situation and, in some manner, abstracts a proton from acetonitrile. It seems reasonable to assume similar behaviour for the acetophenone dimer dianion also. However, it has been shown by Hallcher and Baizer[98] that the azobenzene dianion does not abstract a proton from acetonitrile in very dry conditions and probably the same situation will hold for the dimer dianion. Although it may be argued that the situation in Hallcher and Baizer's experiment is not equivalent to the conditions used in the present studies in that there is a concentration difference, it should be noted that, in the present experiments there is more residual water present and that in the region of the basic dianions, there will be a relatively high concentration of water due to preferential solvation. Given this situation, it is probable that the dianions abstract a proton from the residual water.

If protons are abstracted from water, then hydroxyl anions are formed and these would be expected to be highly active species due to their poor solvation by acetonitrile. The hydroxyl anion could then attack the solvent to form a cyanomethyl anion and water. It seems likely that a water molecule would be able to solvate a cyanomethyl anion more efficiently than acetonitrile would be able to solvate a hydroxyl anion.

Obviously, the abstraction of a proton from water is an equilibrium

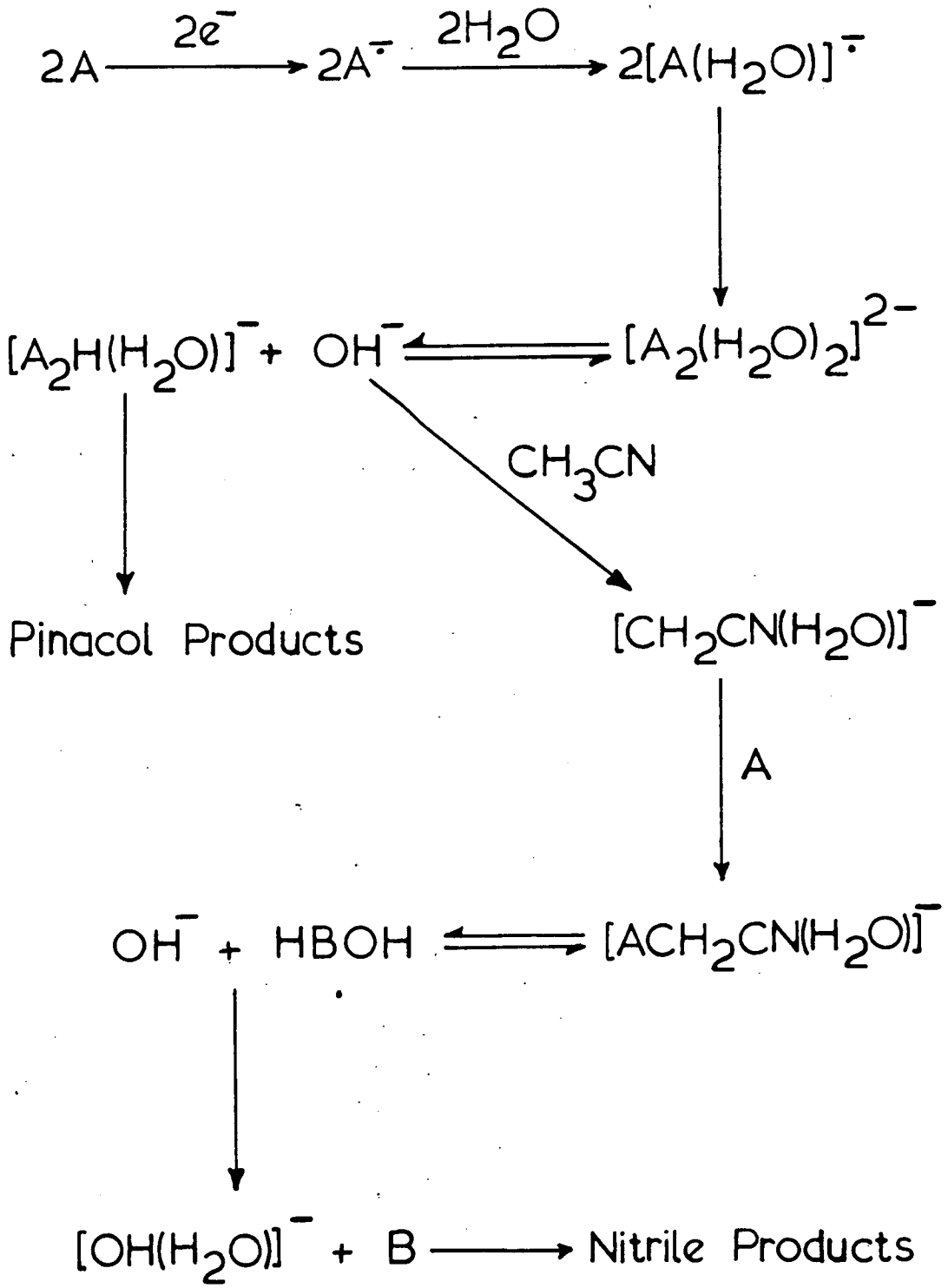

2A
2e⁻
2A⁻·
2H2O
2[A(H2O)]⁻·
[A2H(H2O)]⁻ + OH⁻
[A2(H2O)2]2⁻
CH3CN
Pinacol Products
[CH2CN(H2O)]⁻
A
OH⁻ + HBOH
[ACH2CN(H2O)]⁻
[OH(H2O)]⁻ + B
Nitrile Products

Figure 17

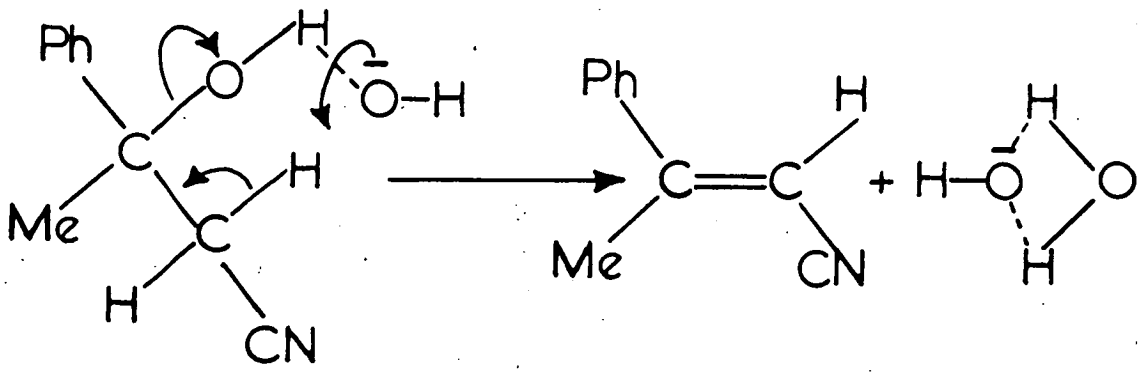
process which is probably more in favour of a water molecule than a hydroxyl anion due to the solvation factors. However, this equilibrium can be displaced by the attack of the hydroxyl anion upon the solvent, thus driving the reaction. As the water concentration is increased, the hydroxyl anion will become more favoured in the equilibrium but less active due to its increased solvation by other water molecules and the attack on the solvent should be less favoured. Even if a cyanomethyl anion is formed at higher water concentrations, then it should be much less nucleophilic due to its more efficient solvation by the extra water. These effects would explain the suppression of nitrile formation observed at higher water concentrations in the reduction of acetophenone in acetonitrile.

The situation is summarised in Figure 17 where A corresponds to acetophenone, B corresponds to 3-methylcinnamonitrile and HBOH the hydroxynitrile. A similar abstraction process with the azobenzene dianion, catalysed by water, would explain the result reported by Hallcher and Baizer[98], since in their very dry solvent there would be too little water present to efficiently catalyse the abstraction process. Indeed, since DMF was used as solvent, the hydroxyl anion should be even less favoured in the equilibrium with the dianion-water complex.

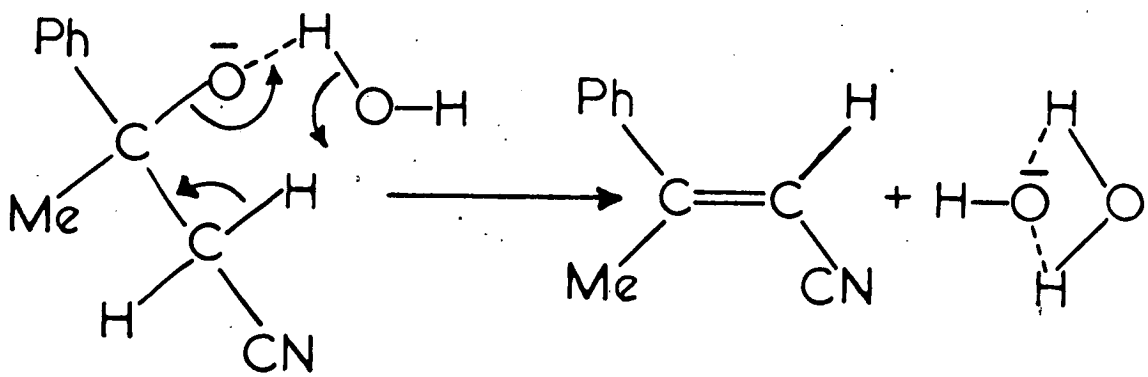
In the voltammetric experiments carried out with acetophenone and azobenzene, the increased reversibility of the acetophenone reduction pattern supports the proposal of the involvement of water in the abstraction process. Further evidence for the involvement of hydroxyl anions comes from the reaction of KOH with acetonitrile and acetophenone.[104] In one such experiment carried out in the present study, 3-methyl-3-phenylglutaronitrile was observed among the products in addition to 3-methylcinnamonitrile, thus showing a striking parallel with the electrochemical distribution of products.

A further point of interest concerning the hydroxyl anion is its

possible role in the dehydration of 3-hydroxy-3-phenylbutanenitrile. In both the chemical and electrochemical reactions, there is no acid present which could catalyse the dehydration. However, if the hydroxynitrile forms, as shown in Figure 17, then a hydroxyl anion would be produced. In order to avoid the production of a poorly solvated anion, the loss of water by the hydroxynitrile would lead to a rather more efficiently solvated anion:



On the other hand, it is possible that the hydroxynitrile itself is never formed but that the water which solvates the ionized form is involved in the dehydration step:



Such a possibility is still consistent with the observation of the hydroxynitrile in the product mixtures, since the ionized form could easily gain a proton on work-up. Probably, the true situation lies somewhere between the extremes described here.

Table 11 lists the results of reduction of 3-methylcinnamonitrile under conditions similar to those used for acetophenone in Table 10. It is noticable that the amount of product corresponding to addition of the cyanomethyl anion to the substrate is significantly lower than that observed with acetophenone. This is in accord with the observation that azobenzene causes very little reduction in the peak height of 3-methylcinnamonitrile in cyclic voltammetry experiments, presumably due to the lower electrophilicity of the olefinic carbon compared with the carbonyl carbon in ketones.

The high yields of 3-phenylbutanenitrile reflect the reversibility observed in the cyclic voltammogram of 3-methylcinnamonitrile (B). This product is probably formed through a slow disproportionation process which competes with the dimerization reaction. Addition of a proton donor such as phenol increases the speed of disproportionation and dimerization through solvation and protonation of the anion radicals:

$$2B + 2e^- \rightleftharpoons 2B^{\cdot -} \xrightarrow[\text{slow}]{k_{disp}} B^{2-} + B$$

$$\xrightarrow[\text{slow}]{k_{dim}} B_2^{2-}$$

$$2B^{\cdot -} + PhOH \rightleftharpoons BH\cdot + B^-$$

$$BH\cdot + B^{\cdot -} \xrightarrow[\text{fast}]{k'_{disp}} BH^- + B$$

$$BH\cdot + B^{\cdot -} \xrightarrow[\text{fast}]{k'_{dim}} B_2H^-$$

$$BH\cdot + e^- \xrightarrow[\text{fast}]{} BH^-$$

The observed variations of peak potential with sweep rate in the

presence of phenol are consistent with such a scheme. At low concentrations of proton donor, the protonation step is relatively fast compared with the disproportionation and dimerization reactions. In other words, the predominant second order reactions are those involving two radical-anions which are slow and give rise to second order kinetics ($\partial E_p/\partial \log \nu$ = -23mV/decade). As the proton donor concentration is increased then disproportionation, dimerization and further reduction involving protonated radical-anions become the predominant reactions. These are likely to be so fast that the protonation of the radical-anion would be the overall rate-determining step leading to the observation of first order kinetics ($\partial E_p/\partial \log \nu$ = -28mV/decade).

In the case where a weaker proton donor like water is added to the solution, it seems that protonation of the radical-anion would not take place but that the water would preferentially solvate it. Such solvation would increase the rate of the disproportionation and dimerization reactions and tends to favour disporportionation over dimerization as seen in Table 12 where the addition of 0.3% water significantly increased the relative amount of monomer formed. This would also account for the relative amount of the cinnamonitrile monomer and dimer formed in the acetophenone reductions since water is produced during the formation of the cinnamonitrile in these reactions.

Stereochemistry and the mechanism of dimerization

Due to the application of high pressure liquid chromatography to the problem of product analysis, it has been a simple matter to measure the isomer ratios of the hydrodimers formed. The dl- and meso- isomers of the acetophenone pinacol were identified by comparison with the retention times of the respective isomers which had been prepared chemically. The isomers of the cinnamonitrile hydrodimer were not definitely identified. However, the factors which favour the formation of the dl-isomer in the

reduction of acetophenone should equally favour the corresponding isomer of the cinnamonitrile dimer. Similarly the factors which favour the faster elution of the meso-isomer of acetophenone pinacol in the liquid chromatograph should be the same for both types of hydrodimer. Consequently, when the isomer ratio of the cinnamonitrile hydrodimer is listed, what is thought to be the isomer corresponding to the dl-pinacol is quoted first. These isomer ratios are listed in parentheses after the yields of the hydrodimers.

The dl/meso isomer ratios measured for the acetophenone pinacol listed in Tables 9 and 10 are considerably lower than those measured by either Stocker and Jenevein[72] or Bewick and Cleghorn[85] for reductions in aprotic solvents. Addition of 0.3% water, which corresponds to conditions similar to that used by Stocker and Jenevein, caused an increase of this ratio to 6.2. Since different methods of measurement were used, the difference between this value and that found by Stocker and Jenevein (7.0) may be due to the analytical method and, if so, acts as a reference to the former work.

The values of the dl/meso ratio did not appear to be sensitive to the electrode material, in agreement with the findings of Stocker and Jenevein,[52] but were affected by the solvent composition. Similar effects were observed for the hydrodimer of 3-methylcinnamonitrile although it should be noted that changes also occurred depending whether the 3-methylcinnamonitrile was formed during the reduction of acetophenone or whether it was the substrate.

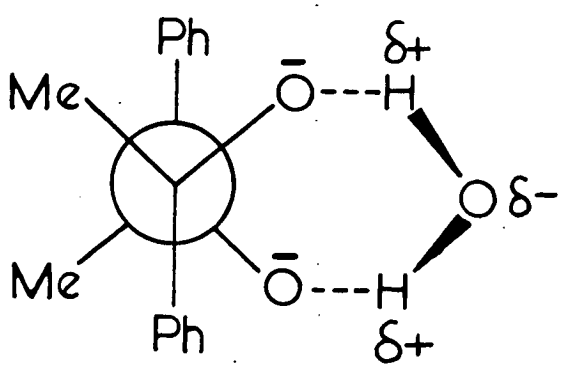
Nearly all of the electroanalytical work carried out on the mechanism of hydrodimerization has shown that the dimerization step involves the coupling of two radical species. Indeed, the studies by Bard and co-workers[28,29,57-59] and Saveant and co-workers[11,60,61] have shown that, in aprotic media, the coupling step proceeds via two radical-anions. Even at preparative scale concentrations, the coupling step has been

shown to involve two radical-anions for p-methylbenzylidenemalononitrile in wet and dry DMF.[68] Saveant and Tessier[87] have made a study of the reduction of acetophenone in acetonitrile containing varying amounts of water and have shown unequivocally that the coupling step takes place between two radical-anions which are preferentially solvated by residual water. No mention of adsorption was made by these authors although Nadjo and Saveant[71] did find evidence for adsorption in aqueous alkaline media. Bard et al.[58] have shown that the maximum coverage on a platinum electrode by 1,2-diactivated olefins in DMF is about 3% indicating that adsorption plays a very small role. The involvement of alkali-metal cations in the dimerization process has also been demonstrated by the same authors.

These results are in conflict with the proposals put forward by Stocker and Jenevein[72] and Bewick and co-workers[85,86] to account for the observed stereochemistry of the product pinacols on reduction of acetophenone in acetonitrile or DMF. Both sets of workers have invoked protonation of one of the radical-anions involved in the coupling step by the residual water to explain the preference for the dl-stereoisomer. However, since the electroanalytical data shows that protonation does not take place, then these explanations must be considered doubtful.

A possible explanation of the preference shown for the dl-isomer based on a homogeneous coupling step is as follows. In an aprotic medium, acetophenone is reduced to the radical-anion. This species is then preferentially solvated by the residual water in the solution (see Figure 17) which helps to decrease the coulombic repulsion between the radical-anions. Now, if there is little or no water present in solution, the coupling step is very slow as indicated by the voltammetric evidence presented earlier[96,97] (reversible behaviour in the presence of azobenzene) which implies that there is little spreading of the charge from the

oxygen to the solvent. Therefore, it would be expected that the meso-isomer would be the most favoured form of the pinacol due to the purely steric factors operating. If, however, there were a small number of water molecules present, then they might be involved in the coupling step. It might be envisaged that a water molecule can act as a hydrogen-bonded bridge between the two radical-anions:

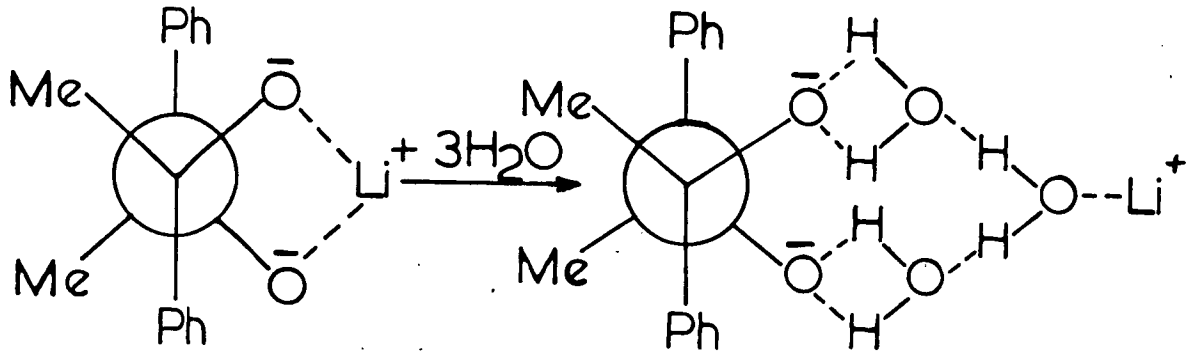


favours dl

When the water concentrations are low, then very few of the couplings will proceed via this mechanism and preference for the meso-form will be expected. As the water concentration increases then more and more couplings will proceed via this kind of mechanism and, consequently, the preference for the dl-form will increase. This will continue until the point where the concentration of water is sufficient for each radical-anion to be surrounded by a cluster of water molecules. At such a point, the charge on the oxygen will be delocalised over the water cluster such that the charge will be diffuse and the strength of the hydrogen-bonding interactions will decrease. Furthermore, as the number of water molecules clustered around the oxygen increases, then the size of the oxygen-water complex will become so great that the steric preference for the meso-isomer will reassert itself.

Such a theory, then, predicts that in very aprotic conditions, the meso-isomer will predominate. As the water concentration increases, an increased preference for the dl-isomer will be observed which will reach a maximum at some point. This is exactly what was observed in this study and in the study by Bewick and Brown.[86] The exact extent of the isomeric preference will vary depending on the solvent. DMF is well known for its inability to solvate small, localised charges effeciently and, consequently, the water solvation effect would be expected to play a more important role in this solvent than in acetonitrile. Nevertheless, since the values of the dl/meso ratio observed in the present study are considerably lower, it appears that the solvent used by Bewick and coworkers was not particularly dry.

It is, of course, possible that the cations of the supporting electrolyte could form ion-pairs with the radical-anions and take over the role of water as described above. For example, it is easy to see how lithium cations would fulfil this role and, since the ion-pairing energies are greater than those for hydrogen-bonding, then a greater effect would be expected. Once again, an increase in the effect would be expected as the concentration of cation is increased until a maximum is reached. The effect of the addition of water (drastic fall in the isomer ratio) is easily explained by preferential solvation of the various ions involved leading to diffuse charges and solvent separated ion-pairs in which the ion-pairing is less strong:



The possibility of ion-pairing by tetra-alkylammonium cations has been put forward by Bewick and co-workers and such ion-pairing has also been proposed by van Tilborg.[91] Jensen and Parker[105] have indeed found evidence for ion-pairing between hydrocarbon dianions and tetra-alkylammonium cations in very dry DMF, although they do not consider the radical-anion as ion-paired. However, it has been shown[87,106] that addition of water or hydroxylic compounds will preferentially solvate anions so that one would not expect tetra-alkylammonium cations to have any effect in the presence of water. This is borne out by the dl/meso ratios observed in the present study when tetrabutylammonium and tetraethylammonium cations were used as the supporting electrolyte. No significant difference was observed when one or the other cation was used. One might expect, if there was any significant effect, that a higher dl/meso ratio would be found in the presence of the tetraethylammonium cations due to their smaller ionic radii.

It is, of course, highly probable that, if the supporting electrolyte

contains a hydroxyl function, e.g. $PhCH(OH)CHCH_3N(CH_3)_3I$,[107] then the cations will be closely associated with the radical-anions since the hydroxyl function will help to solvate the radical-anion in a similar manner to water. If such a hydroxyl-containing cation were to be chiral, then this association could provide an asymmetric environment for the radical-anion in solution and could lead to asymmetric induction in the pinacol. Previous experiments with such electrolytes have not given rise to any asymmetric induction in the pinacol although chirality was induced in the alcohol formed.[108] However, these experiments were performed in water-ethanol solvent mixtures where the radical-anion is probably protonated and the hydrogen bonding in solution will be very weak. Seebach and Oei[83] have induced asymmetry in the pinacol by use of a chiral solvent and van Tilborg and Smit[107] have claimed to be able to induce asymmetry in the pinacol by the use of chiral electrolytes under certain conditions. Unfortunately, no details of the latter are available at present.

The fact that no asymmetric induction in the pinacols has been observed under conditions where there is considerable induction in the alcohols has persuaded certain authors that pinacolization does not take place at the electrode surface.[82] The experiment of Seebach and Oei[83], using a chiral solvent, strongly supports this concept. However Bewick and co-workers[85,86] have contended that the coupling process does, indeed, take place at the surface when DMF is used as the solvent. In support of this, these authors have cited experiments where certain additives, known to adsorb on mercury, have had effects upon the stereochemistry of the products. In particular, Puglisi et al.[78] have found that the addition of tetra-alkylammonium salts to an aqueous acidic solution considerably reduced the dl/meso ratio for benzaldehyde pinacol formation.

Bewick and Brown[86] have proposed that neither the radical-anion nor

the neutral ketyl radical are adsorbed but that only strongly dipolar species such as ion-pairs are adsorbed. The ion-pairs in question were proposed to be those between the radical-anions and tetraalkylammonium or lithium cations. To support this idea, these authors have studied the effect of lithium cations upon the cyclic voltammogram of acetophenone in DMF and have observed effects which they have interpreted as adsorption of ion-paired radical-anions leading to pinacolization on the surface of the electrode.

From the previous discussion, concerning the presence of water and ion-pairing involving tetra-alkylammonium cations, this possibility seems unlikely. However, it must be stressed that the above discussion referred to a homogeneous situation and that, at the electrode, the tetra-alkylammonium cations may well be adsorbed on the electrode where, due to their hydrophobic properties, they may exclude the residual water from the region of the electrode as takes place in the commercial synthesis of adiponitrile. In such a situation, perhaps the conditions at the electrode envisaged by Bewick and co-workers may well exist.

van Tilborg[79] has found evidence for complex formation between ketones and tetra-alkylammonium cations from tensammetric measurements and has found that p-bromoacetophenone is co-adsorbed with tetraethylammonium cations on to mercury from aqueous solution. From this result, he has suggested that a similar situation exists in aprotic solutions, i.e. the ketone and the radical-anion are complexed with the electrolyte cation. In support of this proposal, van Tilborg and Smit[107] have observed that acetophenone is not reducible in acetonitrile containing 0.05M LiF but that on addition of 0.05M tetraethylammonium perchlorate, a reduction wave is observed. This was interpreted as the reduction process requiring, in some manner, the formation of a tetraethylammonium cation complex in order to take place.

Several points, however, must be noted concerning these results. The tensammetric measurements were carried out using an aqueous solution in which the substrate ketone is not too soluble. Tetra-alkylammonium salts are hydrophobic and one might expect their specific adsorption onto mercury to be much stronger from an aqueous solution than from an aprotic solution where they are more soluble. Indeed, it is not surprising that van Tilborg found that the ketone and the cation adsorbed as a complex, since the ketone is fairly insoluble in water and more soluble in organic media. Therefore, if the tetra-alkylammonium cations adsorb onto the electrode then so also will the ketone since it is more "soluble" in the organic medium at the electrode surface. Interestingly, van Tilborg found that the ketyl radical desorbed without the tetra-alkylammonium cation.

Such conditions are difficult to translate directly to aprotic media since the solubilities of the various species in the solution will be considerably different. This is shown by the absence of reduction of acetophenone in acetonitrile in the presence of LiF. It is, in fact, difficult to see how LiF could be appreciably ionized in acetonitrile, especially as the fluoride anion is such a small ion. If this salt was not appreciably ionized, then there would be no supporting electrolyte to carry the reduction current which is not the case upon the addition of TEAP and, hence, one observes a reduction wave.

No evidence for the participation of adsorption in the pinacolization process has been observed in the present study. No significant change in the dl/meso ratios (Table 9) were observed on changing the electrode material (Hg, Pt or C). However, this is not to say that no adsorption processes are taking place. Indeed, when DMF is used as the solvent then a clear adsorption prewave is observed in polarography and, in the comparison of electrode materials, it should be noted that, with

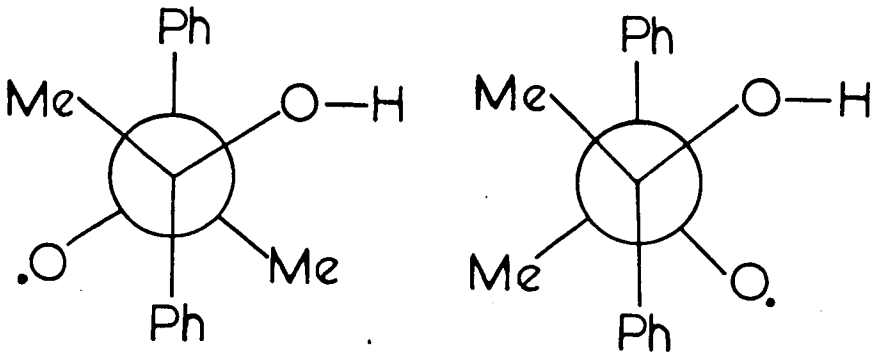
platinum, considerably more nitriles were formed than with either mercury or carbon.

The adsorption prewave was shown by cyclic voltammetry to be irreversible for acetophenone, benzophenone and fluorenone and appears about 150-200mV anodic of the diffusion wave and thus is very similar in position to the peak observed by Bewick and Brown[86] upon addition of lithium cations to the solution. Now, if the process which was taking place at this adsorption prepeak was pinacolization, then it is very difficult to see how this could be faster than the process taking place in solution due to the immobility of the adsorbed species. The irreversibility therefore implies that the surface process is not pinacolization. Since no alcohol is found among the products there then remains the possibility of an attack upon the electrode, i.e. the formation of organomercury compounds. The fact that there is a prewave as opposed to a postwave indicates that it is the product of electron transfer which is attached to the surface.[15,109]

A prewave is only observed in DMF because the radical-anion is much less stable than in acetonitrile due to the less efficient solvation of the charge. The radical-anion is therefore unstable and attacks the electrode surface, forming a film of mercury compound. This film can be destroyed by bubbling nitrogen through the solution. If lithium cations are added to the solution, then the radical-anions can be stabilised by ion-pairing but attack on the surface to form a film which inhibits further reduction as found by Bewick and Brown[86] is still possible. The fact that no inhibition is observed in the absence of Li^+ may be due to a difference in the nature or thickness of the film in the absence of the metal ions. The lack of a prewave in acetonitrile is easily explained by the fact that the radical-anion is better solvated in solution and, hence, less strongly adsorbed such that the adsorption wave is buried under the diffusion wave.

The conclusion of this study, therefore, is that, although adsorption processes take place during the reduction of acetophenone in aprotic conditions, they are not involved in the pinacolization process which takes place in the bulk of the solution. All of the variations of the isomer ratios with the concentrations of water and lithium cations can be adequately explained on this basis, which is also in harmony with the voltammetric results of Saveant and Tessier.[87]

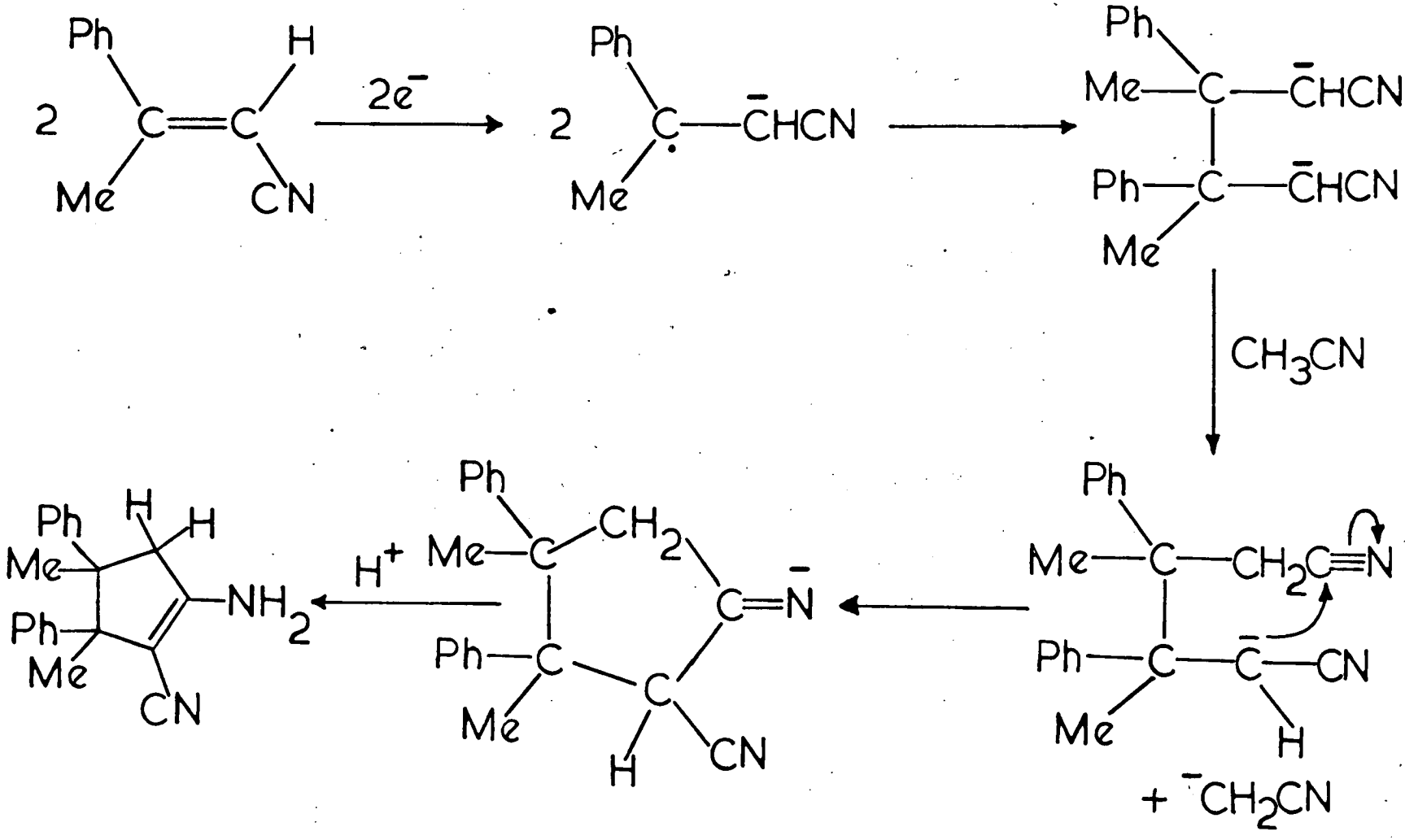
The main piece of evidence which induced Bewick and co-workers to invoke adsorption has, however, not been explained. That is, if the pinacolization process takes place in solution, how can one explain the changes in the isomer ratios which occur upon addition of adsorbable compounds to the solution as observed by Puglisi et al.[78]? In the first place, the evidence presented by Bewick and Cleghorn[85] for this effect in DMF is not very convincing and secondly, Puglisi et al. carried out their experiments in acidic aqueous solution. Under such conditions, the pinacolization process has been shown to be at least as fast as the heterogeneous electron transfer.[43] This means that any decrease in the rate of electron transfer would mean that the formation of the ketyl radical is the rate-determining step. Therefore, it is conceivable that the ketyl radical could attack incoming molecules of unreduced ketone in a radical-substrate coupling process. If this were the case, hydrogen bonding would have little influence, if any, upon the stereochemistry of the product:



meso dl

The presence of strongly adsorbed ions such as tetra-alkylammonium cations could slow down the heterogeneous rate constant. In fact, such an effect has been observed in DMF for certain tetra-alkylammonium cations by Jensen, Ronlan and Parker[41] who have described it as a double layer effect. In aqueous solution, such effects might be expected to be greater due to the stronger specific adsorption of the cations and explain, in a simple manner, not only the effects observed by Puglisi et al.[78] but also the smaller variations observed by Bewick and Cleghorn.[85] Thus, it can be seen that it is not necessary to invoke the adsorption of the acetophenone radicals in order to explain the variation in the isomer ratios and the proposal that coupling does not take place at the surface between adsorbed species but only in solution, seems to be the best explanation of the facts.

The connection between the concentration of water in the solution and the production of nitrile compounds is illustrated by comparison of the dl/meso ratios in Table 9 and Table 10. In Table 10, where the yields


Ph
H
2
C
C
2e⁻
Me
CN
Ph
2
C
CHCN
Me
Ph
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C
CHCN
Ph
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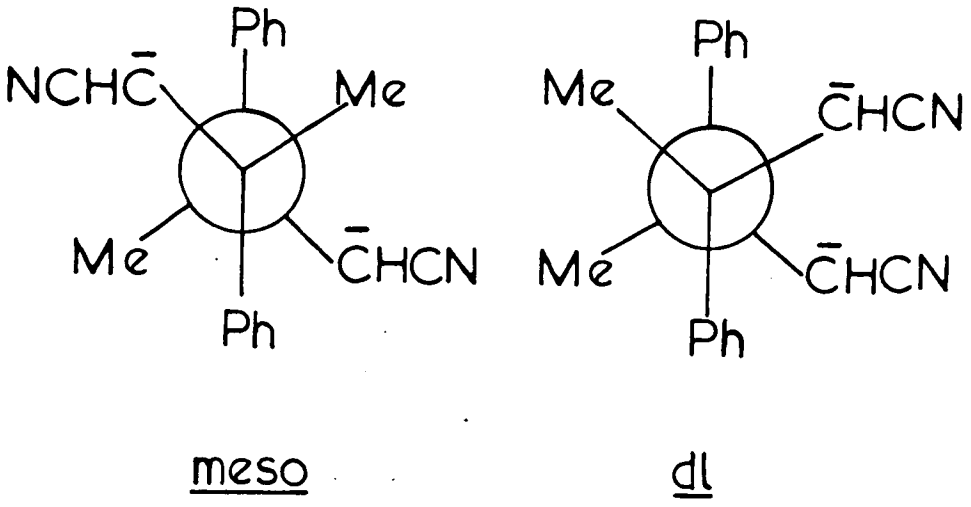
CHCN
Me
CH3CN
Ph
Me
C
CH2C≡N
Ph
C
C
CN
Me
H
+ ⁻CH2CN
Ph
Me
CH2
H+
Me
C
C≡N
Ph
C
Me
C
CN
H
Ph
H
H
Me
NH2
Ph
Me
CN

Figure 18

of nitriles are considerably higher, the dl/meso ratios are considerably lower than those in Table 9. Particularly interesting in this respect, is the variation of this ratio during the course of an electrolysis (see Table 12). It can be seen that the ratio starts off at a low value, increases to a maximum and then falls away. This maximum appears just after the maximum concentration of hydroxynitrile (2, Table 12) has been reached and at about the same time as the maximum concentration of 3-methylcinnamonitrile (3, Table 12). Since, as shown previously, the dl/meso ratio is dependent upon the water concentration, this variation of the isomer ratio is indicative of the production of water during the formation of the nitrile products.

The production of 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcylopent-1-ene upon reduction of 3-methylcinnamonitrile occurs via the coupling of two radical-anions followed by protonation and cyclization (see Figure 18). The preference for one isomer seems to be more pronounced in this case. Since the hydrogen bonding considerations should be approximately the same for this hydrodimer as that outlined for acetophenone, the addition of water should have similar effects as, indeed, is the case although the system appears to be less sensitive. The increased preference for one isomer may be due to the larger size of the charge-bearing nitrile grouping as compared with the oxygen in acetophenone. As shown, the size of this grouping is approximately the same as a methyl group and the steric preference for the meso-form could well be reduced:



meso dl

The system is also sensitive to the presence of Li^+ ions as is the case for acetophenone. Baizer et al.[26] have also found that the presence of Li^+ ions can have effects upon the form of the hydrodimer of cinnamonitrile in that they observed the formation of linear, uncyclised hydrodimers in such conditions. No such products were observed in this study but it is highly probable that they were formed although not detected.

Avaca and Utley[95] have observed similar cyclised hydrodimers upon the reduction of 1-cyano-3-phenylbut-2-enenitrile and 2-cyano-3-phenylprop-2-enenitrile in aprotic solvent with added acetic acid. In this case the hydrodimers were formed in isomer ratios of 3:2 and 1:1 respectively and the presence of Li^+ cations did not lead to the formation of linear, uncyclised hydrodimers. However, the extra cyano group should help to spread the charge in the radical-anions of these compounds such that the ion-pairing and hydrogen-bonding effects will be much smaller than in the ketones and cinnamonitriles. This is supported by the findings of Nadjo, Saveant and Tessier[61] who observed that the addition of water to the solution has a much smaller effect upon the rate constant

of dimerization for such compounds. The decreased preference for one isomer, therefore, may be due, in part, to decreased hydrogen bonding effects. A further cause may be a slightly increased steric effect due to the larger malononitrile grouping.

Presumably, the more localised charge on the cinnamonitrile radical-anions explains, to some extent, the greater reversibility observed for the cinnamonitrile compounds in cyclic voltammetry as compared with 2-cyano-3-phenylbut-2-enenitrile, for example. The rate of dimerization should be slower due to the greater coulombic repulsion of the more localised charge in the cinnamonitrile radical-anions.

The tendency for the radical-anions of 3-methylcinnamonitrile to disproportionate appears to be much larger than that of the acetophenone radical-anions and this may possibly be due to the fact that the cinnamonitrile can better accommodate the extra charge of the dianion. This tendency can be increased by the addition of water to the solution and may be due to the solvating water increasing the bulk of the radical-anions. In such a case, the two radical-anions may have more difficulty in coming close enough together to couple. On the other hand, electron transfer may take place at considerable distances and, indeed, the solvating water may provide a bridge for the passage of the electron. Certainly, the presence of water will favour the formation of the dianion due to solvation effects.[106] Since water solvation plays a much smaller role with 2-cyano-3-phenylbut-2-enenitrile, disproportionation will be much less favoured. With acetophenone, on the other hand, the inability of the molecule to accommodate the two electrons excludes disproportionation. Thus, it is easy to see how much more monomer is produced than dimer when 3-methylcinnamonitrile, produced <u>in situ</u>, is reduced (Tables 9 and 10) than is the case when 3-methylcinnamonitrile is the substrate (Table 11) since when the cinnamonitrile is formed from acetophenone, a molecule of water is closely associated with it.

Finally the possibility that the hydrodimers may decompose in strong base, as shown by Simonet et co-workers[110] has been checked by the reduction of azobenzene in acetonitrile in the presence of acetophenone pinacol. Only the pinacol was recovered with no change in the isomer ratio, indicating that the dimerization of the radical-anions is irreversible under the very alkaline conditions used in the present study.

Conclusion

The study of the reduction of acetophenone in dry acetonitrile just presented has, in some respects, been a failure and also, in some ways, successful. Of the aims set out in the introduction, the synthetic purpose has not been achieved. No real predominance of any of the nitrile products was accomplished and, indeed, the results of this study throw some doubt upon the original findings[93] in that the initial high yields of nitriles have never been entirely reproduced. However, as pointed out previously, there were some experimental differences between the two studies and it has been shown in this study how these differences could affect the product distribution. It has, in fact, proved impossible to reproduce, using an efficient experimental situation, the results of a poorly designed experimental cell. For this reason, it seems unlikely that this system will have any real synthetic value since one would have to deliberately use poor electrode geometry and this would be somewhat difficult to define from one cell design to another.

If the synthetic value of the system has proved to be less than was hoped, the information gained concerning the role of the solvent with respect to mechanism has proved to be of great interest. The concentration of the residual water has shown itself to be critical for both the hydrodimerization mechanism and the production of nitrile compounds. The proposal of the participation of the hydroxyl anion, although the evidence is not clear-cut, appears to provide a reasonable explanation

of the experimental evidence and it is the author's opinion that this facet of the system should be pursued. Obviously, in any further work on this aspect, the residual water content of the solution will require to be strictly controlled which from the extent of irreproducibility evident in the results of the preparative electrolyses, implies the need for more sophisticated purification procedures and cell designs. In short, a vacuum line method of solvent purification will probably be necessary in addition to a vacuum cell similar to that employed by Bard and co-workers.[28]

A further success of this study has been the satisfactory explanation of the stereochemical factors involved in the hydrodimerization process. The theory proposed here, involving the residual water solvation, is able to explain all of the experimental evidence available to date and is supported by the role of the residual water observed in the production of nitriles.

Table 7 Voltammetric data for ketones and 3-methylcinnamonitrile

Polarography

Compound	Conc^{n}. /M x 10^{-3}	Medium	$E_{\frac{1}{2}}(1)$[a]	$E_{\frac{1}{2}}(2)$[a]	$i_d(2)/i_d(1)$[b]
Acetophenone	0.242	0.1M $TEABF_4/CH_3CN$	-2.41	-2.79	0.866
	0.552	0.1M $TBABF_4/CH_3CN$	-2.44	-	-
	0.813	0.1M $TBABF_4$/DMF[c]	-2.38	-	-
Benzophenone	0.233	0.1M $TEABF_4/CH_3CN$	-2.20	-2.48	0.600
	0.911	0.1M $TBABF_4$/DMF[c]	-2.23	-2.75	0.750
3-Methylcinnamo-nitrile	0.220	0.1M $TEABF_4/CH_3CN$	-2.36	-2.69	0.944
Fluorenone	1.000	0.1M TEAP/DMF[c]	-1.72	-2.42	0.967

Table 7 (contd.)

Cyclic Voltammetry (sweep rate = $200mVs^{-1}$)

Compound	Conc^{n}. /M x 10^{-3}	Medium	$E_{pc}(1)$[a]	$E_{pc}(2)$[a]	$i_{pc}(2)/i_{pc}(1)$[b]	$i_{pa}(1)/i_{pc}(1)$
Acetophenone	0.242	0.1M $TEABF_4/CH_3CN$	-2.46	-2.900	0.299	0.518
	0.552	0.1M $TBABF_4/CH_3CN$	-2.49	-	-	0.521
Benzophenone	1.000	0.1M $TEABF_4/CH_3CN$[d]	-2.21	-2.59	0.525	0.932
	0.252	0.1M TBAP/DMF[c]	-2.22	-2.84	0.534	0.926
3-Methylcinnamo-nitrile	1.000	0.1M $TEABF_4/CH_3CN$[e]	-2.30	-2.71	0.723	0.926
Fluorenone	1.000	0.1M TBAP/DMF[c]	-1.75	-2.47	0.756	1.027

a, Volts vs. Ag/0.1M $AgNO_3$; b, ratio of peak or wave heights since several different electrodes used;

c, adsorption prewaves or prepeaks observed; d, second oxidation peak visible at E_p = -0.5V;

e, second oxidation peak visible at E_p = -1.27V.

Table 8 Results of preparative electrolyses of acetophenone (0.1M) in dry acetonitrile (100ml.) at mercury with $TEABF_4$ (0.1M) as supporting electrolyte. Products: 1, acetophenone; 2, 3-phenylbutanenitrile; 3, 3-methylcinnamonitrile; 4, 3-methyl-3-phenylglutaronitrile. Working potential = -2.95V vs. Ag/0.1M $AgNO_3$. Cell uncooled.

i_o[a] (mA)	i_{max} (mA)	n ($Fmol^{-1}$)	Yields (% by glc analyses[b])			
			1	2	3	4
25	35	1.31	-	32	-	15
40	60	1.38	-	26	-	20
57	90	1.38	12	21	-	26
73	139	1.37	0	22	-	28
80[c,d]	121	1.43	5	18	-	2
50[d,e]	-	1.00	15	13	3	1
100[d,e]	-	1.00	12	18	9	2
75[d,e]	-	1.00	5	11	11	4

a, initial current; b, 10% ApL column, 20 min at 160°C, 10°C/min to 220°C, benzophenone used as internal standard; c, 21% 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcyclopent-1-ene by hplc analysis; d, cell cooled by ice-bath; e, constant current electrolyses.

Table 9 Results of preparative electrolyses of acetophenone (0.1M) in dry acetonitrile (50ml) using $TEABF_4$ (0.1M) as supporting electrolyte. Products: 1, acetophenone; 2, 1-phenylethanol: 3, 3-phenylbutanenitrile; 4, 3-hydroxy-3-phenylbutanenitrile: 5, 3-methylcinnamonitrile; 6, 3-methyl-3-phenylglutaronitrile; 7, acetophenone pinacol; 8, 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcyclopent-1-ene. Mercury pool working electrode at -2.95V vs. Ag/0.1M $AgNO_3$ unless otherwise stated.

i_o[a] (mA)	n ($F\ mol^{-1}$)	Temp. (°C)	Yields (% by glc analysis[b])							
			1	2	3	4	5	6	7 (dl/meso)[c]	8 (dl/dl)[c]
121	1.45	0	7.0	trace	7.0	1.2	0.2	1.2	79 (3.9)	0.5 (-)
200	1.01	0	8.0	trace	3.0	2.6	0.3	0.5	72 (2.3)	trace
132	1.47	16	8.0	trace	5.0	0.5	1.3	3	102 (3.0)	4 (14.5)
147	1.59	16	9.0	trace	1.4	2.6	1.0	1.5	100 (4.4)	2.6 (10.1)
102	1.30	-28	17	trace	3.4	6	1.0	0	67 (3.8)	-
43[d]	1.46	20	2.5	trace	15.0	1.4	12.4	3.6	82 (3.6)	5 (10.9)
33[d]	1.79	18	4.0	trace	29.0	2.0	1.0	11.0	81 (3.2)	5 (10.3)
39[e]	2.35	20	2.5	trace	8.4	0	0	7.4	62 (2.6)	2.3 (7.3)
64	1.26	-28	9.5	trace	6.4	1.5	0	0	62 (3.3)	-

Table 9 (contd.)

i_o[a] (mA)	n ($F\ mol^{-1}$)	Temp. (°C)	Yields (% by glc analysis[b])							
			1	2	3	4	5	6	7 (dl/meso)[c]	8 (dl/dl)[c]
104	1.72	16	4.5	trace	13.0	0.5	1.0	7.0	78 (5.9)	2.4 (9.2)
50[f]	1.04	0	15.4	trace	4.0	6.8	2.3	2.8	-	-
310	1.47	81	4.6	8.8	18.2	-	-	1.3	-	-
153	1.93	81	19.0	8.5	23	-	-	4.8	-	-
32[d]	2.3	81	9.0	9.2	29	-	-	3.2	-	-
90[g]	1.6	0	-	-	5.0	-	-	3.0	-	109 (9.6)

a, initial current; b, 10% ApL column, 195°C - benzonitrile as internal standard; c, estimated by hplc analysis, 20% THF (0.5% H_2O w/w) in n-hexane; d, platinum electrode; e, graphite electrode; f, lead electrode; g, 3-methylcinnamonitrile as substrate.

Table 10 Results of preparative electrolyses of acetophenone (0.1M) in dry acetonitrile (50ml) at mercury with $TEABF_4$ (0.1M) as supporting electrolyte. Products: 1, acetophenone: 2, 3-phenylbutanenitrile; 3, 3-methyl-3-phenylglutaronitrile· 4, acetophenone pinacol: 5, 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcyclopent-1-ene. The cell temperature was 16°C and the reference electrode was Ag/0.1M $AgNO_3$.

i_o[a] (mA)	n ($Fmol^{-1}$)	E (V)	Yields (% by glc analysis[b]) 1	2	3	4 (dl/meso)[c]	5 (dl/dl)[c]
500	2.90	-2.97	6	32	9	74 (2.0)	2.4 (12.0)
95	2.14	-2.97	0	21	8	62 (2.2)	7.2 (12.7)
25	1.93	-2.25	0	18	35	25 -	8.0 (6.5)
500[d]	1.22	-2.50	0	0	0	95 (6.2)	0 (-)
280	2.21	-2.61	7	20	18	63 (1.7)	4.8 (11.1)
450[e]	1.93	-2.97	7	8	10	70 (2.5)	0.2 (10.6)
426[f]	1.94	-2.97	5	17	5	-	0.5 (9.3)
20[e]	3.23	-2.20	2	16	5	72 (3.0)	3.5 (5.5)
500[g]	2.49	-2.95	3	15	8	55 (2.8)	2.0 (11.5)
470[g]	2.03	-2.95	4	26	14	47 (2.5)	9.0 (14.1)

Table 10 (contd.)

i_o[a] (mA)	n ($Fmol^{-1}$)	E (V)	Yields (% by glc analysis[b]) 1	2	3	4 (dl/meso)[c]	5 (dl/dl)[c]
20[g]	2.39	-2.25	0	10	13	66 (4.8)	-
*470[h,i]	1.43	-2.95	14	27	0	61 (2.1)	0.2 (5.2)
400[h]	1.97	-2.60	11	14	3	69 (2.4)	5.0 (5.8)
20[k]	2.22	-2.20	2	2	0	83 (8.2)	0 (-)
350	2.71	-2.95	2	13	2	92 (1.4)	1.1 (5.0)
450	1.17	-3.20	4	20	11	78 (3.5)	7.5 (8.5)
10[l]	1.00	-	9	24	3	55 (2.0)	6.0 (10.8)

a, initial current; b, ApL column, 165°C for 12 min, 8°C/min to 230°C, benzonitrile as internal standard; c, estimated by hplc analysis, 20% ethyl acetate (0.5% H_2O w/w) in n-hexane; d, +0.3% H_2O; e, +0.1% H_2O: f, +0.05% H_2O: g, $TBABF_4$ as supporting electrolyte: h, 50% DMF as co-solvent; i, 2% 3-methylcinnamonitrile detected; k, 90% DMF as co-solvent: l, constant current; *, fresh batch of solvent.

Table 11 Results of preparative electrolyses of 3-methylcinnamonitrile (0.1M) in dry acetonitrile (50ml) at mercury with $TEABF_4$ (0.1M) as supporting electrolyte. Products: 1, 3-phenylbutanenitrile; 2, 3-methyl-3-phenylglutaronitrile; 3, 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcyclopent-1-ene. Reference electrode, Ag/0.1M $AgNO_3$. Temperature 16°C.

i_o[a] (mA)	n ($Fmol^{-1}$)	E V	Yields (% by glc analysis[b]) 1	2	3 (dl/dl)[c]
480	1.38	-2.60	18	23	36 (5.2)
140	3.37	-2.60	13	6	23 (5.7)
20[d]	1.41	-2.13	11	6	- -
450[e,f]	1.73	-2.60	31	5	38 (6.3)
260[f,g]	2.26	-2.60	21	7	57 (8.0)
140[f,h]	1.33	-2.50	29	13	50 (10.0)
62	0.70	-2.97	10	17	50 (6.6)
134[i]	1.00	-2.60	15	-	55 (13.1)

a, initial current; b, 10% ApL column, 165°C for 12 min, 8°C/min to 230°C, benzonitrile as internal standard; c, estimated by hplc analysis, 20% ethyl acetate (0.5% H_2O w/w) in n-hexane; g, +0.05% H_2O; h, +10^{-2}M $LiClO_4$; i, DMF as solvent.

d, alumina added to secondary compartment; e, + 0·3% H_2O; f, $TBABF_4$ (0·1M) as supporting electrolyte.

Table 12 Product distribution during the course of an electrolysis of acetophenone (0.1M) in dry acetonitrile, as measured by analysis of samples taken from the catholyte solution. Products: 1, acetophenone; 2, 3-hydroxy-3-phenylbutanenitrile; 3, 3-methylcinnamonitrile; 4, 3-phenylbutanenitrile; 5, 3-methyl-3-phenylglutaronitrile; 6, acetophenone pinacol; 7, 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcyclopent-1-ene. The working electrode was a mercury pool at -2.95V vs. Ag/0.1M $AgNO_3$. The cell temperature was 18°C.

time (min)	i (mA)	coulombs[a] passed	Product concentrations (M x 10^{-2} by glc analysis[b]) 1	2	3	4	5	6 (dl/meso)[c]	7 (dl/dl)[c]
0	104	0	7.63	-	-	-	-	-	-
5	149	36	0.49	0.76	0.09	0.03	0.03	-	-
10	167	91	0.56	0.43	0.02	0.07	-	-	-
15	226	176	0.32	0.49	0.01	0.09	-	-	-
20	184	214	0.25	0.34	0.00	0.07	-	0.27 (-)	0.002 (-)
30	149	335	0.26	0.43	0.01	0.01	0.01	0.62 (4.8)	0.006 (13.2)
40	123	450	0.68	0.91	0.11	0.22	0.29	-	-
60	120	680	0.31	0.73	0.02	0.08	0.65	1.69 (6.8)	0.02 (13.5)
80	109	891	0.46	0.35	0.08	0.17	0.86	2.90 (11.7)	0.05 (8.9)

Table 12 (contd.)

time (min)	i (mA)	coulombs[a] passed	Product concentrations ($M \times 10^{-2}$ by glc analysis[b])						
			1	2	3	4	5	6 (dl/meso)[c]	7 (dl/dl)[c]
100	90	1082	0.44	0.14	0.21	0.57	0.62	2.33 (9.1)	0.03 (11.6)
122	86	1271	0.33	0.43	0.19	0.50	1.18	3.32 (7.5)	0.06 (-)
160	80	1590	0.51	0.10	0.13	1.07	0.81	2.51 (9.0)	0.05 (8.6)
190	60	1840	0.31	0.03	0.08	0.88	0.47	2.67 (5.9)	0.16 (9.2)
300	45	2257	0.11	0	0	1.06	0.39	-	-

a, corrected in order to allow for material removed in sampling; b, 10% ApL column, 195°C, benzonitrile as internal standard; c, estimated by hplc analysis, 20% THF (0.5% H_2O w/w) in n-hexane.

CHAPTER 4

AN ELECTROCHEMICAL INVESTIGATION OF THE RING CLEAVAGE OF CYCLOPROPYL DERIVATIVES

CHAPTER 4

An Electrochemical Investigation of the Ring Cleavage of Cyclopropyl Derivatives

Introduction

In the previous two chapters, the discussion has centred around the reaction of the product of electron transfer with its environment rather than upon what effect the extra electron has upon the structure of the intermediate. Nevertheless, this point, as regards the shape of the intermediate, was touched upon in the stereochemical arguments outlined for the immonium cation reductions. However, since it was shown that the intermediate radical retained the shape of the cation and that the radical was the main intermediate, then the structural considerations were only of interest with regard to the elucidation of the follow-up chemical reactions. Similarly, it was implicit in the stereochemical arguments used in the discussion of the hydrodimerization of acetophenone, that the intermediate radical-anions and radicals were of the same shape as the substrate molecules. On the other hand, any further addition of electrons to these radical species should, as was shown for the immonium cations, result in a change of the molecular shape.

Although the transfer of an electron to the substrate molecule may not have any effect upon the shape of the species, it will obviously cause changes in the electronic energy which, in turn, will cause some reorganisation of the solvent in the region of the intermediate, as was demonstrated in the last chapter. These internal and external energies can be treated separately[111] so that the effects of conjugation and electronic rearrangement can be assessed. The measured polarographic half-wave potentials for the formation of aromatic hydrocarbon radical-anions vary linearly with the Hückel molecular orbital energies of the lowest vacant orbitals.[112-115] Although this correlation is probably[116,117] due

to a fortuitous compensation of errors, it does give an indication of the electronic structure of the intermediate. Similar information can be gained from the epr spectrum of the radical intermediate and some use of this kind of information was made in deciding the shape of the immonium radical in Chapter 2.

In some cases, e.g. the reduction of alkyl halides,[3] the addition of an electron to the molecule has a much more drastic effect in that bonds are cleaved or formed. Sometimes these changes are concerted with the electron transfer and in other cases, the bond cleavage or formation takes place after the formation of a radical-anion. The reduction of alkyl halides is electrochemically irreversible and it has been suggested[3,118] that the mechanism of reduction involves a transition state where the carbon atom has radical character and the halogen atom, ionic character. Examination of benzyl bromides and halobenzenes[119] has lead to some Hammett correlations between the σ-values of the aryl substituents and the half-wave potentials.

If the organic halide compound contains an aromatic group or a reducible function such as a nitro group, then the electron transfer tends to be less irreversible than that to a simple alkyl halide and an actual radical-anion is formed. For example, electron transfer to p-bromo- and p-chlorobenzophenones[90] has been shown to be Nernstian and a radical-anion is formed initially, followed by a cleavage of the carbon-halogen bond. The electron transfer is therefore fast and the rate-determining step consists of the cleavage reaction which follows and is distinct from the electron transfer. A similar situation has been reported in the reduction of certain phosphonium salts in aprotic media[120] where a fast and reversible electron transfer to form a neutral radical is followed by a cleavage reaction to give a radical plus triphenylphosphine.

Another form of cleavage reaction is the hydrogen atom transfer exemplified in Chapter 2 but, in this case, there is both bond cleavage

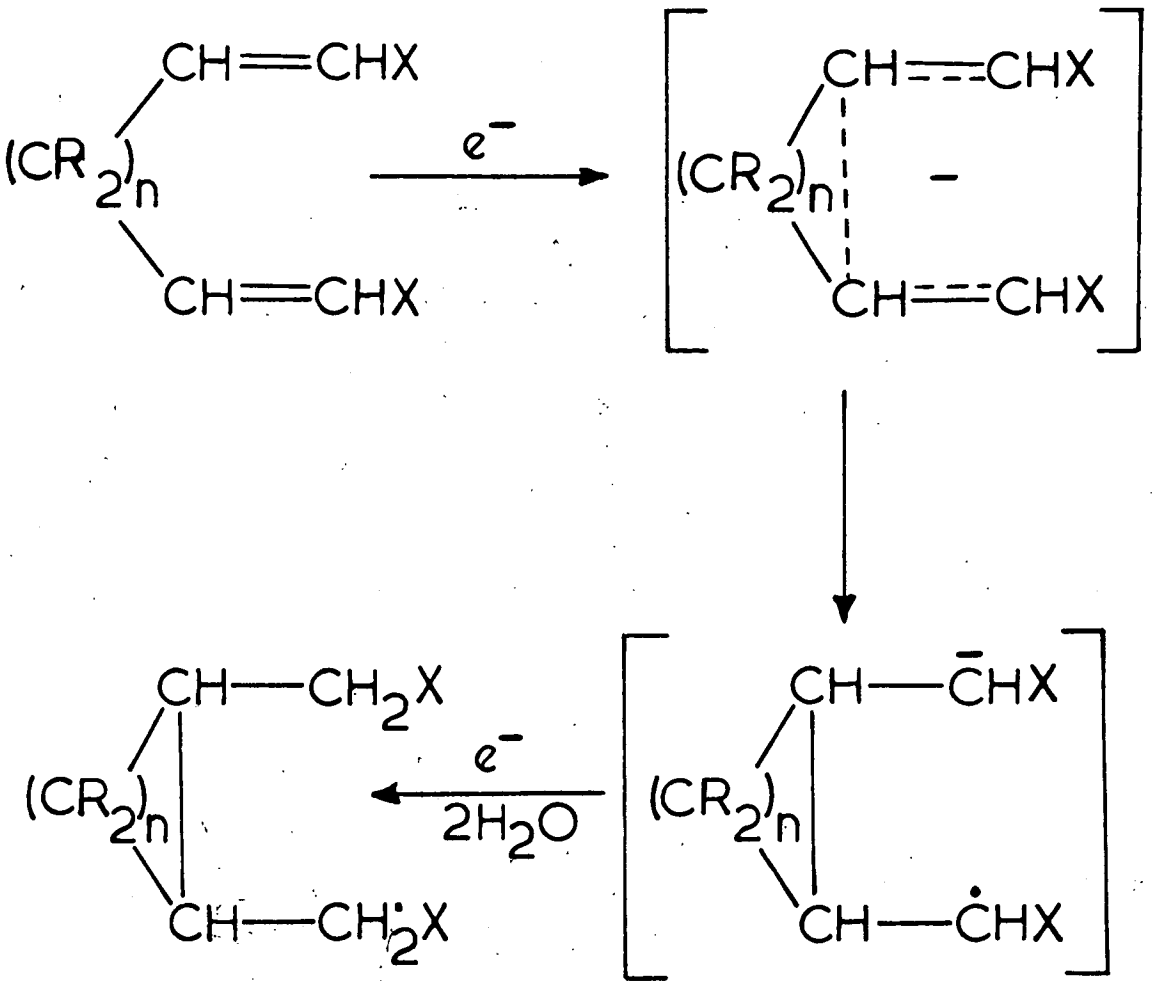

CH=CHX
(CR2)n
CH=CHX
e⁻
CH=CHX
(CR2)n
CH=CHX
CH—CH2X
(CR2)n
CH—CH2X
e⁻
2H2O
CH—CHX
(CR2)n
CH—ĊHX

Figure 19

and bond formation occurring at the same time. Dimerization, on the other hand, only involves bond formation. Both of these reactions are examples of intermolecular reactions, the reaction of the intermediate with a species in its environment being of interest rather than an internal reaction. An example of an intramolecular reaction is the electrohydrocyclization of bis-activated olefins studies by Baizer and co-workers[121,122] who have likened the cyclization reaction to an internal dimerization. From polarographic, coulometric and controlled potential electrolysis data,[122] a concerted reduction-cyclization mechanism has been proposed in which the bis-activated olefin is reduced and cyclized in a single, one-electron, rate-determining step forming a cyclized radical-anion (Figure 19). This radical is subsequently reduced and protonated to yield cyclized products. In a recent study of such compounds in aprotic media,[123] the mechanism of electrohydrocyclization has been reported to proceed through the cyclization of the initially formed radical-anion at low water concentrations. However, it is reported that, at higher concentrations of water, intramolecular radical-radical coupling in the bis-anion competes with the intramolecular radical-substrate process.

The intramolecular pinacolization of dicarbonyl compounds has also been observed[124] and a kinetic and preparative study of the electrochemical cyclization of 1,3-dibenzoylpropane has been carried out by Saveant and co-workers.[125-127] These authors were able to achieve almost quantitative conversion to the cyclized product and, by means of linear sweep voltammetry and convolution potential sweep voltammetry, have shown that the cyclization reaction involves the dianion which is produced by a solution electron transfer:

$$Ph\text{-}CO\text{-}(CH_2)_3\text{-}CO\text{-}Ph + \bar{e} \rightleftharpoons Ph\dot{C}\bar{O}\text{-}(CH_2)_3\text{-}CO\text{-}Ph$$

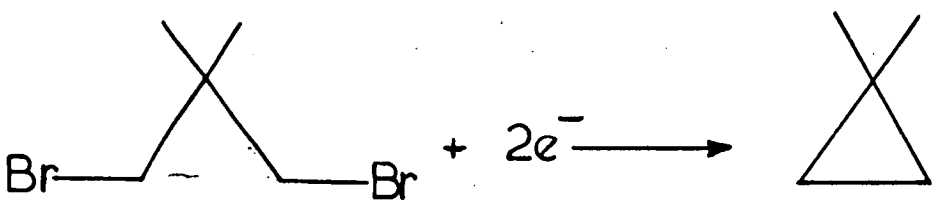
$$2Ph\dot{C}\bar{O}\text{-}(CH_2)_3\text{-}COPh \rightleftharpoons Ph\text{-}\dot{C}\bar{O}\text{-}(CH_2)_3\text{-}\dot{C}\bar{O}\text{-}Ph + Ph\text{-}CO\text{-}(CH_2)_3\text{-}CO\text{-}Ph$$

$$Ph\text{-}\dot{C}\bar{O}\text{-}(CH_2)_3\text{-}\dot{C}\bar{O}\text{-}Ph \rightleftharpoons Ph\text{-}\overline{C\bar{O}\text{-}(CH_2)_3\text{-}C\bar{O}}\text{-}Ph$$

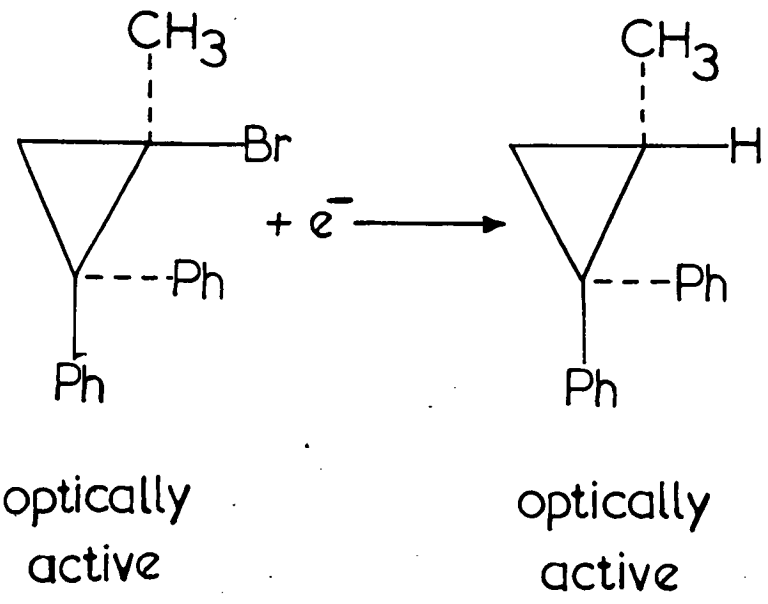
$$Ph\text{-}\overline{C\bar{O}\text{-}(CH_2)_3\text{-}C\bar{O}}\text{-}Ph + H^+ \rightleftharpoons Ph\text{-}\overline{C\bar{O}\text{-}(CH_2)_3\text{-}C(OH)}\text{-}Ph$$

The rate determining step was either the cyclization step or the protonation step, in which case the cyclization reaction is reversible. It was also noted that the cyclization reaction was very fast, almost as fast as electron transfer itself, since charge transfer kinetic control was observed at sweep rates greater than 30V s^{-1}.

Cyclization to form small strained rings has been effected by the reduction of 1,3-dihalogenopropanes[128-130]:



Once again, the initial electron transfer involves the concerted cleavage of at least one carbon-bromine bond. However, it is notable that the reduction of a cyclopropyl halide does not involve the reverse reaction, ring cleavage[131]:



optically active

optically active

The product of this reaction, on the other hand, has been shown to undergo ring-cleavage upon reduction with sodium in liquid ammonia, the cleavage being thought to proceed via a radical-anion.[132] The cleavage reaction was shown to be irreversible for this compound since some starting material was recovered with unchanged optical activity. When a pentyl group replaced the hydrogen geminal to the methyl group, the product mixture was found to be completely racemic. Unfortunately, no starting material was recovered in this case so that nothing could be inferred as regards the reversibility of the cleavage reaction.

Although little attention has been paid to the electrochemical reductive ring-cleavage of cyclopropanes, the reduction has been extensively studied by means of metal ammonia solutions. In particular, when conjugated cyclopropyl ketones are reduced by metals in liquid ammonia,[133] they undergo reductive cleavage of the cyclopropane ring. If the cyclopropane function is contained in a fused bicyclic ring system, then the reaction is highly stereospecific:

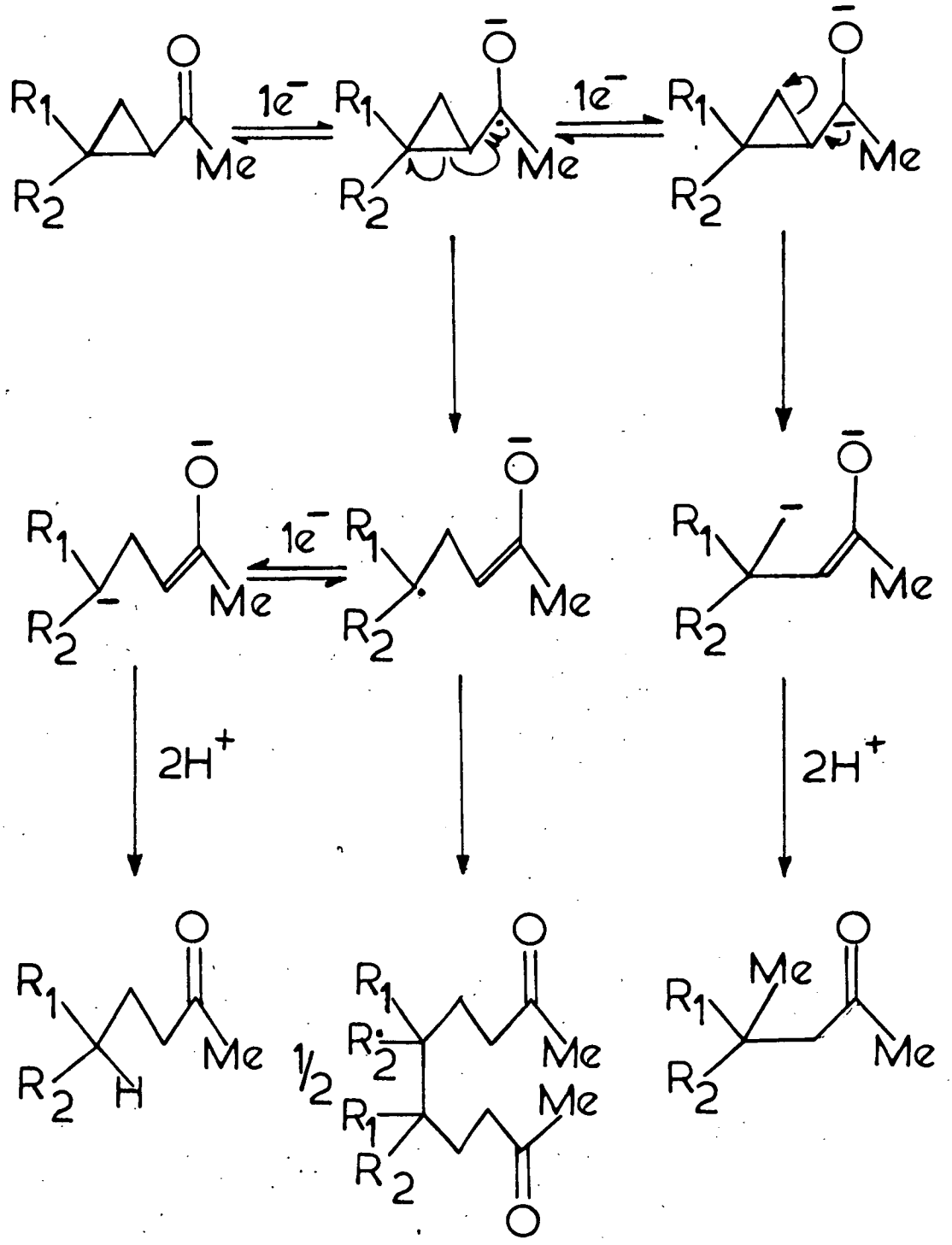
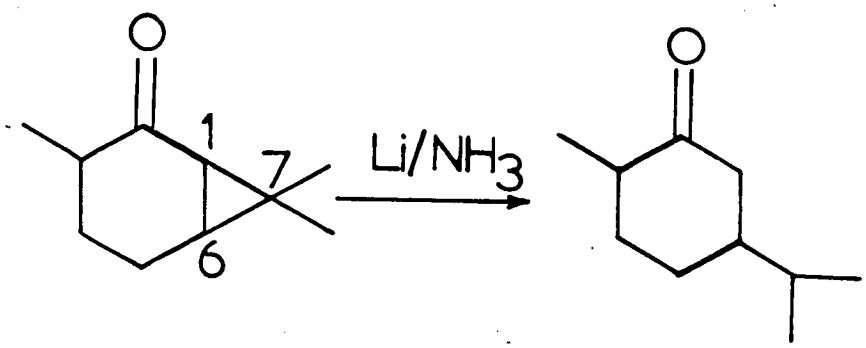


Figure 20

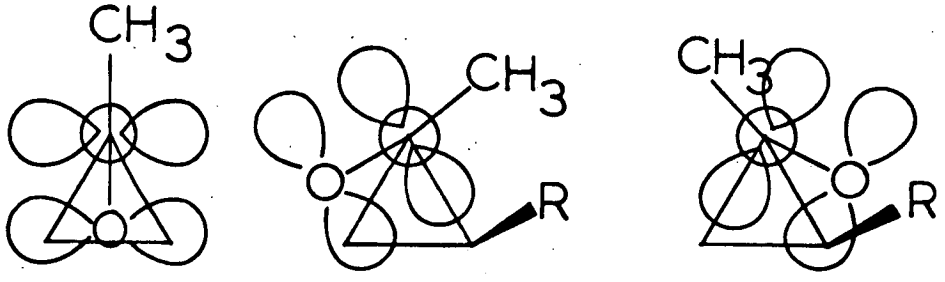


Only the $C_{(1)}$ - $C_{(7)}$ bond is cleaved.[134,135] Several other examples of this stereospecificity have been observed[136,137] and it has been shown that the cyclopropane bond which is cleaved is the one possessing the maximum overlap with the π-orbital of the carbonyl group.

The mechanism of the cleavage is believed to proceed via a dianionic species and this has been borne out by the reduction of conformationally mobile cyclopropyl ketones, e.g. trans-1-acetyl-2-methylcyclopropane, by means of lithium-ammonia solutions.[137-140] The major product from the example quoted, was found to be 4-methylpentan-2-one, indicating that the cleavage reaction takes place via an anionic species rather than a radical species. The situation is illustrated in Figure 20 which shows how a radical intermediate would favour cleavage to form a secondary rather than a primary radical, e.g. hexan-2-one (R_1 = H_1, R_2 = Me) formation, while an anionic intermediate would favour cleavage to form a primary rather than a secondary carbanion, e.g. 4-methylpentan-2-one formation.

In the reduction of cis-1-acetyl-2-methylcyclopropane (R_1 = Me, R_2 = H) and 1-acetyl-2,2-dimethylcyclopropane (R_1 = R_2 = Me), results differing from those expected from the purely electronic control outlined

above were obtained. However, it was pointed out[138-140] that a steric effect due to the cis-methyl on the conformation of the acetyl group could explain these differences. Although the unsubstituted ketone has been shown to exist predominantly in a bisected cisoid conformer, A, in the ground state,[141,142] it was suggested that the gauche conformers, B and C, were of more relevance with respect to the stereoselectivity of bond-cleavage:

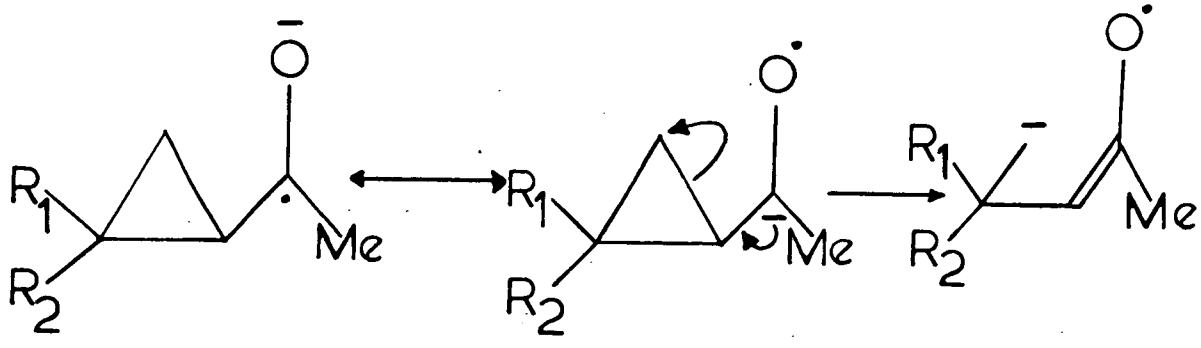


A B C

Because of the presence of the R-group in the cis-2-methyl- and the 2,2-dimethyl- substituted cyclopropanes, conformer B will be more favoured than C. It has been shown that in the cleavage transition-state, the conformer population is similar to that present in the ground state,[139] and, consequently, due to the better overlap with the $C_{(1)} - C_{(2)}$ bond, the cleavage takes place towards the substituent. Therefore, these cleavages are sterically rather than electronically controlled. In the case of the trans-2-methyl derivative, the conformation of the acetyl group is mobile and the cleavage is electronically controlled.

The observation of dimeric products in some cases[140] suggested the participation of a radical species in the reaction scheme although it

was noted that, even when dimers were formed, the cleaved monomeric products still indicated the anionic mode of cleavage to be operating. This suggested that the radical-anion might be able to cleave in an anionic fashion:



Thus, it was not entirely certain that the reductive cleavage of these cyclopropyl ketones proceeded via the dianion. In order to try to distinguish between the possibility of a radical-anion and a dianion intermediate being the species undergoing cleavage, attempts were made to study the electrochemistry of these compounds in liquid ammonia.[143] Unfortunately, these ketones are not reducible within the cathodic limits imposed by the supporting electrolyte-solvent systems employed and, therefore, the number of electrons involved in the reduction could not be directly observed. Preparative reductions were, however, carried out employing electrochemically generated solvated electrons. The results of these experiments were very similar to those found for the metal-ammonia reductions as regards the direction of cleavage, implying a similar intermediate is involved.

Since the reduction of these ketones could not be directly observed by means of polarography or cyclic voltammetry, it was decided to study

some cyclopropyl ring systems which were more easily reducible. Such systems can be readily synthesised by a Knoevenagel condensation of the above ketones with malononitrile, and an examination of the electrochemical reduction of these alkylidene malononitriles provides the subject of the present study. It was hoped that, by means of preparative electrolysis, polarography and cyclic voltammetry studies, the species involved in the cleavage reaction could be identified.

This type of compound has, in fact, been previously studied by Baizer and co-workers[144] who have studied the electrochemistry of an unsubstituted cyclopropyl compound. These authors have shown that, upon reduction in DMF, ring cleavage takes place to give, mainly, an unsaturated, ring opened product. Polarographic experiments indicated that the substrate was reduced in a one-electron wave while cyclic voltammetry experiments demonstrated the completely irreversible pattern which is typical of the presence of a fast follow-up chemical reaction. In addition, it was stated that ring-cleavage takes place via a radical-anion and it was implied that a radical-type cleavage is involved, presumably because of the one-electron reduction behaviour observed by polarography. However, no attempt was made to explain the exact mechanism of ring-cleavage or the irreversibility observed in the cyclic voltammetry experiments. This is the purpose of the present study.

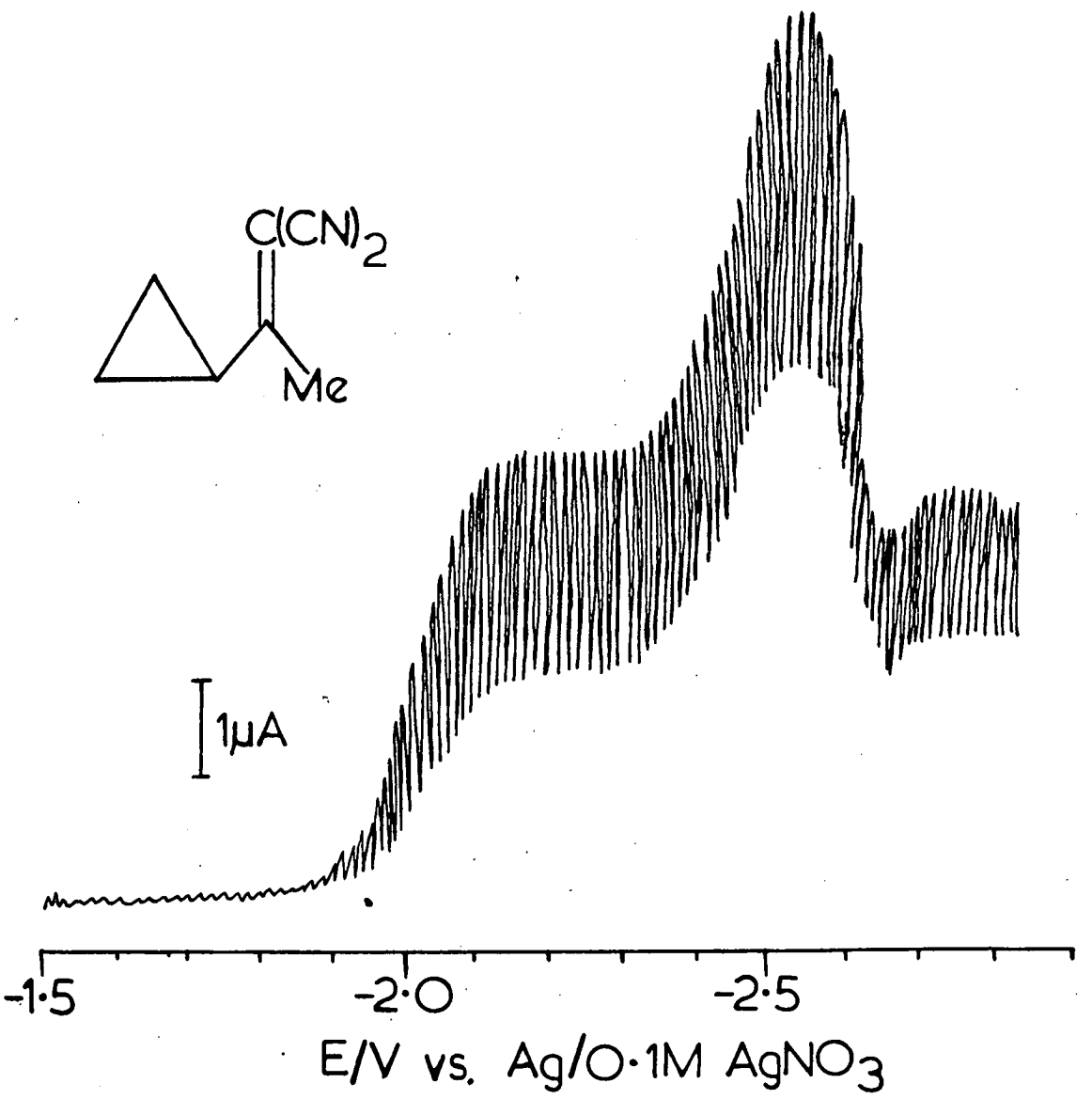
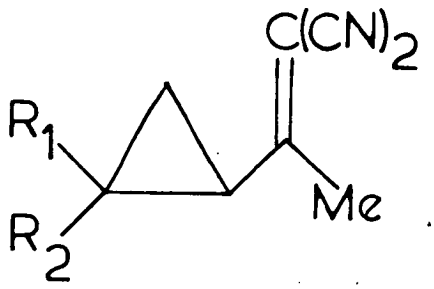


Figure 21. Polarogram of 2-cyano-3-cyclopropylbut-2-enenitrile (f); 0.48mM in 0.1M $TEABF_4$-CH_3CN.

Discussion

Preparation of substituted 1-cyclopropylalkylidenemalononitriles

The compounds of interest were of the form:



f) $R_1 = R_2 = H$

g) $R_1 = R_2 = Me$

h) $R_1 = H$; $R_2 = Me$

These were prepared by a Knoevenagel condensation procedure[145] involving malononitrile and the relevant ketone. Compound f was readily prepared since the unsubstituted cyclopropyl methyl ketone is commercially available. The preparation of compound g involved the preparation of 1-acetyl-2,2-dimethylcyclopropane by the reaction of trimethylsulphoxonium iodide and mesityl oxide, following the procedure of Roberts et al.[146] The product of the condensation of this compound with malononitrile was a colourless liquid which crystallized upon standing to give a low melting, oily solid. Although it was apparently pure by nmr spectroscopy and glc analysis, the elemental analysis of this compound was not satisfactory (see experimental). It was further noted that this compound tended to decompose on standing in air, judging by the dark colouration which appeared after a few hours. The accurate mass analysis, however, was found to be correct.

The preparation of compound h was rather more involved due to the difficulty experienced in obtaining trans-1-acetyl-2-methylcyclopropane. Initially, the preparation of this ketone was attempted by means of a Simmons-Smith reaction[147] upon trans-pent-3-en-2-ol, which was obtained

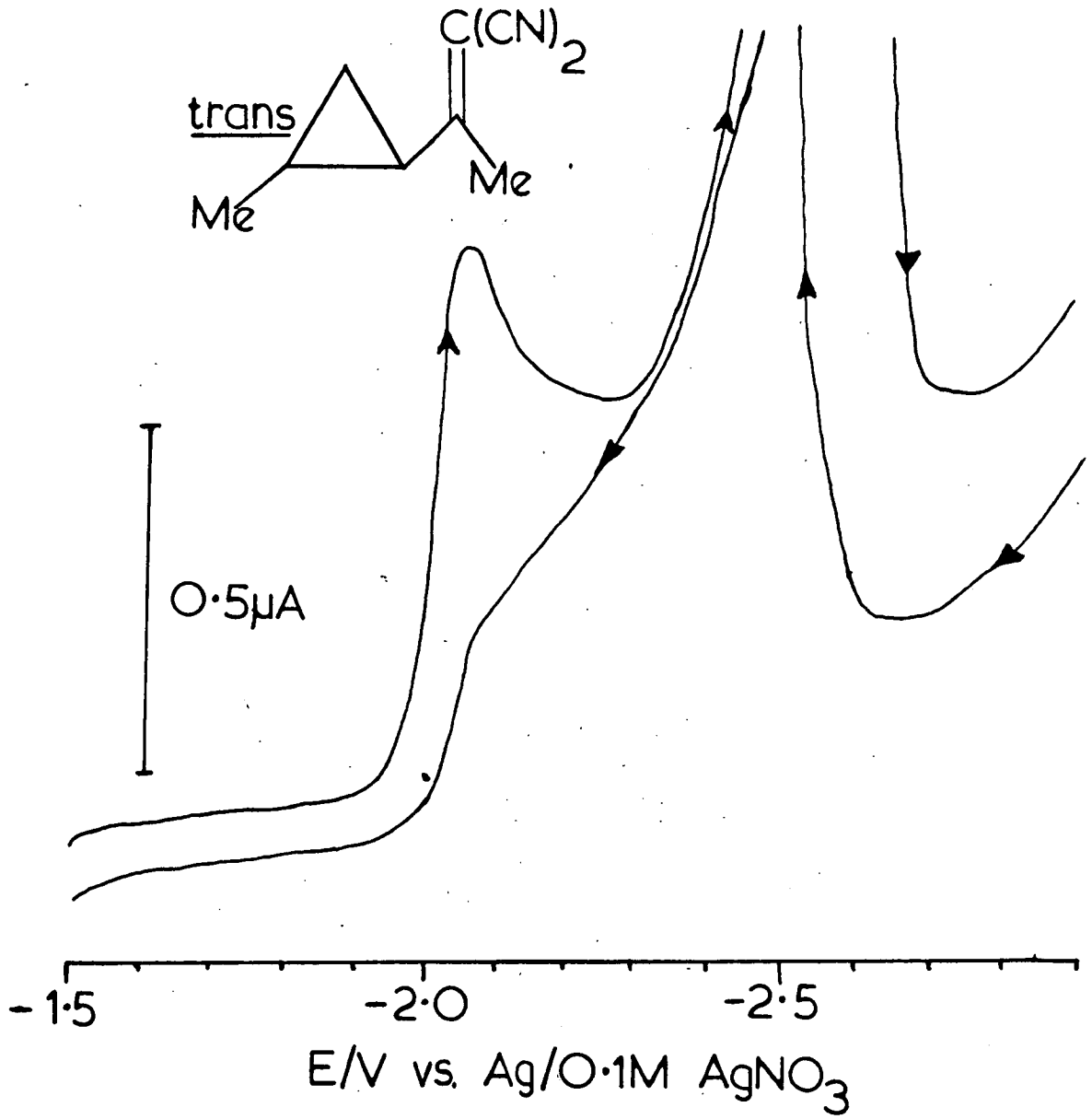


Figure 22. Cyclic voltammogram of 2-cyano-3-(trans-2-methylcyclopropyl)but-2-enenitrile (h); 0.5mM in 0.4M $TBABF_4$ – CH_3CN; electrode, hmde; sweep rate: $200mVs^{-1}$.

by the reaction of crotonaldehyde and methylmagnesium chloride.[148] This reaction was successful when carried out on a small scale and gave trans-1-(2-methylcyclopropyl)ethanol from which the desired ketone was obtained by oxidation with 6N chromic acid. Unfortunately, the preparation could not be reproduced on a large scale, a complex mixture of products resulting. Consequently, it was decided to prepare the cyclopropyl ketone in a similar manner to the preparation of 1-acetyl-2,2-dimethylcyclopropane described above. For this, trans-pent-3-en-2-one was required and it could be prepared via a Wittig reaction of acetylmethylenetriphenylphosphorane with acetaldehyde in methylene chloride.[149] Another possible method involves the oxidation of trans-pent-3-en-2-ol, which was found to be readily accomplished by means of pyridinium chlorochromate as the oxidizing agent.[150] This latter method was found to be the most convenient route to trans-pent-3-en-2-one and the desired trans-1-acetyl-2-methylcyclopropane was readily prepared from this compound by the use of trimethylsulphoxonium iodide.[146] Condensation of this ketone with malononitrile gave the desired product, h, which was found to be pure by nmr spectroscopy and glc analysis. Furthermore, its accurate mass analysis and elemental analysis were also found to be satisfactory. This compound is a colourless liquid and it was observed that, on standing in air, a dark colouration appeared in a similar manner to that observed for compound g.

Voltammetry

The half-wave potentials and the peak potentials of the three 1-cyclopropylalkylidenemalononitriles are listed in Table 13 together with those of a ring-opened alkylidenemalononitrile (a) for comparison. The values are all very similar, indicating that the cyclopropyl group is not involved to any significant extent in the initial reduction process. This is in agreement with the findings of Baizer and co-workers.[144] The

polarograms and cyclic voltammograms of compounds f and h are unusual, examples of which are illustrated in Figures 21 and 22. These unusual effects are not present at the same concentrations for compounds g and a although compound g does exhibit maxima phenomena at higher concentrations.

The height of the polarographic waves correspond to a one-electron reduction for compounds a and g. This was deduced by comparison of the wave heights with those of the one-electron reduction wave of benzophenone under similar conditions at various concentrations. The variation of the current with concentration was found to be the same for benzophenone and compounds a and g. Compounds f and h, on the other hand, exhibit a variation with concentration which is slightly larger than that of benzophenone, indicating that the reduction wave corresponds to slightly more than one electron. However, it is not known how the unusual effects illustrated in Figure 21 would affect this. In all cases, the addition of phenol caused the heights of the waves to double but no change in the half-wave or peak potentials was observed.

The unusual effects observed in the polarography and cyclic voltammetry patterns of compounds f and h (Figures 21 and 22) appear to involve adsorption of some kind. The large currents appearing at -2.5V are probably due to polarographic maxima effects. This can be seen most effectively in the cyclic voltammogram where a cathodic current is observed during the anodic sweep similar to that reported in Chapter 2 for the immonium cations. However, the effect in this case appears to be somewhat different in that the maximum is not associated with the initial faradaic reduction and, therefore, cannot be a maximum of the first kind.[34] Thus, it seems likely that the effect is a maximum of the third kind[33] where the depolariser is very strongly adsorbed. If the depolariser is strongly adsorbed, then the adsorption wave is negative of the diffusion wave, the separation between the diffusion wave and the

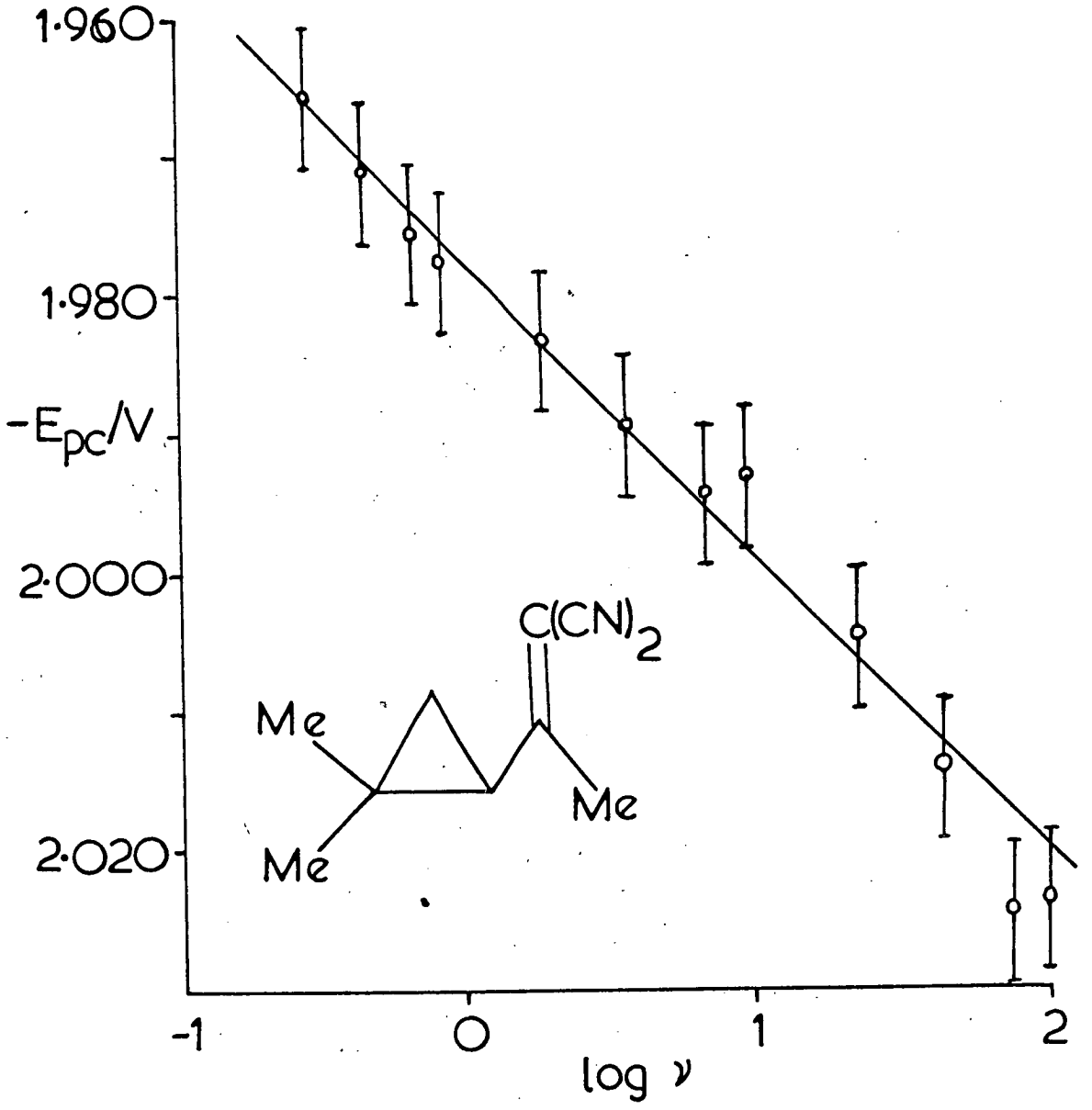


Figure 23. E_p-log ν diagram for 2-cyano-3-(2,2-dimethylcyclopropyl)-but-2-enenitrile (g); 1mM in 0.4M $TEABF_4$-CH_3CN; working electrode: hmde; reference electrode: $Ag/0.1M\ AgNO_3$.

adsorption wave increasing as the strength of the adsorption increases.[15,109] Due to shielding of the drop by the glass mounting of the electrode, some parts of the surface will be more negative than others so than when reduction of the adsorbate begins, the electrode has an uneven coverage. This results in inequalities in the surface tension which lead to the streaming of the solution. Such a theory accounts for the sudden drop in current back to the diffusion current value and also for the cathodic current during the anodic sweep in cyclic voltammetry experiments. Indeed, as the sweep rate in increased in cyclic voltammetry, the anodic sweep maximum disappears while the current peak on the cathodic sweep becomes much smaller and resembles an adsorption pattern.[15,109]

Compound g does not exhibit these phenomena at low concentrations. However, as the concentration is increased a maximum appears immediately after the diffusion peak in the cyclic voltammogram and the anodic sweep effect tends to occur. This behaviour is much more similar to that observed for the immonium cations in Chapter 2 and may be due to the effects of a maximum of the first kind.[33,34] On the other hand, it may also be that the depolariser is much less strongly adsorbed, such that the adsorption wave is very close to the diffusion wave.

These adsorption and streaming phenomena interfered with the study of the kinetics of reduction by linear sweep voltammetry. However, in agreement with the report of Baizer and co-workers,[144] all the compounds studied here exhibit totally irreversible behaviour in cyclic voltammetry. As noted above, the addition of phenol has no effect upon the peak potential. For both compounds f and h, the peak potential did not vary with the initial depolariser concentration. Compound g, on the other hand, did show a definite anodic shift upon increasing the initial concentration, but this was difficult to measure since, at high concentrations, the maximum interfered and no further shift of peak potential was observed.

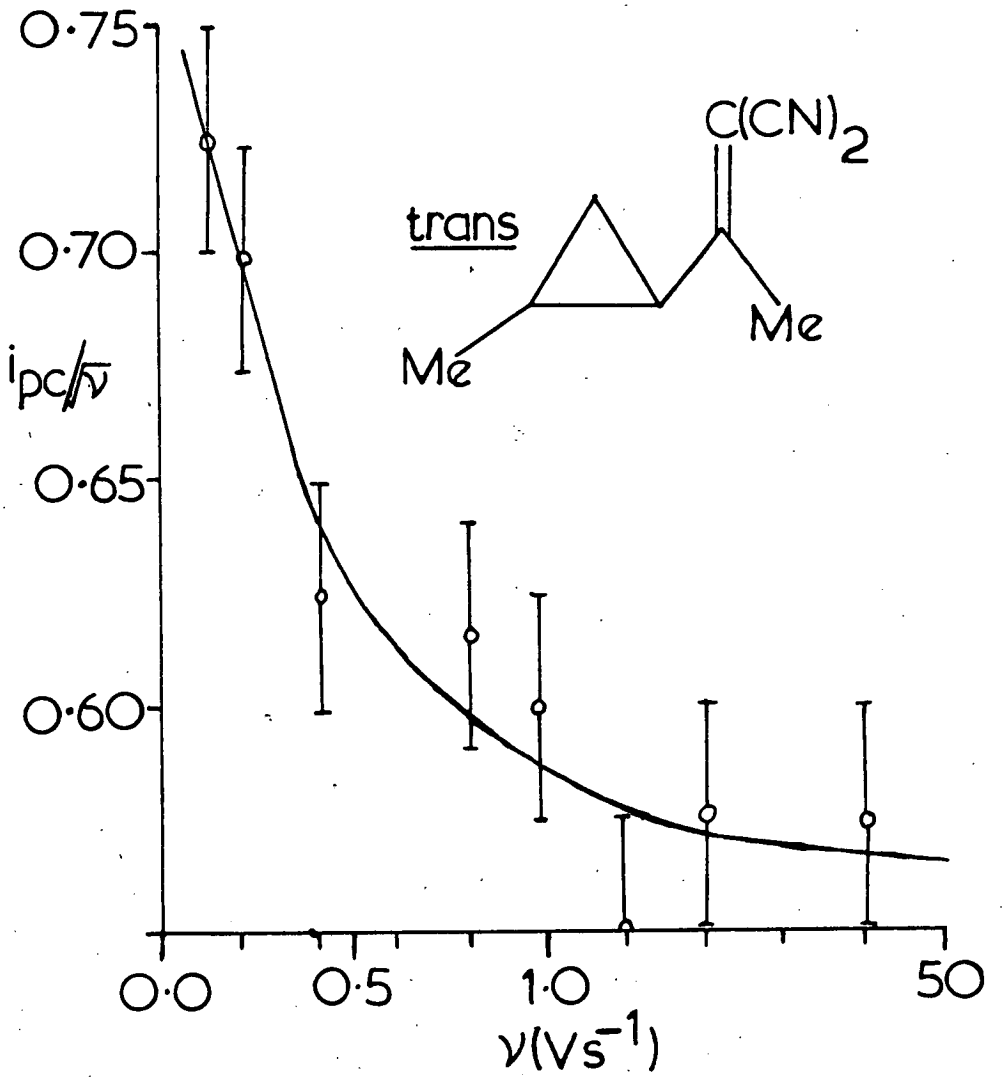


Figure 24. Current function variation with sweep rate for 2-cyano-3(trans-2-methylcyclopropyl)but-2-enenitrile (h); 0.5mM in 0.4M $TEABF_4$-CH_3CN; working electrode: hmde; reference electrode: Ag/0.1M $AgNO_3$.

A study of the variation of peak potential with sweep rate proved to be very difficult for compounds f and h. At concentrations greater or equal to 1mM, no discernable shift could be seen since the peak potential values were found not to be reproducible. At lower concentrations (0.1 - 0.5mM), a cathodic shift in the region of 30mV/decade could be detected. However, discontinuities in the E_p-log ν diagrams were observed at higher sweep rates which cast some doubt upon the validity of the measurements made at the lower sweep rates. The study of the peak potential variation of compound g, by contrast, was relatively straight forward and two different measurements of the variation with log ν gave slope values of 20.3mV/decade and 22mV/decade with correlation coefficients greater than 0.99 (see Figure 23).

Since the study of the peak potential variation of compounds f and h was inconclusive, a study of the variation of the current function, $i_{pc}/\nu^{\frac{1}{2}}$,[151] with the sweep rate was carried out on all three cyclopropyl compounds. With compound g, the current function appeared to be independent of the sweep rate but both compounds f and h exhibited behaviour, illustrated in Figure 24, in which, at low sweep rates, the current function increases markedly as the sweep rate is decreased. This type of behaviour is characteristic of an ECE process as shown by Nicholson and Shain.[152]

Preparative electrolyses

Preparative electrolyses were carried out on the unsubstituted cyclopropyl compound, f (10mM), in 0.1M $TEABF_4$-CH_3CN using a mercury electrode at -2.4V vs. Ag/0.1M $AgNO_3$. Coulometric measurements were also carried out during the electrolyses using the method devised by Avaca and Utley[95] and the n value was found to be approximately 1 $Fmol^{-1}$. Analysis of the product mixtures by glc showed that 40% of the starting material was recovered and 20% of the ring-opened alkylidenemalononitrile,

a, was detected. On repeating the experiment, 36% of the starting material and 24% of the ring-opened compound, a, were detected. Examination of the product mixtures by mass spectrometry showed that no dimers had been formed, the highest peak having m/e = 134. Electrolysis of f in the presence of phenol (0.1M) gave 6% of starting material, 7% of the ring-opened alkylidenemalononitrile, a, and 40% 2-cyano-3-methylhexanenitrile which corresponds to the two-electron reduction product of a. The n value was considerably greater than 2 $Fmol^{-1}$ but, at the potential employed (-2.4V), reduction of phenol was probably occuring.

In all three electrolyses, the material balance was deficient by around 40%. Since no dimeric, involatile material could be detected by mass spectrometry, then either the products were decomposing to volatile compounds, such as the corresponding ketones, which were lost during the work-up procedure or the analytical method was in error. The possibility of decomposition occurring during the work-up was checked for some of the electrolysis mixtures arising from the reduction of compound g by using careful distillation techniques to remove the solvents. However, since only ca. 1% of ketone was found, it would appear that the products are stable to work-up. We conclude, therefore, that there was a systematic error in the analytical method since it is improbable that even compound a, b.p. 94°C/4mm, would be volatile enough to be lost upon rotary evaporation. Nevertheless, the analyses do show that cleavage of the cyclopropyl ring takes place and that the major part of the reduction process concerns this reaction.

The results of preparative electrolyses of the substituted 1-cyclopropylalkylidenemalononitriles, g and h, are listed in Tables 14 and 15 respectively. The results of lithium-ammonia reductions of these compounds are also included for comparison. In Table 14, the resulting product distribution of a preparative reduction of 2-cyano-3,6-dimethylhept-2-enenitrile is also listed which allows comparison of the reduction

of the ring-opened alkylidenemalononitrile with that of the cyclopropyl compounds.

When the dimethylsubstituted cyclopropyl compound, g, was examined by glc analysis using a stainless steel column packed with a 10% Carbowax 20M stationary phase, two peaks were obtained. However, the same sample, when examined using a 10% ApL glass column, gave only one peak, indicating that some thermal rearrangement is taking place in the chromatograph inlet when steel columns are used. Dauben and Wolf[138] have reported some thermal rearrangement of 1-acetyl-2,2-dimethylcyclopropane to 5-methylhex-5-en-2-one on a gas chromatograph column. It is probable that a similar rearrangement takes place with the corresponding malononitrile derivative and since the quantitative analyses listed in Table 14 were carried out using a stainless steel column, the amounts of starting material are only approximate due to the uncertainty created by this rearrangement.

As was observed with the unsubstituted cyclopropyl compound, no evidence for dimeric material was found in the mass spectra of the products from the substituted cyclopropyl compounds. Coulometry carried out as described by Avaca and Utley[95] gave n values of approximately 1 $Fmol^{-1}$ when no proton donor was present. The value was increased upon the addition of phenol to the solution.

It is noticable that, in the absence of a proton donor, a large amount of starting material is recovered, even though the current at the end of the electrolysis had dropped from initial values of ca. 200mA to ca. 1-2mA and indicated that all the reducible material had been consumed. Indeed, the main cleavage product from most of the electrolyses is, in fact, reducible at the potentials employed. Since, in the presence of phenol, the reduction tends to proceed more to complete saturation, then it may be that some deprotonation reaction is preventing complete reduction and any proposed mechanism will have to account for this.

The mechanism of reduction of the 1-cyclopropylalkylidenemalononitriles, f, g and h.

The results of the preparative electrolyses listed in Tables 14 and 15 consistently demonstrate that the cyclopropyl ring is cleaved in a radical manner, both the trans-2-methylcyclopropyl derivative and the 2,2-dimethylcyclopropyl derivative favouring cleavage towards the substituted position by factors of 2-5 and >30 respectively. The corresponding ketones, when cleaved by a radical reaction involving di-t-butyl peroxide and butan-2-ol, gave very similar product ratios as regards the direction of ring cleavage[140].

In agreement with the findings of Baizer and co-workers,[144] the half-wave potentials of the alkylidenemalononitriles listed in Table 13 show little change upon replacing the cyclopropyl group with a propyl group. Since increased conjugation within a compound tends to increase the reducibility,[153] this observation implies that the cyclopropyl group is not conjugated with the adjacent olefinic group, at least in the ground state.

The fact that no sign of reversibility is observed in cyclic voltammetry experiments for any of the cyclopropyl compounds, even at the highest sweep rates ($500Vs^{-1}$), indicates that the follow-up chemical reactions are very rapid. However, since the slopes of the E_p-log ν diagrams are 20mV/decade or 30mV/decade, the electron transfer step must be a faster process. On the other hand, on close inspection of Figure 23, it can be seen that there appears to be a bending of the line at the highest sweep rates. This may, in fact, be due to insufficient compensation of the residual cell resistance or it may be due to the onset of charge transfer kinetic control.[42,43] In any case, the fact remains that the follow-up chemical reactions are very fast, probably approaching the speed of electron transfer. Consequently, it is not possible to study

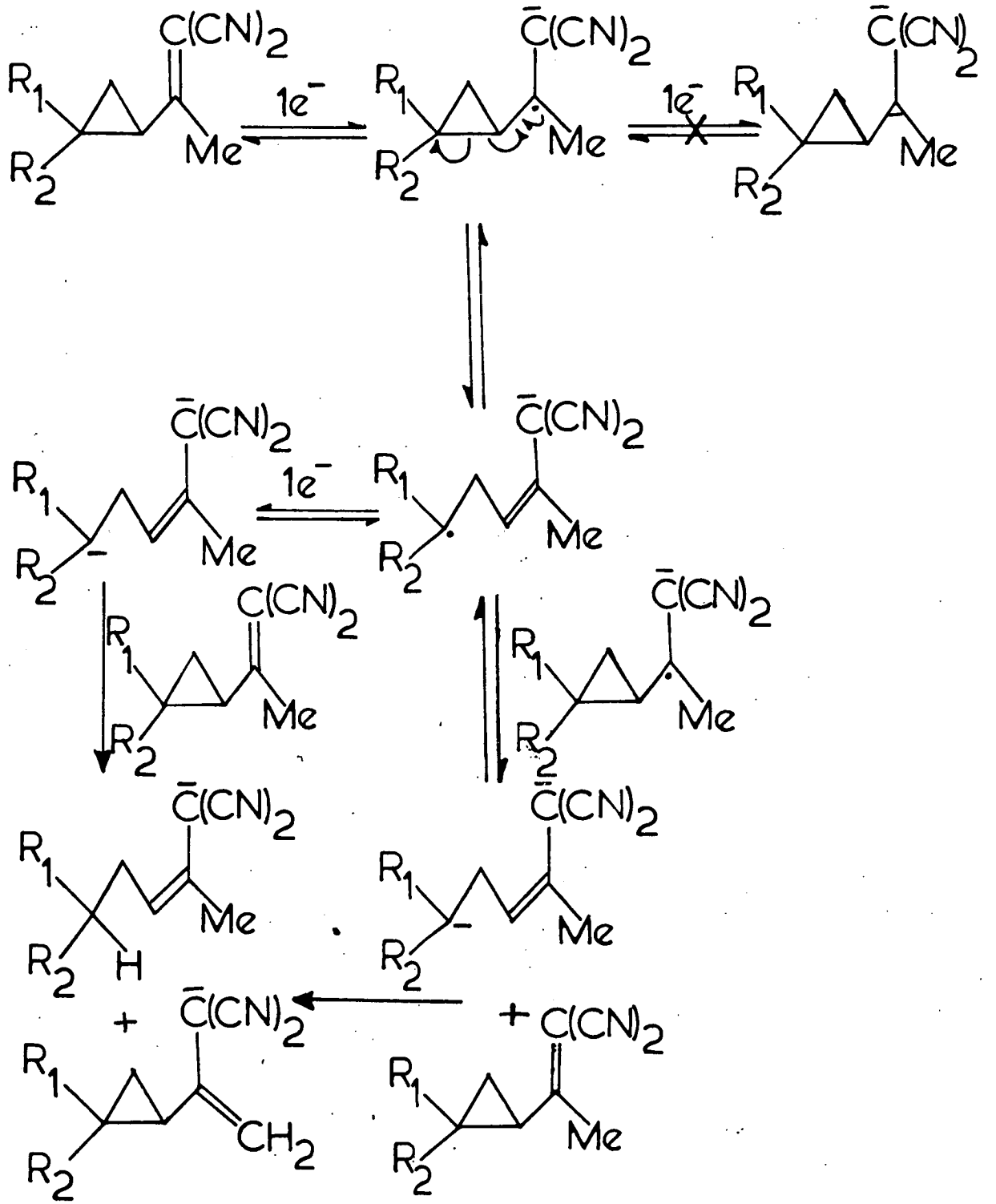


Figure 25

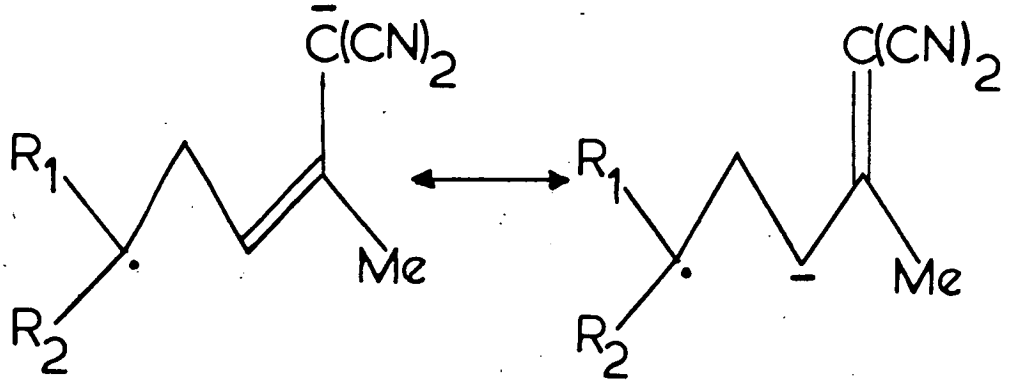
the epr spectra of the radical-anions.

The intermediate radical-anion may react in a number of ways. It may be further reduced by means of an electron transfer either at the electrode surface or in solution, it may be protonated or it may undergo an internal cleavage of the cyclopropyl ring. Examination of the products of the preparative electrolyses show that all of these possibilities take part in the reaction mechanism. The question is to decide which order they come in and which is the rate-determining step.

Further reduction of the initially formed radical-anion is not consistent with the products of the preparative reductions, since this would result in a dianionic species, the cleavage of which would yield a different product distribution from that actually observed. Protonation of the radical-anion does not seem likely either, since it has been previously shown that similar radical-anions are not protonated under these conditions.[11,60,61] Indeed, it has been shown that a radical-anion containing the same malononitrile function is not protonated even in DMF with 10% added water.[68] Therefore, the most likely reaction of the initially formed radical-anion is that involving the cleavage of the cyclopropyl ring which would be consistent with the observed product distributions. Some possible reaction schemes are illustrated in Figure 25.

Diagnostic criteria for linear sweep voltammetry have not so far been formulated to deal specifically with an internal ring cleavage reaction. However, such criteria have been presented by Andrieux and Saveant[125] for the reverse reaction, viz. the internal cyclization of radical-anions, protonated radical-anions and dianions. Since the cyclization reaction can be regarded as reversible, in particular when cyclization precedes the rate-determining step, such criteria can be applied to the reverse reaction of ring-cleavage. These criteria are listed in Table 16, the slope values and the reaction schemes being, in fact, taken

from Table 4, reference 125 and can be used with the proviso that the reaction designated by the letter c denotes cleavage rather than cyclization. Since the protonation of the radical-anion has been shown to be unlikely, then it seems reasonable that the protonation of the cleaved radical-anion would be even less likely due to the increased delocalization of the charge:



From this, it seems that the protonated radical-anions are unlikely to contribute to the reaction and, therefore, only cleavages of the radical-anion or the dianion are considered.

The measured E_p-log ν slopes for the disubstituted cyclopropyl compound, g, were 20.3mV/decade and 22mV/decade. Comparison with the slope values given in Table 16 allows five reaction schemes to be discarded immediately. The peak potential does not vary with the concentration of proton donor and therefore a further scheme can be eliminated. Of the remaining four possibilities, two show no variation with the initial concentration. Although it was not possible to measure accurately the variation of the peak potential with concentration due to the adsorption effects described earlier, it was possible to discern a positive shift at low concentrations, thus giving grounds for the elimination of these two schemes. The remaining possibilities are:

e - c - D - p - p and e - D - c - p - p.

The E_p-log ν slopes for the unsubstituted and the trans-substituted cyclopropyl compounds, f and h, were found to be ca. 30mV/decade while the peak potentials do not vary with either the initial concentration or the concentration of proton donor. Only two of the reaction schemes listed in Table 16 are compatible with these observations:

e - C - e - p - p and e - C - d - p - p.

As mentioned before, some doubt must be placed upon the peak potential measurements made for compounds f and h due to the effects of the adsorption phenomena and, consequently, it is necessary to take into account the observed behaviour of the current function illustrated in Figure 24. This behaviour is characteristic of an ECE mechanism where the intervening chemical reaction is irreversible and rate-determining.[152] The only two reaction schemes listed in Table 16 which fit the ECE mechanism are the two which were suggested by the peak potential measurements.

Since the reduction pathways of the unsubstituted and trans-substituted cyclopropyl compounds proceed via a ring cleavage of the radical-anion, there seems to be no apparent reason, from a structural point of view, why the disubstituted cyclopropyl compound should behave differently. Indeed, the radical cleavage of the disubstituted cyclopropyl compound should be more favoured than in the less substituted compounds since cleavage leads to the formation of a tertiary radical as opposed to a primary or a secondary radical. Therefore, cleavage of the dianion can safely be eliminated as a possible route leaving as the only possible mechanism for the disubstituted cyclopropyl compound:

e - c - D - p - p

That is, a fast reversible electron transfer to form a radical-anion followed by a fast and reversible ring cleavage of the radical-anion. The

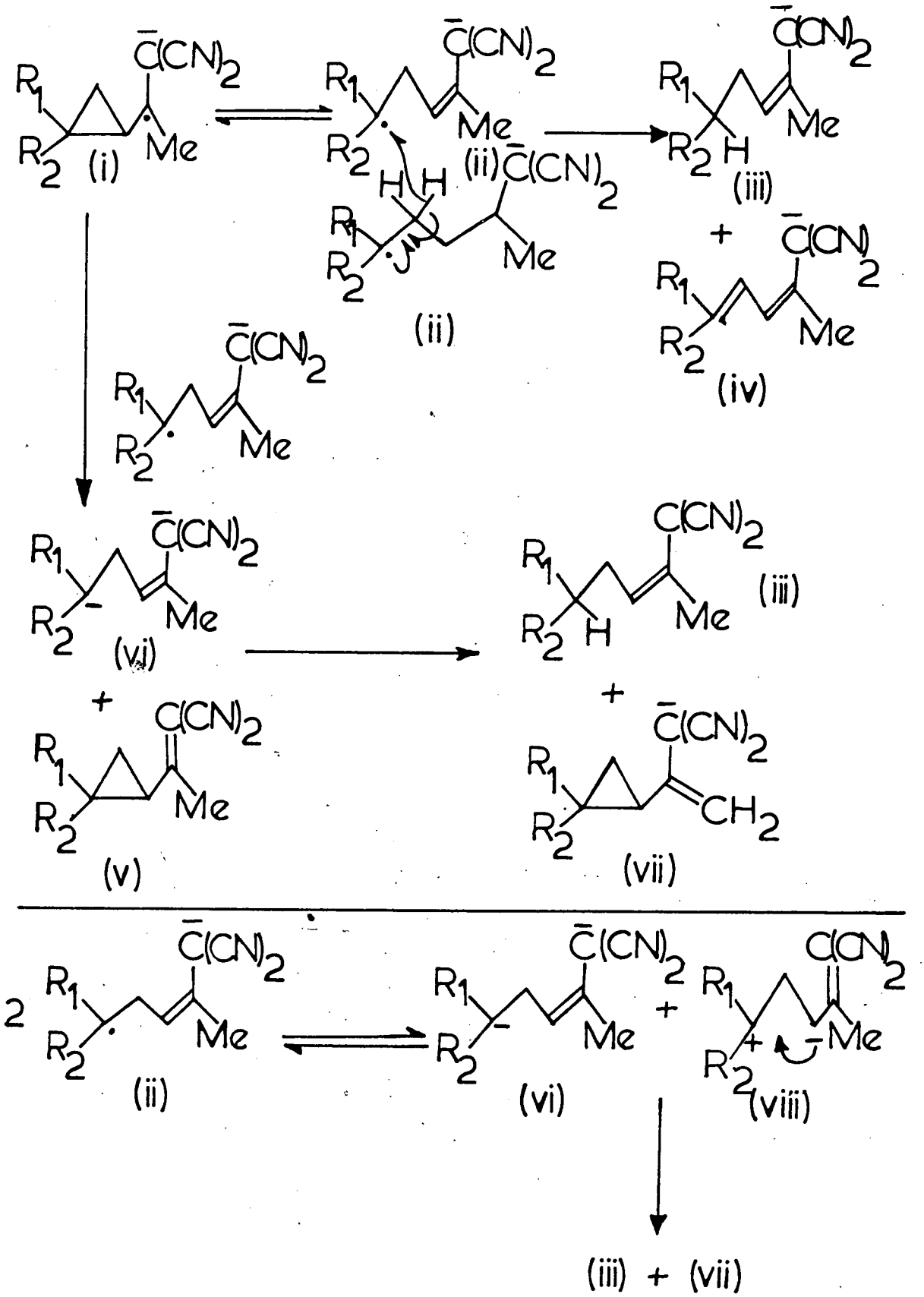


Figure 26

rate-determining step of the process is a disproportionation reaction which is followed by protonation to give the products. This mechanism is entirely compatible with the preparative results as regards the direction of the ring cleavage and, hence, the species involved in the cleavage reaction.

Although it is not possible to distinguish between the remaining mechanistic possibilities for the less substituted cyclopropyl compounds by means of lsv, it does seem that, since the reduction of the disubstituted compound proceeds via a disproportionation reaction, so also will the reduction of the other cyclopropyl compounds. Thus, it is most probable that the e - C - d - p - p mechanism is the correct one and this mechanism is compatible with the preparative results. It only remains to discuss the nature of the disproportionation reaction and how it produces the observed products.

As shown in Chapter 2, disproportionation reactions may involve either electron transfer or atom transfer. In this case, however, two different species may also be involved. In other words, disproportionation may take place between two ring-opened radical-anions or between one ring-opened and one cyclized radical-anion. The three major possibilities are shown in Figure 26.

The reducibility of the ring-opened radical-anion should be greater than that of the cyclized radical-anion due to the greater charge separation in the ring-cleaved dianion. The progressive increase in the ease of reduction with greater charge separation has been shown for the case of polynitro-compounds.[111] Thus, the disproportionation equilibrium constant should be greater for electron transfer between a cyclized radical-anion and a ring-cleaved radical-anion than for electron transfer between two ring-cleaved radical-anions due to the differing reducibilities of the two species concerned in the reaction. The rapid protonation of the dianion by the substrate molecule then provides the

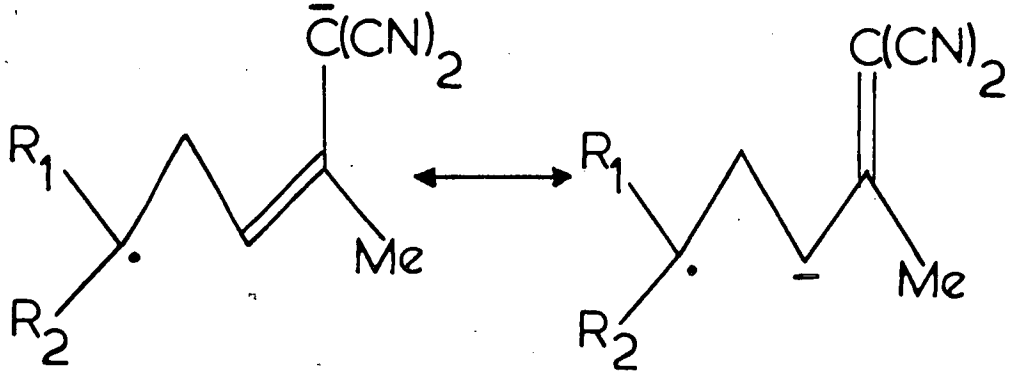
driving force to produce the two monoanions iii and vii (Figure 26). These anions are unlikely to be rapidly protonated in aprotic conditions and are not reducible at the working potentials employed. Consequently, they will survive until the solution is worked-up, when they gain a proton, and give the unsaturated alkylidenemalononitrile and the starting compound respectively, which are observed among the electrolysis products.

Electron transfer disproportionation between two ring-cleaved radical-anions can also give rise to the same products. The electron transfer produces the dianion, vi, plus the species, viii, which may not exist but only describe a transition state between the radical-anion (ii) and the substrate (v). Rapid proton transfer would then lead to the products. However, as pointed out above and in Chapter 2, such an electron transfer disproportionation would be an equilibrium process, strongly favouring the radical-anions (ii), and would probably only contribute to the reaction in the presence of a non-reducible proton donor such as phenol.

A disproportionation reaction between two ring-cleaved radical-anions may, however, involve a hydrogen atom transfer to give the monoanions, iii and iv. Unfortunately, no attempt to search for the protonated form of iv was made, and it may be that it was present among the reaction products. However, such a mechanism cannot explain the recovery of starting material which was observed in every reaction, even though little or no current was flowing at the end of the electrolysis. On these grounds, therefore, the hydrogen-atom transfer mechanism must be considered extremely doubtful although it cannot be ruled out as a minor pathway.

In the reduction of the unsubstituted and trans-substituted cyclopropyl compounds, f and h, the cleavage reaction is the rate-determining step while the disproportionation step is comparatively fast. Therefore,

when the ring-cleaved radical-anion (ii) is formed the concentration of the cyclized radical-anion (i) will be much higher than that of the ring-cleaved radical-anion and electron transfer between these two species will be the most likely mode of reaction. In the disubstituted case, however, the cleavage reaction is a fast and reversible equilibrium while the disproportionation is relatively slow. The cleavage equilibrium should favour the ring-cleaved form of radical-anion since the unpaired electron lies in a more favourable tertiary position and the negative charge can be more effectively delocalized:



Since the disproportionation process is slow compared with the cleavage step, the concentration of the ring-cleaved species will be relatively high. Thus, on the grounds of frequency alone, one would expect electron transfer to take place between two ring-cleaved species. However, as discussed above, the disproportionation equilibrium is not very favourable for electron transfer between two identical radical-anions. Electron transfer between the ring-cleaved radical-anion and the cyclized radical-anion, although not favoured by the relative concentrations of the species, is, however, a much more favoured process due to the greater reducibility of the ring-cleaved radical-anion. This then, is probably

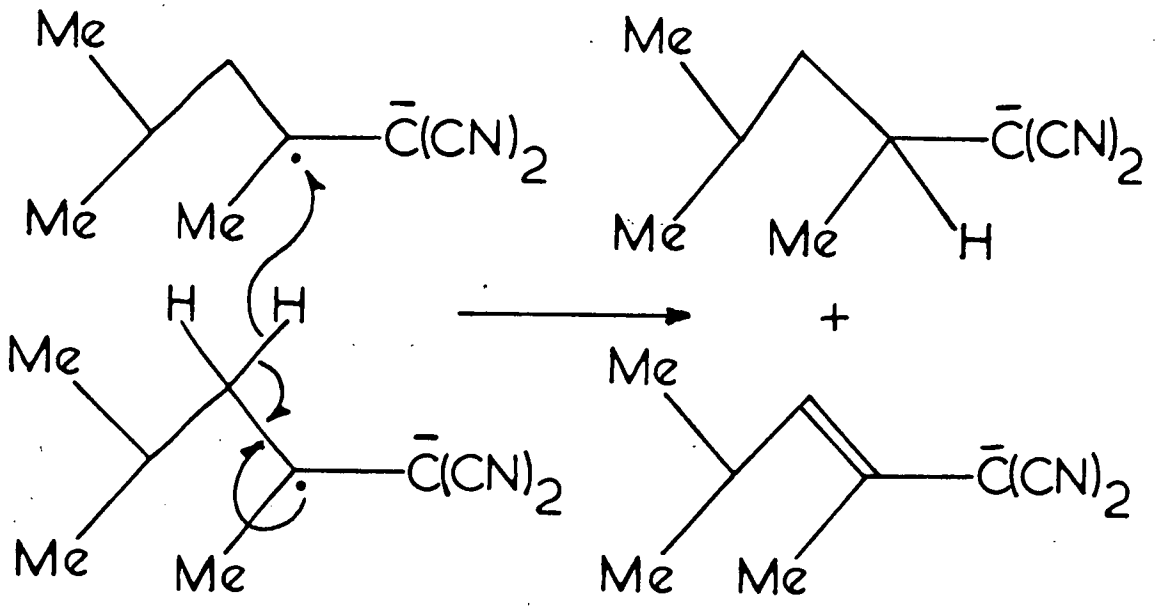
the correct route, the disproportionation reaction displacing the cleavage equilibrium towards the cyclized form of the radical-anion.

In passing, it is worth noting that the resonance forms shown above for the ring-cleaved form, in conjunction with the fact that the cleavage reaction is fast and reversible for the 2,2-dimethylsubstituted cyclopropyl compound may explain the slightly less cathodic reduction potential observed for this compound (Table 13). Since the cleavage reaction is not reversible for the other cyclopropyl compounds, then the form of conjugation shown above can make no contribution to the reduction process.

The difference in the observed kinetics between the 2,2-dimethyl substituted cyclopropyl, compound, g, and the less substituted cyclopropyl compounds, f and h, neatly reflects the difference in the intermediates involved in the reactions. Since the cleavage reaction results in the formation of what is essentially a free-radical site, it is interesting to note how the tertiary radical seems to be more favoured than the primary or secondary radicals. Similarly, the disproportionation reactions produce anions and again, the relative stabilities of the product anions may be reflected in the relative disproportionation rates, viz. the formation of the tertiary anion being slower than that of the primary and secondary anions.

The suggestion that the anions produced by protonation of the ring-opened dianions by the starting molecules, are relatively stable in the aprotic media employed, explains the presence of reducible material in the product mixture despite the lack of current. However, some of these anions must be protonated in order to explain the formation of the completely saturated products. The reduction of the ring-opened alkylidenemalononitriles is exemplified by Expt. No. 11, Table 14. In this case, it is possible that the reduction proceeds by a disproportionation mechanism, hydrogen atom transfer perhaps being more likely in this case

since the species involved in the disproportionation are both equally reducible:



Lithium-ammonia reductions

From Tables 14 and 15, it can be seen that the lithium-ammonia reductions of the cyclopropyl compounds g and h were very inefficient. Even though a large excess of lithium was employed, considerable amounts of substrate were recovered. In addition, the gas liquid chromatograms of the product mixtures showed a large number of unidentified peaks, all of which were quite small in area. However, from the small amount of cleaved product which was observed it is possible to see that the trans-substituted cyclopropyl compound, h, is reduced in a similar manner to the electrolytic reductions, the cleavage taking place mainly towards the substituent. The disubstituted cyclopropyl compound, on the other

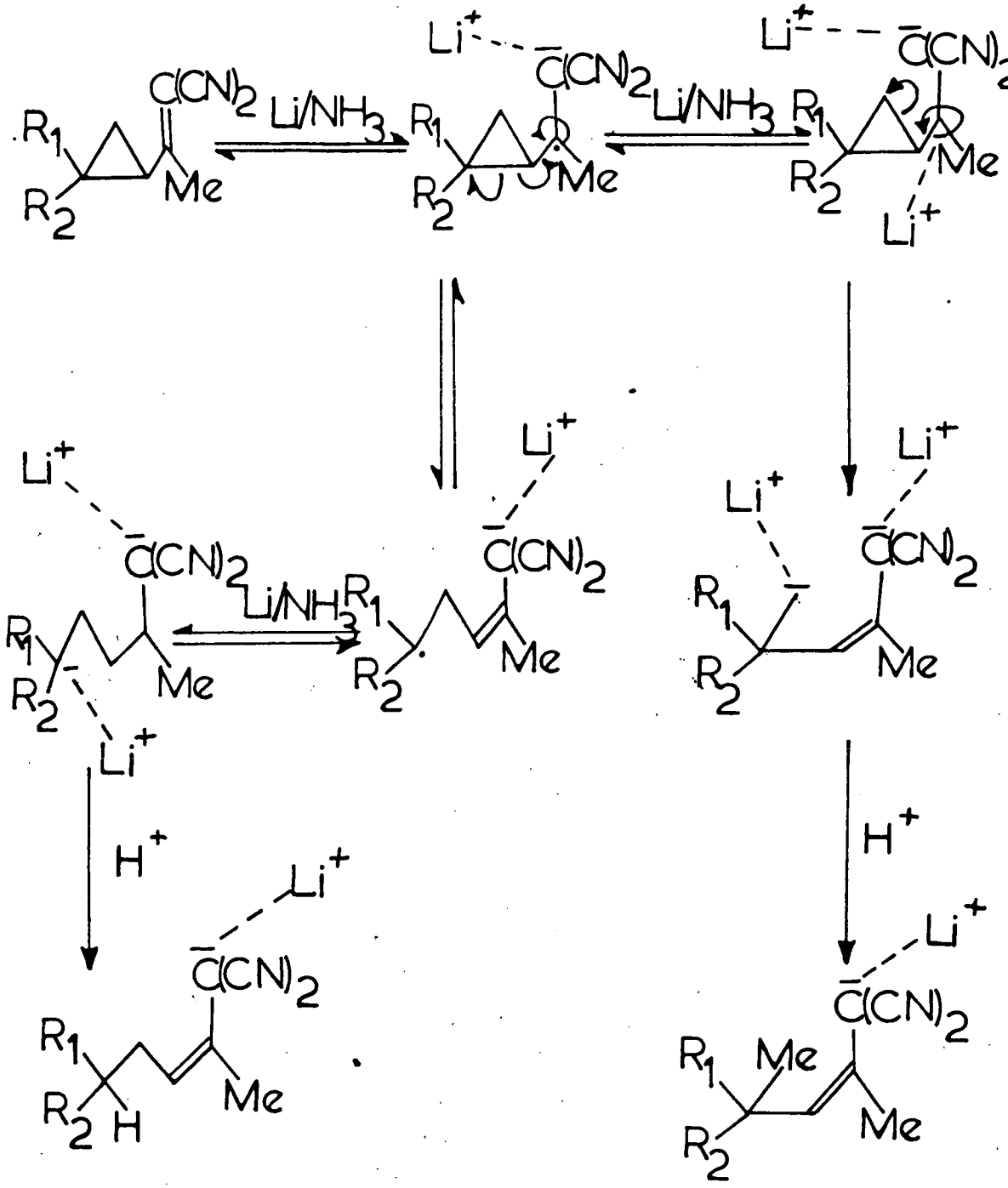


Figure 27

hand, shows a striking change in that the products reflect an anionic mode of cleavage rather than a radical mode.

An explanation for this behaviour may lie in the relative rates and the reversible character of the various cleavage and reduction processes. As shown in Figure 27, the initial reduction process can be represented by the transfer of an electron from the lithium-ammonia solution to the substrate to form a radical-anion. The radical-anion can then undergo cleavage and the resulting species is reduced to the ring-cleaved dianion. Alternatively, it is possible that in the lithium-ammonia solutions, the radical-anion may be further reduced to the cyclized dianion. A fast and irreversible ring-cleavage followed by protonation would then lead to the products.

The difference in the product distributions observed for the two cyclopropyl compounds must lie in the reduction processes of the different forms of radical-anion present. The further reduction of the cyclized radical-anion is equally likely for both compounds, since the substituent methyl groups on the cyclopropyl ring are too far removed from the reaction centre to have any significant effect on the reduction process. However, the reduction of the ring-cleaved radical-anion will be much more favourable for the trans-substituted compound since a secondary anion is formed rather than a tertiary anion as is the case for the dimethylsubstituted compound. From the product distributions, it appears that the cyclized radical-anion of the dimethyl-substituted cyclopropyl compound is more reducible than the ring-cleaved form of the radical-anion in the lithium-ammonia reductions. This is the opposite conclusion to that reached for the electrochemical reductions where the ring-cleaved form must be the more reducible species in order that the observed radical-cleavage products can be formed. Since it appears from the electrochemical reductions in the presence of lithium cations that these cations have no effect upon the reaction, the difference must lie

in the effect of the solvent. In other words, liquid ammonia must be able to stabilise the cyclized dianion much better than acetonitrile can.

Some indication of this solvent effect may perhaps be drawn from a comparison of the difference in the reduction potentials of the two waves of benzophenone in liquid ammonia and DMF. Demortier and Bard[154] have measured this value as being 530mV for the reversible formation of the dianion of benzophenone in liquid ammonia at -50°C using a gold electrode. Measurements made by Jensen and Parker[38b] show that this difference is 770mV in DMF using a platinum electrode at ambient temperature. Similar measurements made in this laboratory[155] show that the difference is 760mV at -40°C in DMF using a Pt disc. The dianion is therefore more easily formed in ammonia than in DMF and this may indicate that in ammonia the coulombic repulsion of the charges in the dianion is less important due to solvation effects. In order to test such a hypothesis, the electrochemical behaviour of the 1-cyclopropylalkylidenemalononitriles, g and h, in liquid ammonia would need to be studied.

Table 13 Half-wave potentials ($E_{\frac{1}{2}}$) and peak potentials (E_p) for various alkylidenemalononitriles of the form $Me(R)C:C(CN)_2$ (1mM) in 0.1M $TEABF_4$-CH_3CN. Reference electrode: $Ag/0.1M\ AgNO_3$.

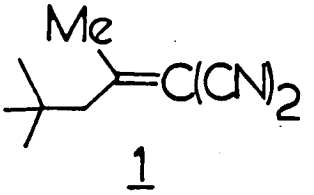
R	$E_{\frac{1}{2}}$/V	E_p/V *
propyl (a)	-2.08	-2.13
cyclopropyl (f)	-2.01	-2.08
2,2-dimethyl-cyclopropyl (g)	-1.93	-2.00
trans-2-methyl-cyclopropyl (h)	-2.03	-2.10

* hmde, sweep rate = 200 mVs^{-1}.

Table 14 Results of preparative electrolyses of 2-cyano-3-(2,2-dimethyl-cyclopropane)-but-2-enenitrile (10mM) in 0.1M $TEABF_4$-CH_3CN at a mercury pool electrode. The working potential was -2.4V vs. Ag/0.1M $AgNO_3$.

Expt. No.	Yields (% by glc analysis[a])				
	1	2	3	4	5
1	0	0	15	0	50
2	0.6	0.8	21	8.5	38
3[b]	0	1.1	27	9	59
4	0	trace	32	8	20
5[c]	0	trace	14	18	20
6[c,d]	0	trace	10	15	25
7[e]	0	1.9	44	20	30
8[e]	0	2.2	24	20	18
9[i]	0	0.7	21	1.6	75
10[k]	0.74	5.8	3.9	0.5	19
11[l]	-	-	38	40	-

a, 10% Carbowax 20M, 170°C; b, n = 0.96 $Fmol^{-1}$; c, +0.1M phenol; d, n = 1.6 $Fmol^{-1}$; e, + 0.1M $LiClO_4$; i, reduction be means of an electrochemically preformed lithium-amalgam; k, Li/NH_3 reduction; l, electrolysis of 3.



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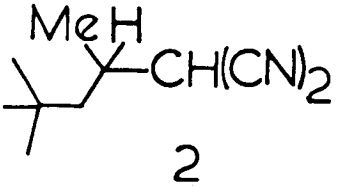

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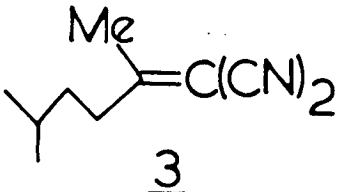

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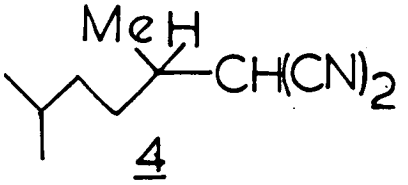

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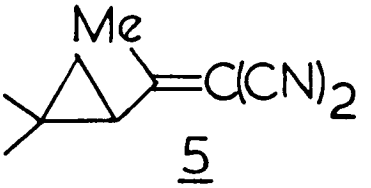

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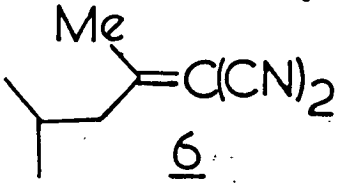
Table 15 Results of preparative electrolyses of 2-cyano-3-(trans-2-methylcyclopropane)-but-2-enenitrile (10mM) in 0.1M $TEABF_4$-CH_3CN at a mercury pool electrode. The working potential was -2.4V vs. Ag/0.1M $AgNO_3$.

Expt. No.	Yields (% by glc analysis[a])				
	6	7	8	9	10
1	2.0	trace	12.8	5.2	4.3
2[b]	12	4	55	24	5
3	15	1	29	3	24
4	3.2	0.5	17	2.6	9
5[c]	8	3	25	8	22
6[d]	2.3	trace	0.6	4.2	42
7[d]	1.7	0.9	2.4	1.3	64

a, 10% Carbowax 20M, 170°C; b, DMF as solvent; c, n = 0.67 $Fmol^{-1}$; d, Li/NH_3 reduction.



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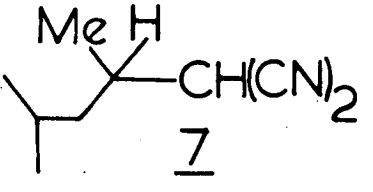

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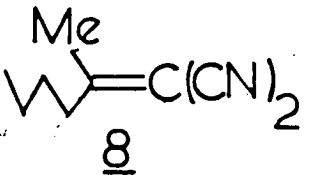

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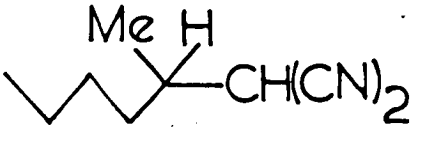

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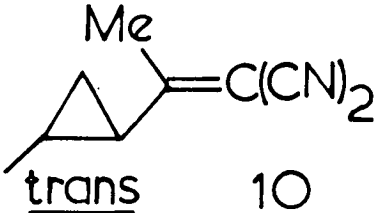


trans 10

Table 16 Diagnostic criteria for lsv analysis of cleavage reactions.

Reaction Scheme[a]	$-\frac{\partial E_p}{\partial \log \nu}$	$\frac{\partial E_p}{\partial \log C_o}$	$\frac{\partial E_p}{\partial \log Z_o}$[b]
	/mV per decade at 25°C		
Cleavage of the radical-anion:			
e-c-e-P-p	14.8	0	14.8
e-C-e-p-p	29.6	0	0
e-c-d-P-p	19.7	0	0
e-c-D-p-p	19.7	19.7	0
e-C-d-p-p	29.6	0	0
Cleavage of the dianion:			
e-e-c-P-p	14.8	0	14.8
e-e-C-p-p	14.8	0	0
e-d-c-P-p	19.7	0	19.7
e-d-C-p-p	19.7	0	0
e-D-c-p-p	19.7	19.7	0

a, e denotes electron transfer at the electrode, c the cleavage reaction, p protonation and d electron transfer in solution. The capital letter denotes the rate-determining step;

b, denotes the conc^{n}. of proton donor.

CHAPTER 5

EXPERIMENTAL

CHAPTER 5

Experimental

Infrared spectra were recorded on a Unicam SP200 or a Perkin-Elmer 157G spectrophotometer. Suffixes to infrared bands quoted are abbreviated weak (w), medium (m), strong (s).

^{1}H nuclear magnetic resonance spectra were recorded on a Varian Associates EM360 (60MHz) or an H.A.100 (100MHz) spectrometer. ^{13}C nmr spectra were recorded on a Varian Associates CFT-20 spectrometer system. Samples were run as solutions (5-10%) in deuterochloroform with tetramethylsilane as internal reference. In the tabulation of nmr data the following abbreviations are used: singlet (s), doublet (d), doublet of doublet (d of d), triplet (t), quartet (q) and multiplet (m).

Analysis figures were obtained using a Perkin-Elmer 240 elemental analyser.

Mass spectra were run on an AEI MS902 double-focusing mass spectrometer.

Melting points are uncorrected.

Analytical glc was performed, in the case of the immonium salt reductions, on a Hewlett-Packard 5711A Gas Chromatograph, equipped with flame ionization detectors and coupled to either an H-P 3370B or an H-P 3380A Integrator for data reduction. Temperature programming was required and therefore double column operation was used. The columns were 2m x ¼" O.D. glass columns packed either with 10% Carbowax 20M, 1% KOH on Chromosorb W (87-100 mesh) or with Chromosorb 103. For the other studies, analytical glc was carried out on a Perkin-Elmer F11 instrument using flame ionization detectors coupled to a Chromolog 3 digital integrator for data reduction. The columns used were either two 6' x ¼" O.D. glass columns packed with 10% ApL on Chromosorb G (80-100 mesh) for use in temperature programming, or 6' x ⅛" O.D. stainless steel

columns packed either with 15% Carbowax 20M on Chromosorb P (80-100 mesh) or with 15% PEGA on Chromosorb P (80-100 mesh) for isothermal analyses.

Preparative glc was performed, in the case of the immonium salt study, on a Perkin-Elmer F21 Gas Chromatograph with a 3 x 1m $\frac{3}{8}$" O.D. SS column packed with 10% Carbowax 20M, 3% KOH on Chromosorb W (60-87 mesh). For the other studies a Wilkens Instrument and Research Inc. Aerograph Autoprep instrument, model A-700 was employed. The columns used were 6' x $\frac{1}{4}$" O.D. SS packed with either 10% SE-30 on Chromosorb P (45-60 mesh) or 10% Versamid 200 on Chromosorb P (45-60 mesh).

High pressure liquid chromatography was carried out using a 100mm x 5mm stainless steel column, slurry packed with Sperisorb Alumina (7μm) at ambient temperature in conjunction with a Du Pont 820 or a Chromatronix Model 3100 liquid chromatograph. The detection systems used were ultraviolet detectors operating at 254nm and integration of the peak areas was carried out by triangulation or by use of an Autolab 6300 Digital Integrator.

Polarographic experiments were carried out with either a Metrohm P305 three-electrode polarograph in conjunction with a Metrohm E506 Polarecord, or a Chemical Electronics TR 70/2A potentiostat driven by a Chemical Electronics Linear Sweep Generator. Tensammetry was carried out using the Metrohm P305 polarograph in the ac mode with a phase angle of 90°. Linear and triangular sweep voltammetry were performed with either a home-built operational amplifier or a Chemical Electronics TR 70/2A potentiostat driven by a Chemical Electronics Waveform Generator Type R.B.1. Voltammograms were recorded on either a Hewlett-Packard 7045A or a Bryans Model 21005 X-Y recorder for slow sweep rates ($400mVs^{-1}$) and on a Tektronik 5103N storage oscilloscope for higher sweep rates. Preparative electrolyses and coulometry were carried out by means of either a Juul Electronic 100V/3A or 300V/1A potentiostat (immonium salts only), a Chemical Electronics TR 70/2A potentiostat or a Hermes Controls series 50, 100V/0.5A potentiostat. The consumption of

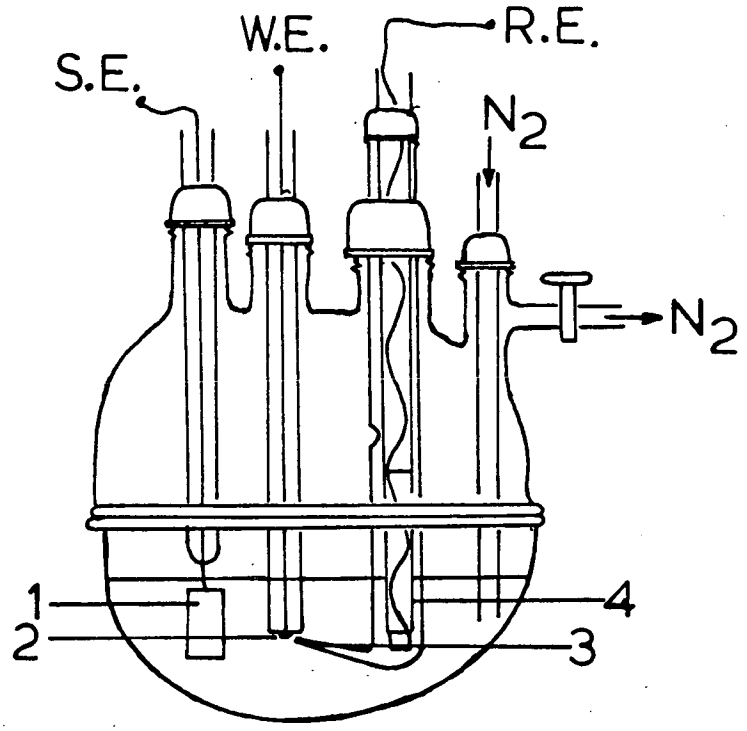


Figure 28. Analytical cell; 1, counter electrode (S.E.); 2, working electrode (W.E.); 3, Luggin capillary; 4, reference electrode (R.E.).

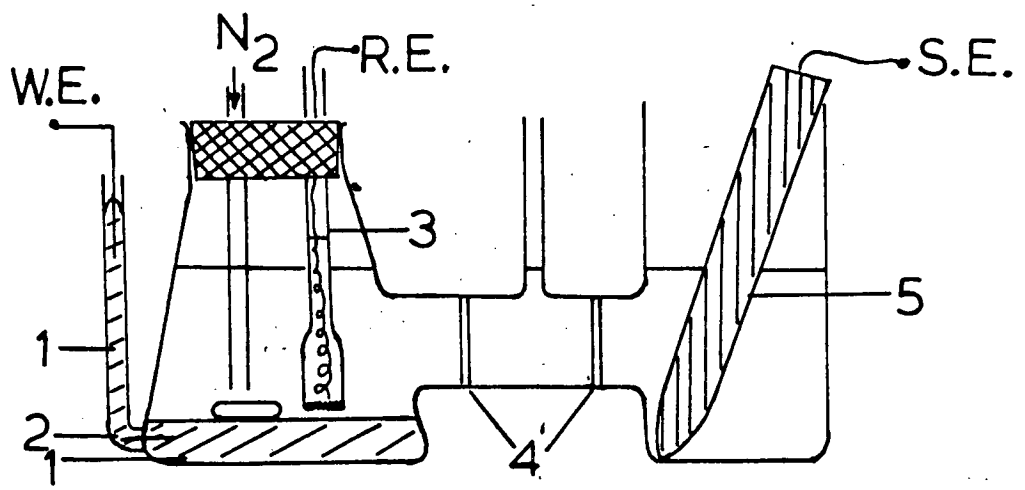


Figure 29. H-type preparative cell; 1, mercury (W.E.); 2, platinum wire contact; 3, reference electrode (R.E.); 4, glass frits; 5, counter electrode (S.E.).

electricity was measured by means of either an electromechanical integrator or a hydrogen-nitrogen coulometer.

Polarography and voltammetry were carried out in a Metrohm analytical cell or in the cell illustrated in Figure 28 which closely resembles the Metrohm cell. The counter electrode was a platinum wire or strip and the reference electrode was either SCE, Ag/0.1M $AgNO_3$ or Ag/AgI/0.1M-TBAI. For polarography the working electrode was a dropping mercury capillary electrode (dme) with a natural drop-time of about 4s in acetonitrile and a flow rate of around 1mg Hg s^{-1}. In order to regulate the drop-time which can be irregular in aprotic solutions, a forced drop device (Metrohm) was sometimes used to give a constant drop-time of 0.8s. The solid working electrodes for stationary electrode voltammetry were either polished platinum wire or glassy carbon rod set in glass. Mercury electrodes consisted of either a long drop-time capillary electrode or a hanging mercury drop electrode (hmde).

The hmde was prepared in two ways from a platinum disc electrode constructed as above. The platinum electrode was first cleaned by treatment with boiling nitric acid followed by polishing. The electrode was then immersed in an aqueous 0.1M $HClO_4$ solution with a mercury pool in the bottom of the flask. A platinum counter electrode was also immersed in the solution and the two electrodes were connected to a 3V battery, the negative terminal being connected to the clean platinum disc electrode. Hydrogen was evolved at the negative electrode and this was allowed to continue for ten minutes. The electrode was then dipped into the mercury pool several times while still connected to the battery until a mercury drop adhered to the surface. The electrode was then washed with water and acetone and allowed to dry.[156] Alternatively, the platinum disc electrode could be immersed in an aqueous solution of $HgClO_4$ (0.1M) and connected to the negative terminal of a potentiostat. A mercury pool anode and an SCE reference electrode were also employed while

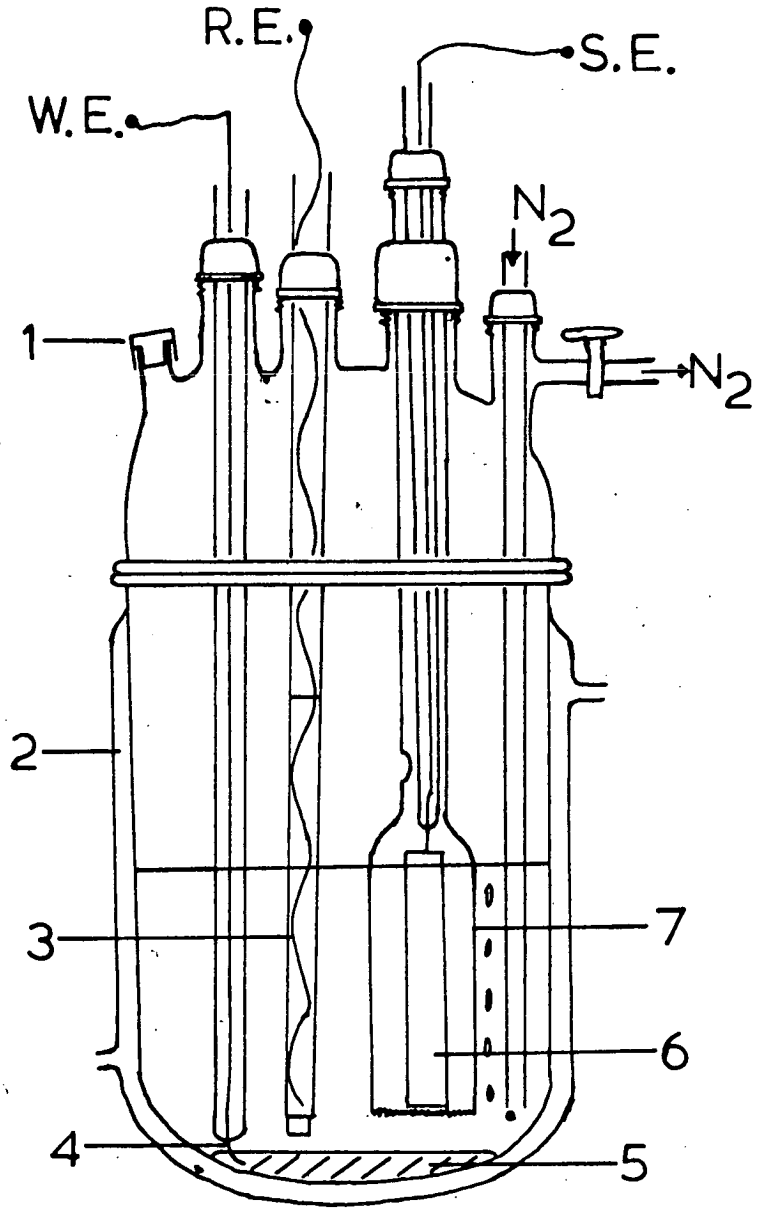


Figure 30. Preparative electrolysis cell; 1, septum to allow sampling of solution; 2, water jacket; 3, reference electrode (R.E.); 4, platinum wire contact; 5, mercury pool (W.E.); 6, counter electrode (S.E.); 7, secondary compartment.

electrolysis was carried out at -1.2V until a mercury drop had formed on the platinum disc. The electrode was then disconnected, washed and dried.

Preparative electrolyses of the immonium salts were carried out in a conventional H-type cell[157] illustrated in Figure 29 for a mercury working electrode whose surface area was about 15cm^2. Platinum working electrodes consisted of a platinum gauze of similar surface area to that of the mercury electrode while carbon working electrodes were graphite rods of undetermined surface area. Counter electrodes were either platinum gauze or graphite rod. The reference electrode was Ag/AgI/0.1M-TBAI in all cases.

Preparative electrolyses of all other compounds were carried out in the cell illustrated in Figure 30 for a mercury pool whose surface area was about 3cm^2. Platinum and carbon working electrodes were as described above, while the counter electrode was a platinum strip. The reference electrode was Ag/0.1M $AgNO_3$. Temperature control of the cell was achieved by means of a thermostat.

The solvents used were acetonitrile and DMF. Acetonitrile (technical grade) was purified and dried by the method of Forcier and Olver.[158] This consisted of refluxing the acetonitrile over sodium hydride (2g per litre) for 2h, followed by distillation through a 50cm Vigreux column. The middle 80% of the distillate was collected and distilled similarly from phosphorus pentoxide (1g per litre). The distillate was finally distilled in the same manner from powdered calcium hydride (2g per litre) and the pure acetonitrile was stored over Molecular Sieves Type 4A. The water content of this acetonitrile was found to be ca. 100ppm by Karl-Fischer titration. DMF (Fluka, Purum in most cases) was purified by drying over Molecular Sieves Type 4A and passed through a column of activated alumina immediately prior to use.

Supporting electrolytes (tetrabutyl- or tetraethyl- ammonium perchlorate or fluoroborate) were prepared by neutralising an aqueous

solution of the tetra-aklylammonium hydroxide with either perchloric or fluoroboric acid. The aqueous solutions were concentrated and the white solids recrystallized (2x) from absolute ethanol. The electrolyte was dried *in vacuo* at 60°C before use. Lithium salts (Fluka, anhydrous) were used without further purification.

Procedures for recording voltammograms and correcting for the effects of uncompensated cell resistances

Voltammograms were carried out using about 20-25ml of solution (acetonitrile or DMF) containing supporting electrolyte (0.1M to 0.4M) and the depolariser (0.1mM to 5mM). Before experiments were commenced the solution was thoroughly de-aerated by passing a stream of nitrogen through the solution for at least 10min prior to recording the voltammograms. It was important that this nitrogen stream should be pre-saturated with the relevant solvent by passing through a solvent bubbler before its introduction into the cell since otherwise, especially in the case of acetonitrile, the solvent may be volatile enough for such a de-aeration procedure to seriously alter the solution concentrations by removal of the solvent in the gas stream. A nitrogen atmosphere was maintained over the solution during the recording of voltammograms by means of a gas stream which did not disturb the solution.

It was important to de-aerate and stir the solution with the nitrogen stream between each voltage sweep, especially in the case where a solid electrode, such as a platinum disc, or an hmde was in use as the working electrode. The reason for this is aptly demonstrated by the behaviour of the adsorption prepeaks of aromatic ketones in DMF which is described in Chapter 3. Such stirring with nitrogen can destroy any films formed on the electrode surface during previous voltage sweeps. This is important because surface films can alter the heterogeneous rate constants of electron transfer and, hence, alter peak potentials and

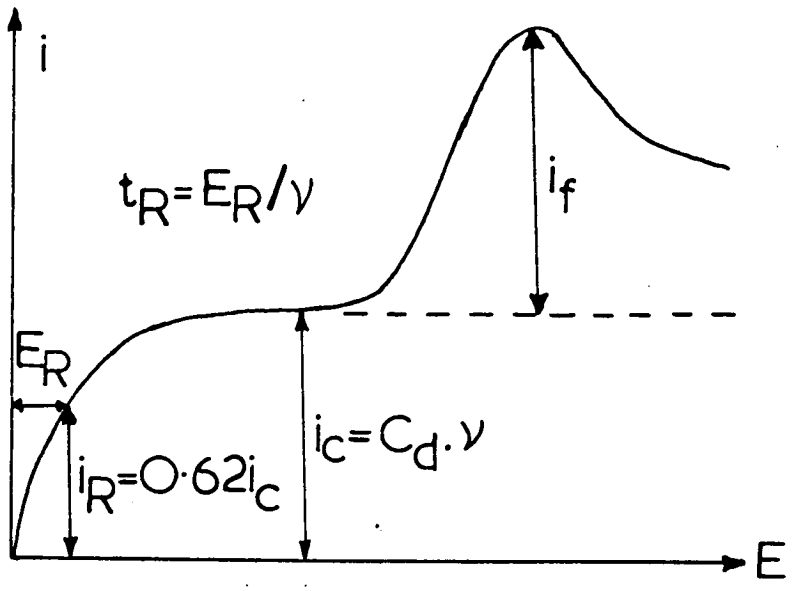


Figure 31a. Schematic representation of faradaic and double layer charging current.

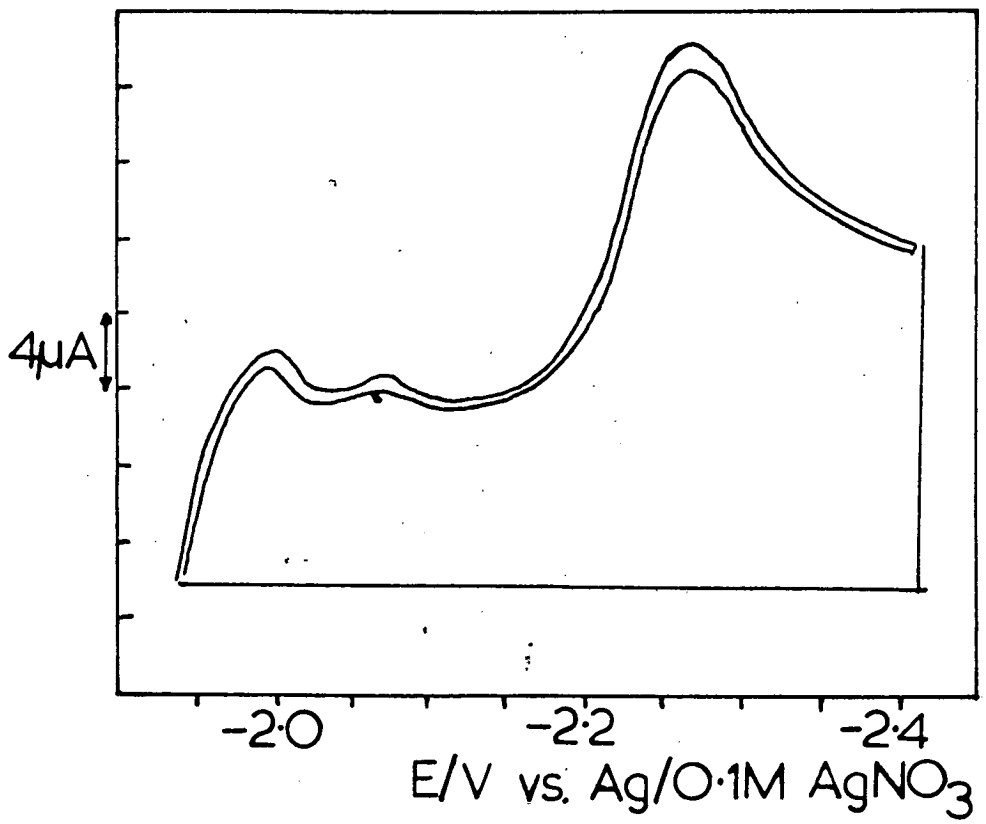


Figure 31b. Linear sweep voltammogram of benzophenone (0.113mM) in 0.1M $TEABF_4$-CH_3CN; reference electrode: Ag/0.1M $AgNO_3$ with Luggin capillary; working electrode: long drop-time capillary electrode; sweep rate: $100Vs^{-1}$.

currents.

A further distortion of voltammograms can arise through the effects of the uncompensated cell resistance and the double layer charging on the polarization curves. In order to allow for this, these effects had to be studied for a system of known behaviour and, for this reason, benzophenone was chosen as a standard on which to study the effects of ohmic drop on the peak potentials since it exhibits a one-electron reversible reduction pattern in the potential range of interest (-2.0 to -2.4V vs. Ag/0.1M $AgNO_3$). Several procedures were employed to allow for the uncompensated resistance of the cell.

Initially, the uncompensated resistance was minimised as far as possible. The cell resistance depends to some extent upon the cell geometry. When an SCE or an Ag/AgI/0.1M TBAI reference electrode was used, the cell resistances were high (ca. 3kΩ for 0.1M TBAP-CH_3CN). This was due to the large size of the medium porosity glass frits which separated the reference electrode from the working compartment and which prevented positioning of the reference electrode close to the working electrode, the intervening distances being at least 1cm. When an Ag/0.1M $AgNO_3$ reference electrode with a smaller, less porous glass frit was used, which allowed closer positioning of the reference and working electrodes, the uncompensated resistance was about 1.5kΩ (0.1M $TEABF_4$-CH_3CN). The introduction of a Luggin capillary, as illustrated in Figure 28, where the tip of the capillary was positioned about 1-2mm from the working electrode surface, caused the resistance to fall to around 1.2kΩ for the above conditions. An increase of the supporting electrolyte concentration to 0.4M reduced the resistance still further (370Ω).

The uncompensated cell resistances and the double layer capacitances were measured using the method described by Saveant and co-workers.[159,160] The double layer charging current (i_c in Figure 31) was measured and from this the double layer differential capacitance (C_d) was calculated. The

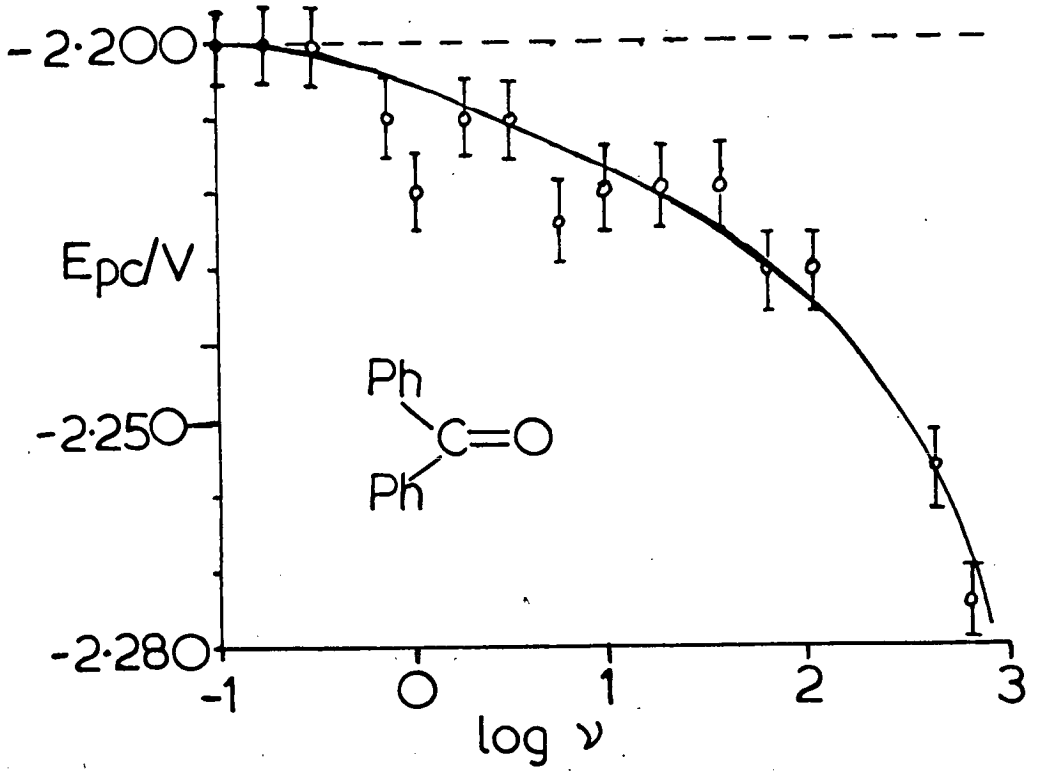
response time (t_R) was measured by finding the point on the initial rising portion of the curve where the current is 63.2%[160] of that on the plateau. Knowing this and the sweep rate, the response time could be calculated. The response time is related to the uncompensated resistance (R_u) and the double layer capacitance according to:

$$t_R = C_d \bullet R_u$$

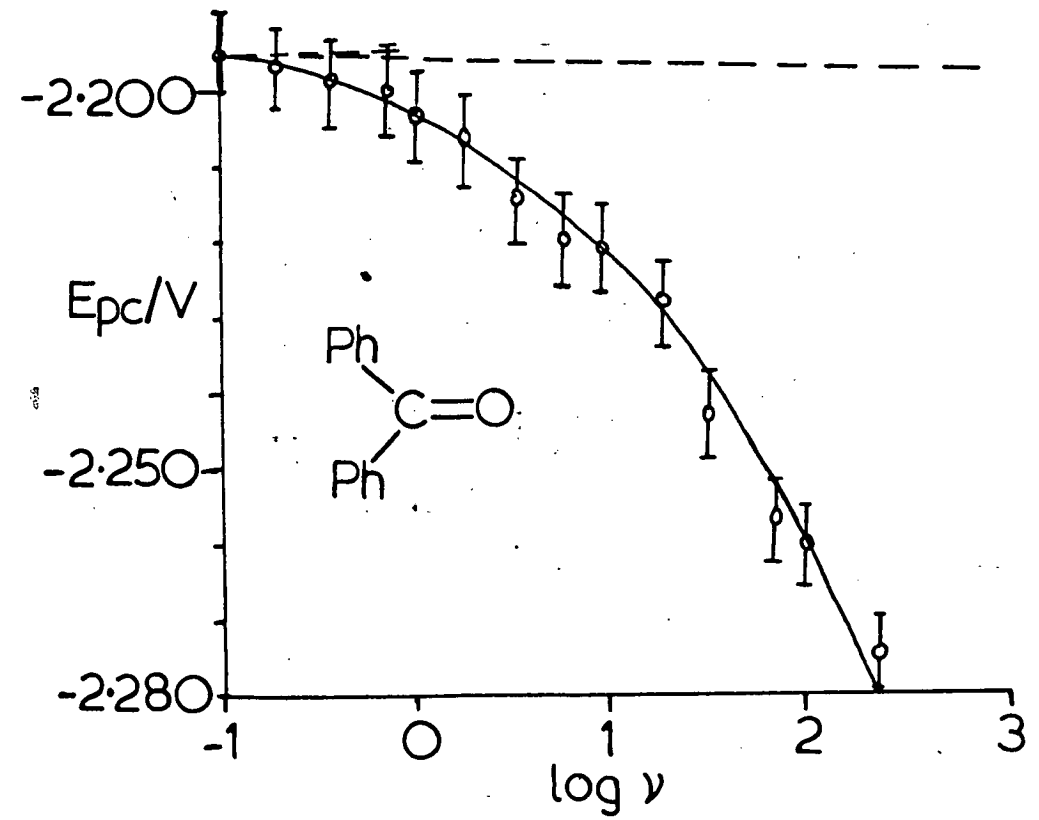
and, hence, R_u could be found. In the experimental example shown in Figure 31b, the value of the charging current (i_c) was 10.62μA which gave a capacitance of 0.1062μF (C_d). The response time (t_R) was found to be 15.5×10^{-5}s, giving an uncompensated cell resistance (R_u) of 1.46kΩ.

Once the uncompensated resistance has been minimised, the next step was to minimise its effects upon the current-voltage measurements. Since the effect of the uncompensated resistance is ohmic, then reduction of the effect on the peak potential can be achieved by reducing the peak current. This implies a reduction of the concentration of the electro-active species. The efficacy of this procedure is illustrated in Figure 32 (a and c) which show the effect of the uncompensated resistance on the peak potential as a function of the sweep rate. Unfortunately, at such low concentrations the signal to noise (50 Hz pick-up) ratio becomes quite small and the error on the peak potential determination becomes larger. This is illustrated by the greater spread of points in the curves for the two lower concentrations (a and b). Thus, the noise pick-up constituted a lower limit to practical concentrations and therefore a limit to the usable sweep rates.

By lowering the concentration, only the faradaic component of the current is varied. However, it is possible to vary both the faradaic and the capacitance components by the use of a long drop-time capillary electrode. By suitably adjusting the delay time between the start of a new drop and the beginning of the sweep, it is possible to keep the total

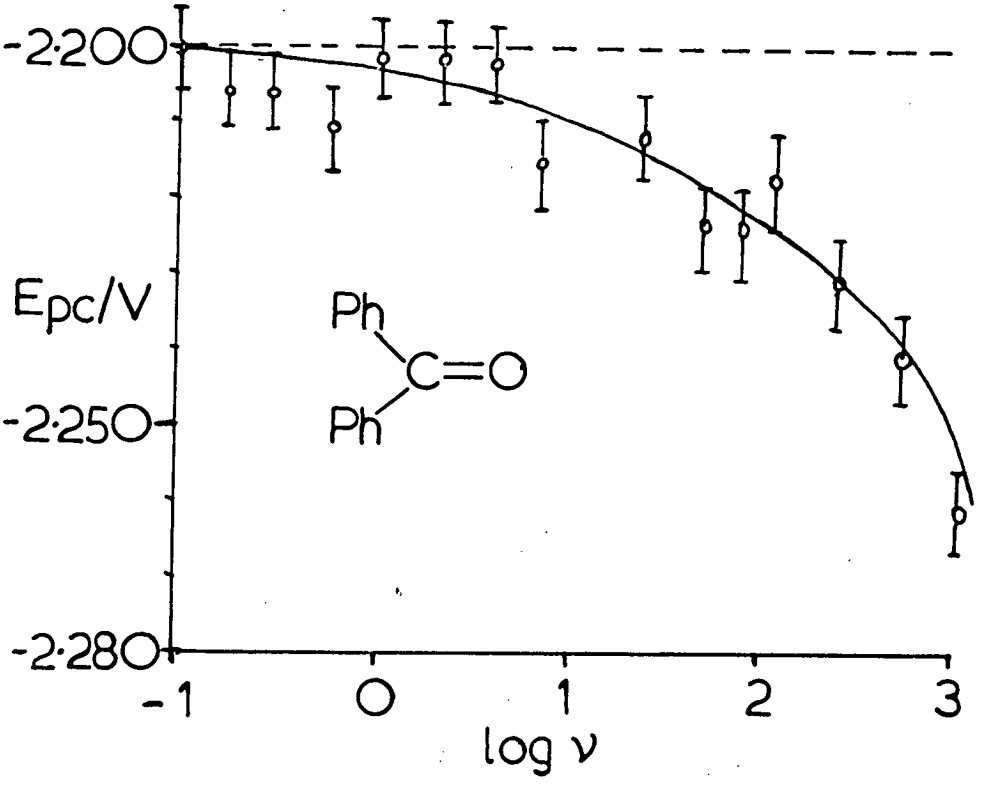


(a) c_o = 0.12mM; hmde; 0.1M $TEABF_4$, R_u = 1.51kΩ

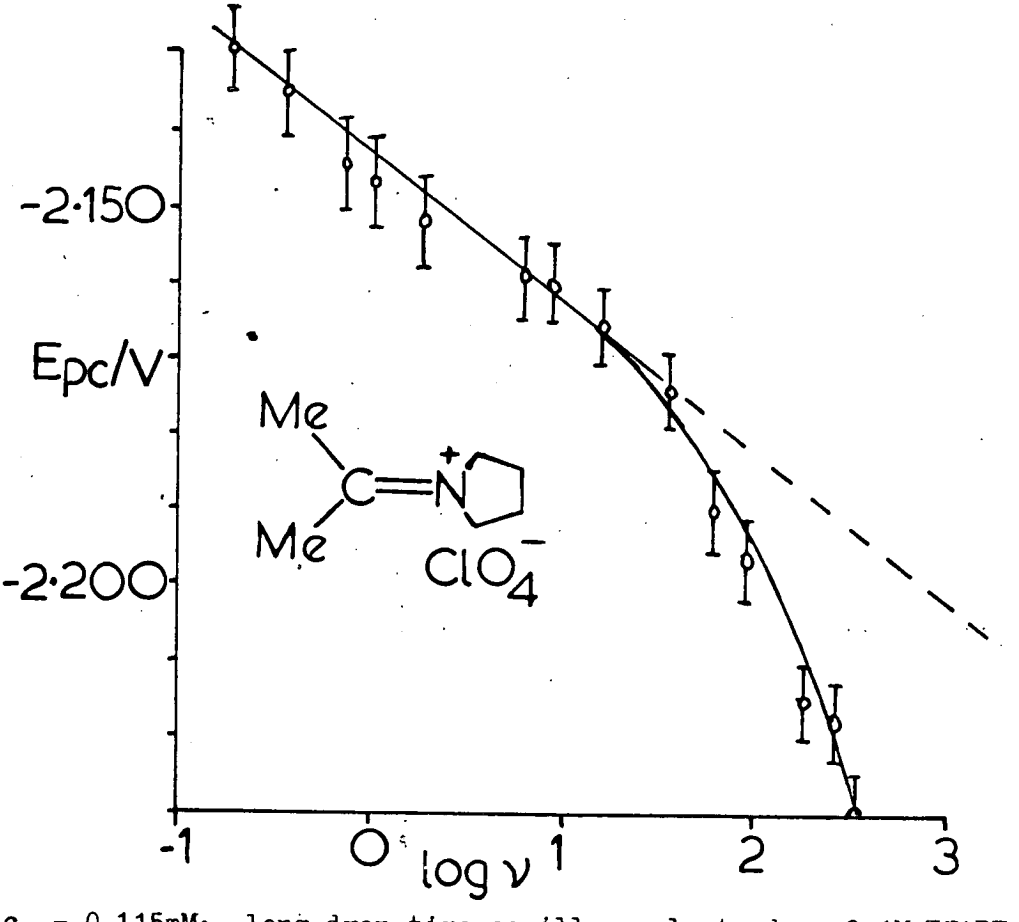


(c) c_o = 1.01mM; hmde; 0.4M $TEABF_4$, R_u = 0.369KΩ

Figure 32. Variation of peak potentials with sweep rate for the first peak of benzophenone (a-c) and N-prop-2-ylidenepyrrolidinium



(b) c_o = 0.136mM; long drop-time capillary electrode; 0.1M $TEABF_4$; R_u = 1.37kΩ



(d) c_o = 0.115mM; long drop-time capillary electrode; 0.1M $TEABF_4$; R_u = 1.67kΩ

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perchlorate (d) in acetonitrile; reference: Ag/0.1M $AgNO_3$

current (faradaic plus capacitance) approximately constant. This is due to the fact that both components are dependent upon the surface area of the electrode which could be suitably adjusted by this means. Such a capillary electrode was constructed from glass capillary tubing (thermometer) which had been softened in a flame to narrow the internal diameter of the capillary. The use of this as a dme (drop-time, 50-100s) helped to eliminate the effect of the ohmic drop when the variation of the peak potential with sweep rate or concentration was under study since the resistance affected each measurement approximately to the same extent. Thus the slope of the oblique line in such a study is not affected although its position is shifted depending upon the resistance. Of course, in a case where reversibility is reached (e.g. acetophenone at higher sweep rates), then the onset point of the horizontal portion of the line is shifted and this must be taken into account in any measurement of standard potentials.

The improvement gained by the use of such an electrode is illustrated by comparison of Figure 32b with Figure 32a where an hmde was used. A further advantage of this dropping electrode is that the surface is renewed before every measurement, making it invaluable in the study of adsorption phenomena.[15] However, it has drawbacks in that the electrode proved to be much less convenient to use than the hmde. The drop-time was sometimes erratic in non-aqueous solutions and the capillary was more prone to blockage than an ordinary capillary. Furthermore, the actual preparation of the capillary proved to be somewhat difficult.

It can be seen from Figure 32b that it was impossible to eliminate entirely the effect of the ohmic drop upon the peak potential. Therefore, in order to perform mechanistic diagnosis by the use of linear sweep voltammetry, it was necessary to make corrections to the measured peak potentials. The procedure used was as follows.

The reduction pattern of benzophenone was studied first as described above under the conditions in which it was proposed to study the compound of interest; the linear sweep voltammogram was recorded on the X-Y recorder using a sweep rate of $200mVs^{-1}$. The compound of interest was then studied in a similar manner under the same conditions: since it was impossible to reproduce the conditions exactly, there were small differences in the peak currents. Comparison of the two voltammograms recorded at $200mVs^{-1}$ allowed the differences to be corrected for, since the effect of the uncompensated resistance is purely ohmic. The range of sweep rates used were the same for all the studies so that the corrections to the peak potentials could be directly applied after adjustment for current differences. Strictly speaking, the standard used to make the corrections should be very similar in structure to that of the compound of interest so that their diffusion coefficients are similar, e.g. an immonium salt with a reversible reduction pattern should have been used for the immonium salt study. However, consideration of the size of the error that this would introduce shows that this is an unnecessary precaution. The correction procedure is illustrated in Figure 32d for the case of N-prop-2-ylidenepyrrolidinium perchlorate; the peak potentials were measured directly on the oscilloscope with an accuracy of $\pm 5mV$.

Using the above precautions, it was possible to distinguish between first order (ca. 30mV/decade) and second order (ca. 20mV/decade) kinetics. Further refinement of the system would require the incorporation of a positive feedback loop into the potentiostat to compensate further for the cell resistance[160,161] and more sophisticated data handling procedures, leading ultimately to convolution potential sweep voltammetry.[62]

If the voltammetric pattern of the compound of interest is completely irreversible, then only the kinetic order of the reaction can be determined by linear sweep voltammetry. If, on the other hand, the

voltammetric pattern should become reversible upon raising the sweep rate, then it is possible to measure the rate constant of the reaction. This is illustrated for the case of acetophenone in Figure 13 where, after the application of the procedures described above, the plot of the peak potential against log ν exhibited an oblique line and a horizontal line. From the intercept of these two lines, the rate constant could be calculated.

An alternative method for rate constant determination is asymmetric triangular sweep voltammetry.[19] This method also required that reversible behaviour of the voltammetric pattern be attainable. Since it is also necessary for the mechanism to be known in order to calculate the rate constant, the preliminary steps for use of this method are the diagnosis of the mechanism by lsv and determination of the sweep rate range where the peak potential is independent of the sweep rate.

The triangular scan method is similar to cyclic voltammetry in that the potential is first scanned in one direction followed immediately by a scan in the reverse direction. The essential difference lies in the speed of these scans. For a reduction process like that of acetophenone, the initial cathodic scan-rate is less than that required for reversibility to be achieved. The anodic scan-rate, on the other hand, must be within the range of sweep rates where the voltammetric pattern is reversible. The peak currents for these scans are measured and compared to give a ratio $(i_a)_p/(i_d)_p$ where $(i_a)_p$ is the cathodic scan peak current. This procedure is repeated for a range of sweep rates for the cathodic scan, keeping the anodic scan-rate constant. A range of values of the ratio $(i_a)_p/(i_d)_p$ are thus obtained.

If the mechanism is known from the lsv measurements, then one can immediately proceed to the calculation of the rate constant. For example, if the chemical reaction consists of a consecutive dimerization reaction

then a plot of the current ratios determined above against $\theta^{-\frac{1}{3}}$, where θ is the switching time corresponding to each measurement, gives a straight line. The slope of this line is equal to $(\frac{2\pi}{3}kC_o)^{\frac{1}{3}}$ and from this the rate constant (k) can be calculated. Procedures for other mechanisms can be found in reference 19.

Preparation of immonium salts. - The method of Leonard and Paukstelis[30] was employed for the synthesis of the immonium salts. Freshly distilled pyrrolidine (1mol) was dissolved in dry ether (500ml) and perchloric acid (70% 1:1 in ethanol) was added until the solution was just acid to congo red. A few drops of pyrrolidine were added and the solvent was then removed under vacuum. The residual solid was recrystallized from propan-2-ol/ether to give pyrrolidinium perchlorate (m.p. 240-242°C). A similar procedure with pyrrolidine and fluoroboric acid gave pyrrolidinium fluoroborate (m.p. 221-223°C).

Compounds 7-9, Table 1 were prepared according to the following procedure. Pyrrolidinium perchlorate or fluoroborate (0.2mol) and the corresponding ketone (0.4mol) were placed in a flask with sodium-dried benzene (400ml). A few drops of pyrrolidine were added and the heterogeneous mixture was refluxed with stirring for several days; water was continuously removed by means of a Dean and Stark trap. The separated solid was then collected by filtration, washed with ethanol and ether and recrystallized from either absolute ethanol or propan-2-ol. The yields are shown below:

Salt	m.p. (°C)	Yield %	ν_{max}(nujol) (cm^{-1})	calculated %C	%H	%N	found %C	%H	%N
N-cyclohexylidene-pyrrolidinium fluoroborate (7)	214-7	88	1670	50.24	7.59	5.86	50.22	7.51	5.87
N-cyclopentylidene-pyrrolidinium fluoroborate (8)	202-4	81	1670	48.04	7.17	6.22	47.97	7.15	6.19
N-(2-methylcyclohexylidene) pyrrolidinium fluoroborate (9)	147-9	52	1660	52.20	7.97	5.54	52.05	7.89	5.48
N-(2-methylcyclohexylidene) pyrrolidinium perchlorate (9)	173-4	61	1660	-	-	-	-	-	-

Salt 10, N-prop-2-ylidenepyrrolidinium perchlorate was prepared by stirring pyrrolidinium perchlorate (33.4g) with acetone (23.2g) for 48h. Anhydrous ether was then added to precipitate the salt (m.p. 227-233°C) which was collected by filtration and washed with ether. Recrystallization (twice) from propan-2-ol gave 16.81g of material, m.p. 233-5°C (lit.[30] 232-3°C).

Preparation of Enamines. - The enamines were prepared according to the method of Stork et al.[162] A solution of 2-methylcyclohexanone (33.6g, 0.3 mol), pyrrolidine (43g, 0.6 mol) and toluene-p-sulphonic acid (0.5g) in dry benzene (100ml) was heated under reflux (40h), while water was continuously removed by means of a Dean and Stark trap. The solvent was removed by rotary evaporation and the remaining liquid was distilled under reduced pressure (b.p. 140°C/2mm) to give N-(2-methylcyclohex-1-en-1-yl)pyrrolidine (33.6g, 0.19 mol). This liquid was initially colourless but rapidly turned brown on exposure to air. Examination by glc analysis (10% Carbowax 20M, 1% KOH) showed the product to contain pyrrolidine and 2-methylcyclohexanone. The attempted purification of the enamine by preparative glc (10% Carbowax 20M, 3% KOH) still gave material containing the same impurities, indicating that the enamine is unstable and decomposes on exposure to air.

The following enamines were also prepared by a similar procedure: N-cyclopent-1-en-1-ylpyrrolidine, b.p. 93-5°C/15mm, in 77% yield; N-cyclohex-1-en-1-ylpyrrolidine, b.p. 115-7°C/13mm, in 67% yield; N-(2-methylcyclohex-1-en-1-yl)morpholine, b.p. 121-3°C/15mm, in 62% yield.

Formic acid reduction of enamines. - The procedure of Madsen and Iversen[46] was followed. On adding an excess (50-100%) of formic acid (98-100%) to the enamine (0.05 - 0.1 mol), the temperature of the mixture usually rose rapidly and was accompanied by a vigorous evolution of gas. The resulting mixture was refluxed overnight and then stirred with 4N HCl (100-200ml) for several hours in order to hydrolyse any unchanged enamine. After extraction with ether (2 x 100ml), the acidic aqueous solution was made strongly alkaline by the addition of solid NaOH, and was then continuously extracted with ether for 16h. The combined ether extracts were dried over solid KOH, the solvent was removed and the residue was distilled under reduced pressure, giving the saturated amine. Final

purification of the amines (and separation of isomers in the case of the 2-methyl-substituted compounds) was achieved by preparative glc (10% Carbowax 20M, 3% KOH). The yields were somewhat uncertain due to the instability of the substrate enamine but the procedure appears to give yields of about 50% with respect to the weight of enamine used. The following amines were prepared according to this method:

N-cyclopentylpyrrolidine, b.p. 82-4°C/15mm;

N-cyclohexylpyrrolidine, b.p. 102-5°C/15mm;

N-(2-methylcyclohexyl)pyrrolidine, b.p. 108°C/10mm;

N-(2-methylcyclohexyl)morpholine, b.p. 110°C/12mm.

The 2-methyl substituted amines were a mixture of two isomers (cis and trans), the cis isomer predominating by 84:16 for the pyrrolidine amine and 85:15 for the morpholine amine. The ^{1}H nmr spectra (60M Hz) of these compounds were complex but the absorptions of the substituent methyls could be easily distinguished; N-(2-methylcyclohexyl)pyrrolidine - cis: δ0.92, J = 6.5Hz; - trans: δ0.92, J = 5.0Hz; N-(2-methylcyclohexyl)morpholine - cis: δ0.90, J = 6.4Hz; - trans: δ0.95, J = 4.9Hz.

Preparation of N-prop-2-ylpyrrolidine.[163] - Pyrrolidine (3.60g, 0.051 mol) and 2-iodopropane (8.82g, 0.052 mol) were stirred together overnight and the mixture was then distilled to give a colourless liquid, b.p. 125-8°C (3.95g, 0.038 mol). The liquid was finally purified by preparative glc. ^{1}H nmr spectra (60M Hz): δ1.12 (d, 6H, J = 6.1Hz; $(CH_3)_2CH$), 1.79 (m, 4H; $-CH_2-\underline{CH}_2-\underline{CH}_2-CH_2-$), 2.58 (m, 4H; $N-\underline{CH}_2-$), 2.35 (m, 1H; $(CH_3)_2\underline{CH}$). ^{13}C nmr spectrum ($CDCl_3$): δ 22.07 and 23.56 ($-CH_2\underline{CH}_2\underline{CH}_2CH_2-$ and $(\underline{CH}_3)_2CH$), 52.04 ($N-\underline{CH}_2-$), 55.07 ($(CH_3)_2\underline{CH}$).

The N-prop-2-ylpyrrolidine was acidified with perchloric acid (70%) and the resulting salt was recrystallized from absolute ethanol to give white crystals of the perchlorate (m.p. 190°C). Examination of the salt by ^{1}H nmr spectroscopy (60M Hz) showed slight differences in the spectrum

compared to that of the free amine:
δ1.52 (d, 6H, J = 6.2Hz; $(C\underline{H}_3)_2CH$), 2.22 (m. 4H; $-CH_2C\underline{H}_2C\underline{H}_2CH_2-$), 3.55 (m, 4H; $N-C\underline{H}_2-$). The tertiary hydrogen absorption ($CH_3C\underline{H}$) was not visible.

Attempted preparation of N-(2-methylcyclohexylidene)morpholinium perchlorate. - Attempts to prepare this immonium salt by the method of Leonard and Paukstelis[30] described above, resulted in the recovery of the starting materials. A modification of the method, using a soxhlet apparatus filled with activated Molecular Sieves Type 4A and chloroform as the solvent, also resulted in recovery of the starting materials.

N-(2-methylcyclohex-1-en-1-yl)morpholine (9.12g, 0.05 mol) was dissolved in dry ether (100ml) and dry hydrogen chloride gas was bubbled through the solution for 5 min; a white, oily precipitate separated out. The ether was removed by rotary evaporation and the oily residue was dissolved in dry acetonitrile (50ml). To this solution was added a solution of sodium perchlorate (5.95g, 0.05 mol) in dry acetonitrile (50ml). The precipitated sodium chloride was filtered off and dry ether (600ml) was added to the remaining solution. The white perchlorate which precipitated was filtered off and dried (5.37g), m.p. 165-7°C. Examination of this solid by infrared spectroscopy showed an absorption band at 1640cm^{-1}, indicating the presence of the immonium function. On attempted recrystallization from absolute ethanol, the salt decomposed to the ketone and morpholinium perchlorate.

Attempted preparation of 1,2-dipyrrolidin-1-yl-1,1,2,2-tetramethylethane. - N-prop-2-ylidenepyrrolidinium perchlorate (10.13g, 0.047 mol) was added to a stirred mixture of freshly cut pieces of sodium (1.16g, 0.051 mol) in freshly distilled tetrahydrofuran (150ml) and the mixture was refluxed for 24h. Methanol (50ml) was added to destroy any remaining sodium, followed by water (100ml). The solution was extracted with ether (3 x 100ml)

and the combined ether extracts were washed with water, dried ($MgSO_4$) and concentrated. The residual liquid (1.023g) was examined by glc (10% Carbowax 20M, 1% KOH) and was shown to consist of mainly one component of long retention time (33 min for 8 min at 85°C, then 4°C/min to 180°C). This component was collected by preparative glc (10% Carbowax, 20M, 3% KOH) for spectral analysis. ^1H nmr spectrum (60M Hz): δ1.05 (s), 1.92 (m), 2.10 (m), 5.79 (m); ^{13}C nmr spectrum: δ 24.52, 28.35, 33.57, 45.39, 50.86. These values did not correspond to the expected spectral patterns and no satisfactory structure has been proposed to account for this.

General procedure for preparative electrolyses of the immonium salts (7-10). - The composition of the solution and the electrolysis conditions were varied as indicated in Tables 2-4 and Table 6. The total volume of solution used was 65ml when a mercury pool electrode was employed and 100ml with the platinum and carbon electrodes. When no more current was observed to be flowing, the cell was disconnected and a known amount of the glc internal standard (butan-1-ol or cyclohexanol) was added to the catholyte solution. Samples (0.5μl) of the catholyte solution were then injected into the gas chromatograph which had previously been calibrated by the internal standard method for quantitative analysis. Different temperature programs were employed, depending upon the initial immonium salt and the solvent used, and these are given later for the respective salts.

The accuracy of the analyses were limited by several factors. As mentioned previously, one of the products of electrolysis, the enamine, is unstable, making an accurate determination exceedingly difficult. Furthermore, injection of a mixture of pyrrolidine and a ketone, e.g. cyclohexanone, gave not only peaks corresponding to these compounds but also a small peak corresponding to the respective enamine. Another complication is illustrated by the blank run in Table 2 where no current

was passed for the duration of a normal electrolysis, followed by injection (0.5μl) of the catholyte into the gas chromatograph. The presence of cyclohexanone in 6% yield could be explained by decomposition of the immonium salt in solution or on-column. Subsequent electrolysis and analysis showed the formation of the saturated amine, the two-electron reduction product from the immonium salt. This indicated that most of the decomposition was taking place on-column. Decomposition of the supporting electrolyte was also apparently occurring on-column providing base-line drift. This was corrected to a small extent by simultaneous injection of a solution of supporting electrolyte (0.1M) onto the reference column.

Due to the factors outlined above, each catholyte mixture was injected at least five times to ensure repeatability. Under these conditions, the best accuracy obtainable was ±5% in the case of the saturated amines and ±10% at the very best for the other compounds.

The cis- and the trans- isomers of the 2-methylcyclohexyl amines were identified by comparison of the ^{1}H nmr spectra and glc retention times with those of previously assigned samples.[46]

Electrochemical reduction of N-cyclohexylidenepyrrolidinium fluoroborate. - Table 2 shows the results of reductions using the general procedure described above. The product distributions were calculated using molar response correction factors and these factors differed slightly depending on which glc temperature program was employed. When the solvent was DMF, the temperature conditions were 16 min at 80°C, then 16°C/min to 180°C. With acetonitrile, the program was 8 min at 60°C, then 8°C/min to 180°C. The columns used were Carbowax 20M, 1% KOH and the standard was butan-1-ol.

Electrochemical reduction of N-cyclopentylidenepyrrolidinium fluoroborate. - Table 3 lists the results of reductions carried out as above.

Once again, the glc standard used was butan-1-ol and the glc columns were 10% Carbowax 20M, 1% KOH. Molar response factors were used to calculate the product distributions and the temperature programs employed were:

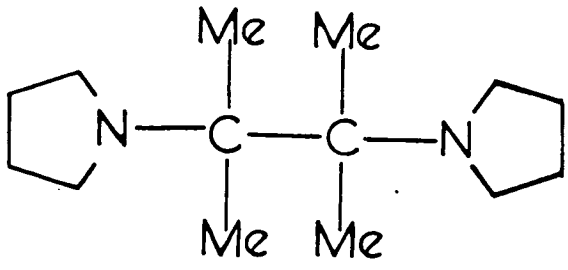
DMF, 80°C for 16 min, 8°C/min to 180°C

Acetonitrile, 60°C for 8 min, 8°C/min to 180°C

Electrochemical reduction of N-(2-methylcyclohexylidene)pyrrolidinium fluoroborate or perchlorate. - The results of reductions carried out in the same manner as the two previous cases are listed in Table 4. The glc standard was again butan-1-ol and the glc columns were 10% Carbowax 20M, 1% KOH. Molar response factors were used to calculate the product distribution as above. The sensitivities of the cis- and the trans-isomer of N-(2-methylcyclohexyl)pyrrolidine were assumed to be the same and the temperature program employed for both DMF and acetonitrile was: 60°C for 8 min, then 8°C/min to 180°C. Unfortunately, when DMF was used as the solvent, the 2-methylcyclohexanone peak was badly masked by the solvent peak, making accurate estimation difficult and at times impossible. The experiments in Table 4 are listed in chronological order.

Electrochemical reduction of N-prop-2-ylidenepyrrolidinium perchlorate. - A preliminary reduction at mercury was carried out on the same scale as that used for the three previous salts (65ml. 0.1M TBAP-CH_3CN). The uptake of electricity was 1.01 F mol^{-1}. Addition of butan-1-ol as glc standard to the catholyte and direct injection of this solution into the gas chromatograph (10% Carbowax 20M, 1% KOH; 85°C for 8 min, 4°C/min to 180°C) gave rise to two peaks apart from that corresponding to the standard. The first peak (2 min) corresponded to either pyrrolidine or N-prop-2-ylpyrrolidine, the column used being unable to resolve these two compounds. The second peak (28.5 min) may possibly have been due to the

dimeric diamine, 1,2-dipyrroli-din-1-yl-1,1,2,2-tetramethylethane:



In order to try and confirm this assignment, the experiment was repeated on a larger scale (5g salt in 300ml 0.1M TBAP-CH_3CN). The uptake of electricity was again close to 1 F mol^{-1} after the current had fallen to zero. Water (200ml) was added to the catholyte and the solution was extracted with ether (3 x 100ml). The ether extracts were washed with water (2 x 100ml), dried ($MgSO_4$) and the solvent was removed by rotary evaporation. The residual white solid was recrystallized from absolute ethanol and washed with ether to give a white, crystalline solid (4.33g), m.p. 190°C. Examination of the ^1H nmr spectrum (60M Hz) of this solid (δ1.0 (s), 1.05 (d), 1.55 (m), 3.25 (m)) appeared to indicate the presence of both the dimeric diamine and the saturated monoamine by comparison with the spectra of the monoamine and its hydroperchlorate salt described above and with the spectrum of the diamine.[164]

Unfortunately, it proved impossible to obtain the free amines from the salt forms obtained which were presumably hydroperchlorate salts. Even the presence of the strong base, $^-CH_2CN$ (prepared by addition of sodium hydride to acetonitrile), apparently did not free the amines from their salt forms. Consequently, outright identification of the dimeric diamine was not achieved and analysis for the dimer by glc was not possible.

It proved possible to separate pyrrolidine and N-prop-2-ylpyrrolidine on the gas chromatograph by the use of a glass column packed with Chromosorb 103 (180°C). Analysis for N-prop-2-ylpyrrolidine was therefore possible and the results of these analyses on several catholyte mixtures are listed in Table 6. The procedure used was the same as for the cyclic immonium salts (7-9) and the internal standard was cyclohexanol. Only traces ($<1\%$) of pyrrolidine and acetone were detected.

Preparation of 1-phenylethanol. - Acetophenone (5.02g, 0.042 mol) in absolute ethanol (100ml) was cooled to 0°C, and sodium borohydride (2.50g, 0.66 mol) was added in small amounts with vigorous stirring. When the addition was complete, the solution was stirred at room temperature for 30 min. A saturated aqueous sodium chloride solution (100ml) was added to the solution and the mixture was extracted with ether (3 x 100ml). The ether extracts were dried ($MgSO_4$) and concentrated to give the crude product (4.23g) which was distilled to give 1-phenylethanol (3.95g, 0.032 mol), b.p. 55°C/0.4mm; ^1H nmr (60M Hz) spectrum: δ 1.36 (d, 3H; CH_3), 3.20 (s, 1H; OH), 4.69 (q, 1H; CH), 7.25 (s, 5H; C_6H_5). Infrared spectroscopy (film) showed the absence of a carbonyl absorption and the presence of a OH band at 3400cm^{-1} (s). Examination by glc analysis (15% Carbowax 20M) showed the presence of one peak with a retention time different from that of acetophenone.

Preparation of 3-hydroxy-3-phenylbutanenitrile. - The method of Ivanov and Anghelova[165] was employed. Anhydrous liquid ammonia (250ml) was placed in a three-necked flask equipped with a mechanical stirrer and a dry-ice condenser. A small piece of lithium was added to the stirred liquid and, after the appearance of a blue colouration, a few crystals of ferric nitrate were added. Further small pieces of lithium were added (1.80g, 0.26 mol) and, after stirring for about 30 min, the blue colour was discharged; a grey suspension of lithium amide remained. Acetonitrile (17.14g, 0.24 mol) in dry ether (30ml) was added and the solution was stirred for a further 10 min. Acetophenone (23.97g, 0.20 mol) in dry ether (30ml) was then added and the solution was stirred for 1h. An excess of solid ammonium chloride, water (100ml) and ether (250 ml) were added while the ammonia was allowed to evaporate. The ether layer was separated, washed with water, dried ($MgSO_4$) and concentrated. The residue was distilled to give acetophenone (0.38g, 0.003 mol),

b.p. 50°C/4mm and 3-hydroxy-3-phenylbutanenitrile (14.56g, 0.09 mol), b.p. 157°C/4mm. The product solidified, m.p. 51-55°C and was recrystallized from absolute ethanol (2x), m.p. 55-58°C (lit 56-57°C). Analysis by glc (10% ApL) indicated that the solid was impure and contained acetophenone (ca. 10%); ^{1}H nmr (60M Hz) spectrum: δ 1.78 (s, 3H; $C\underline{H}_3$), 2.84 (s, 2H, $C\underline{H}_2$), 7.45 (m, $C_6\underline{H}_5$); ν_{max} (nujol): 3435 (s, OH), 2250cm^{-1} (s, CN).

Dehydration of 3-hydroxy-3-phenylbutanenitrile to form 3-methylcinnamonitrile. - 3-Hydroxy-3-phenylbutanenitrile (5.25g, 0.036 mol) was refluxed for four min with a mixture of glacial acetic acid and concentrated sulphuric acid (25:1 by volume, 23ml). The reaction mixture was cooled, diluted with cold water and extracted with ether (2 x 100ml). The combined ether extracts were washed with water (2 x 100ml), dried ($MgSO_4$) and concentrated. The residue was distilled to give 3-methylcinnamonitrile (2.13g), b.p. 103°C/6mm. Analysis by glc (10% ApL) indicated that the product contained three components, one of which (ca. 10%) was acetophenone, and the other two were the two isomers of 3-methylcinnamonitrile. The acetophenone impurity was removed by preparative glc (10% Versamid 200); ^{1}H nmr (100M Hz) spectrum: δ 2.25 (d, J = 1.5Hz, $C\underline{H}_3$ minor isomer), 2.45 (d, J = 1.0Hz, $C\underline{H}_3$ major isomer), 5.39 (q, J = 1.5Hz, C = C$\underline{H}$, minor isomer), 5.60(q, J = 1.0Hz, C = C$\underline{H}$, major isomer), 7.40 (s, 5H, $C_6\underline{H}_5$, both isomers); ν_{max}(film): 2210 (s, CN), 1609cm^{-1} (s, C = C). When this procedure was repeated on a larger scale (9.5g), mainly starting material (5.70g), b.p. 123°C/9mm, was recovered; only ca. 20% 3-methylcinnamonitrile was present (nmr and glc).

Preparation of 3-methylcinnamonitrile from acetophenone. - The method of Gokel et al.[104] was used. Acetophenone (6.03g, 0.050 mol) was quickly added, with stirring, to boiling acetonitrile (40ml) containing freshly powdered potassium hydroxide (2.84g) and the mixture was refluxed for

10 min. The solution was then poured onto cracked ice (50g) and the aqueous solution was extracted with methylene chloride (3 x 100ml) and the extracts were dried ($MgSO_4$) and concentrated. Distillation of the residue gave a liquid (4.15g), b.p. 74°C/6mm, which on examination by glc analysis and nmr spectroscopy was shown to be acetophenone. The procedure was repeated except that the reflux was extended to 5h. Work-up and distillation gave 3-methylcinnamonitrile (0.50g), b.p. 105-6°C/5mm, a large amount of intractable, tarry material remaining after distillation. The experiment was repeated but, on this occasion, was monitored by glc analysis of samples (0.5µl) of the mixture. This procedure showed that the optimum period of the reaction for the production of 3-methylcinnamonitrile was 2.5h. On a larger scale (24.70g of potassium hydroxide in 160ml acetonitrile) and with refluxing for 2.5h, the reaction gave acetophenone (3.94g), b.p. 116°C/3mm and 3-methylcinnamonitrile (6.59g), b.p. 108°C/3mm; the latter contained less than 1% impurity by glc analysis. A similar experiment (25.97g, 0.22 mol of acetophenone, 11.15g of potassium hydroxide in 160ml acetonitrile), but with refluxing for 4h gave three fractions: (i) b.p. 140°C/9mm (6.67g), 3-methylcinnamonitrile; (ii) b.p. 143-7°C/4mm (2.36g), 3-methylcinnamonitrile plus an impurity (40% by glc analysis); (iii) b.p. 170°C/4mm (0.885g); this fraction exhibited the same glc behaviour and nmr spectrum as 3-methyl-3-phenylglutaronitrile (see pg. 152 for spectral details).

Preparation of 3-phenylbutanenitrile by catalytic hydrogenation of 3-methylcinnamonitrile. - The conditions employed by Baldwin et al.[166] were used. 3-Methylcinnamonitrile (2.65g, 0.020 mol) was hydrogenated in the presence of 10% palladium or charcoal (0.20g) in a mixture of ethyl acetate (150ml) and glacial acetic acid (10ml) at one atmosphere pressure of hydrogen. After the uptake of hydrogen had ceased (1 mole-equivalent uptake), the mixture was warmed and then filtered. Ether (200ml) was

added to the filtrate and the solution was washed with saturated, aqueous sodium bicarbonate solution (2 x 100ml) and dried ($MgSO_4$). Removal of the solvent and distillation of the residue gave 3-phenylbutanenitrile (1.109g), b.p. 122°C/1.3mm; nmr spectrum (100M Hz): δ 1.40 (d, 3H, J = 7.0Hz; $C\underline{H}_3$), 2.50 (d, 2H, J = 7.0Hz; $C\underline{H}_2$), 3.11 (m, 1H, J = 7.0Hz; $C\underline{H}$), 7.25 (m, 5H, $C_6\underline{H}_5$); ν_{max}(film) 2242cm^{-1} (s, CN).

Preparation of 1-amino-2-cyano-3,4-dimethyl-3,4-diphenylcyclopent-1-ene. - To a suspension of small pieces of sodium (0.915g, 0.04 mol) in tetrahydrofuran (150ml), 3-methylcinnamonitrile (5.713g, 0.04 mol) was added and the mixture was refluxed with stirring for 12h. Methanol (50ml) was added to destroy any remaining sodium followed by water (100ml). The mixture was extracted with ether (2 x 100ml) and the extract was dried ($MgSO_4$). Removal of the solvent left an oil which was crystallized from n-hexane to give white crystals, m.p. 165-7°C; nmr spectrum (60M Hz): δ1.01 (s, $C\underline{H}_3$), 1.10 (s, 3H; $C\underline{H}_3$), 2.34 (d, 1H, J = 16Hz; $C\underline{H}H$), 3.31 (d, 1H, J = 16Hz; $CH\underline{H}$), 4.79 (s, 2H, NH_2), 7.20 (m, 10H; $2C_6\underline{H}_5$); ν_{max}(nujol) 3425cm^{-1} (m, NH_2), 2170cm^{-1} (s, CN) and 1690cm^{-1} (s, C = C).

Preparation of 3-aminocrotononitrile.[101] - Small pieces of sodium (1.0g) were placed in a 3-neck flask containing dry benzene (25ml) and the flask was flushed with nitrogen before acetonitrile (4.0g) was added. When all of the sodium had dissolved, the mixture was refluxed for a further 4h. On filtration, a white solid was obtained which was divided into two portions. In an attempt to obtain the two geometrical isomers, one portion was added to water at 30°C and the other was added to ice. The resulting aqueous mixtures were extracted with ether and the extracts were dried ($MgSO_4$) and concentrated. Examination of the residues (oily solids) by glc analysis and nmr spectroscopy indicated that both products contained both isomers although the relative amounts varied slightly; nmr spectrum (60M Hz): δ 1.90 and 2.10 (s, 3H; $C\underline{H}_3$ groups),

3.75 and 4.09 (s, 1H; C<u>H</u> = C), and 5.05 (s, 2H; N<u>H</u>$_2$).

<u>Attempted preparation of</u> 4-<u>amino</u>-2,6-<u>dimethylpyrimidine</u>.[167] - Potassium (10.59g, 0.27 mol) was cut into small pieces under toluene and was placed in a 500ml three-necked flask fitted with a reflux condenser, magnetic stirrer and dropping funnel, and which was flushed with nitrogen. The flask was immersed in a cooling bath at -30°C and absolute methanol was slowly added through the funnel until all the potassium had reacted. The excess of methanol was removed by rotary evaporation and the potassium methoxide was dried <u>in vacuo</u> over P_2O_5. The dried product (15.25g, 0.22 mol) was placed in a 50ml flask together with acetonitrile (8.94g, 0.22 mol). The flask was fitted with a sublimation unit consisting of a water-cooled cold finger which extended into the bulb of the flask and a side arm attached to a water pump. The flask was evacuated until the acetonitrile began to boil (condensation on the cold finger) and the system was then sealed. The flask was heated in an oil bath at 140°C for 5h. The mixture was allowed to cool and water (20ml) was added. The expected precipitate did not form and the solution was left for several hours; the presence of ammonia (detected by smell) indicated that some decomposition had occurred. The mixture was extracted with ether (2 x 50ml) and the extracts were dried ($MgSO_4$) and concentrated to give green, oily crystals (0.805g). Examination by nmr spectroscopy and glc analysis indicated that 3-aminocrotononitrile had been formed together with another compound. Allowing for the known absorptions of 3-aminocrotononitrile in the nmr spectrum, the nmr spectrum (60M Hz) of the second component was : δ2.31 (s, 3H; C<u>H</u>$_3$), 2.49 (s, 3H; C<u>H</u>$_3$), 4.70 (broad absorption, N<u>H</u>$_2$) and 6.11 (s, 1H; C<u>H</u> = C). This spectrum is consistent with the second component being 4-amino-2,6-dimethylpyrimidine and this assignment is further supported by m/e 123 in the mass spectrum.

Preparation of 3-methyl-3-phenylglutaronitrile. - (i) A solution of cyanomethylsodium was prepared by reacting sodium (0.54g, 0.024 mol) with dry acetonitrile (300ml) which had previously been flushed with nitrogen. Tetraethylammonium chloride (3.57g, 0.022 mol) was added and the solution was left for 30 min until all of the sodium chloride had precipitated. 3-Methylcinnamonitrile (3.12g, 0.022 mol) was added and the solution was refluxed under nitrogen for 14h. The solution was cooled, an excess of aqueous ammonium chloride solution was added and the mixture was extracted with ether (3 x 100ml). The ether extracts were dried ($MgSO_4$) and the solvent was removed to yield the crude product (5.99g). The crude product was examined by nmr spectroscopy and by analysis by glc/ms. The nmr spectrum indicated that a large amount of starting material (ca. 50%) was present; 3-methylcinnamonitrile was also identified by its glc retention time and by the mass spectrum of the corresponding peak (m/e 143, 128, 115, 103, 77). Other small peaks in the glc analysis were similarly identified: 3-aminocrotononitrile (m/e 82, 67, 54), acetophenone (m/e 120, 105, 77) and 4-amino-2-6-dimethylpyrimidine (m/e 123, 96, 83). A large peak of long retention time exhibited the following mass spectrum: m/e 184, 144, 118, 103, 91, 77, which was consistent with the component being 3-methyl-3-phenylglutaronitrile. The crude product was chromatographed on a 20" x 1½" dry column packed with 10% deactivated alumina; elution with ether gave five different fractions. Fraction (i) (0.123g) contained mainly 3-methylcinnamonitrile, fraction (ii) (0.998g) contained 3-methyl-3-phenylglutaronitrile, nmr spectrum (60M Hz): δ1.67 (s, 3H; $C\underline{H}_3$), 2.80 (s, 4H; $2C\underline{H}_2$), 7.32 (s, 5H, $C_6\underline{H}_5$), ν_{max}(film) 2245cm^{-1} (s, CN). Fraction (ii) was purified by distillation, b.p. 190°C/5mm. The other fractions contained small amounts of 3-aminocrotononitrile and 4-amino-2,6-dimethylpyrimidine.

(ii) A similar reaction was carried out using sodium hydride (0.58g,

0.024 mol) instead of sodium metal. Tetraethylammonium chloride (4.05g, 0.025 mol) and 3-methylcinnamonitrile (3.00g, 0.021 mol) were added as above and the mixture was refluxed under nitrogen for 14h. Work-up and chromatographing of the crude product as in (i) gave 3-methyl-3-phenylglutaronitrile (1.32g, 0.007 mol). Very little starting material was detected in the product mixture in this case, indicating a more efficient formation of cyanomethyl anions, although the low yield of product indicates some polymerisation had occurred under these conditions.

(iii) 3-Methylcinnamonitrile (1.007g, 7.04×10^{-3} mol) was electrolysed in a 0.1M solution of $TEABF_4$ in freshly purified acetonitrile (150ml) using a mercury pool cathode at -2.5V vs. Ag/0.1M $AgNO_3$. After about 0.5 F mol^{-1} had been passed, the current fell to zero and the electrolysis was discontinued. An excess of aqueous ammonium chloride solution was added to the catholyte and the mixture was extracted with ether (3 x 100ml). The ether extracts were dried ($MgSO_4$) and concentrated to give a brown, viscous oil which was extracted with boiling n-hexane. The extract was cooled to -78°C and the white crystals which appeared were filtered off, but they melted on warming to room temperature. Examination by nmr spectroscopy and glc analysis indicated that this product was 3-methyl-3-phenylglutaronitrile (0.488g). The mother liquor was evaporated and examination of the residue (0.105g) by nmr spectroscopy and glc analysis showed that it contained both 3-methyl-3-phenylglutaronitrile and 3-phenylbutanenitrile.

Preparation of 1,2-dihydroxy-1,2-diphenylbutane (acetophenone pinacol). - Chemical preparation[74]

(i) Lithium (0.683g, 0.099 mol) was placed in a flask with dry ether (50ml) and a magnetic stirrer bar, and phenylbromide (15.16g, 0.103 mol) was slowly added followed by diacetyl (4.263g, 0.050 mol). The solution

was refluxed for 4h, after which time an excess of an aqueous solution of ammonium chloride was added and the mixture was extracted with ether (2 x 100ml). The ether extracts were dried ($MgSO_4$) and concentrated to give an oily product (2.315g). The crude product was crystallized from n-hexane and recrystallized 5 times from n-hexane to give pure dl-1,2-dihydroxy-1,2-diphenylbutane, m.p. 122-3°C; nmr spectrum (60M Hz): δ1.52 (s, 6H; $2CH_3$), 2.54 (s, 2H, 2OH), 7.17 (s, 10H, $2C_6H_5$).

(ii) A similar procedure using lithium (0.349g, 0.050 mol), methyl iodide (3.525g, 0.050 mol) and benzil (5.141g, 0.025 mol) gave light yellow crystals (1.024g) which on examination by nmr spectroscopy and hplc analysis (7μm Spherisorb Alumina column, 20% ethyl acetate in n-hexane) were shown to consist mainly of benzil. However, the nmr spectrum showed an absorption at 1.58 which was thought to be due to the methyl protons of the meso-pinacol. A minor peak in the liquid chromatogram corresponded to one of the isomers of the pinacol synthesised by the electrochemical method described below; this was not the dl-pinacol prepared in (i).

Electrochemical preparation

(a) A 40% aqueous solution of tetrabutylammonium hydroxide (19.44g) was diluted to 300ml with dry ethanol to give a 0.1M solution. This solution was placed in an H-type electrochemical cell equipped with a mercury pool cathode, platinum foil anode and an SCE reference electrode. Acetophenone (5.77g, 0.048 mol) was added to the cathodic compartment and, after deoxygenation of the solution with nitrogen, electrolysis was carried out at -2.0V vs. SCE. After the passage of nearly 1 F mol^{-1}, the electrolysis was discontinued. The catholyte solution was added to water (150ml) and the mixture was extracted with ether (3 x 100ml). The ether extracts were dried ($MgSO_4$) and the solvent was removed to give a brown viscous oil. Acetophenone pinacol crystallized from this oil upon

addition of n-hexane, giving off-white crystals (0.59g), m.p. 115-8°C; nmr spectrum (60M Hz): δ 1.49 (s, $2CH_3$ of dl-isomer), 1.57 (s, $2CH_3$ of meso-isomer), 2.59 (s, 2OH) and 7.17 (s, $2C_6H_5$). The ratio of dl- to meso-isomers was, as measured by the peak height method,[168] 2.0.

(b) Acetophenone (3.018g, 2.51×10^{-2} mol) was reduced at a mercury cathode at -2.50V vs. Ag/0.1M $AgNO_3$ in a solution of 0.1M $TEABF_4$ in acetonitrile (150ml) containing 1% water. When approximately 1 F mol^{-1} had been passed, the electrolysis was discontinued, aqueous ammonium chloride was added to the catholyte and the mixture was extracted with ether (3 x 100ml). After drying the ether extracts ($MgSO_4$), the solvent was removed, leaving a brown, oily liquid. Examination of this crude product by nmr spectroscopy showed that it contained mostly pinacol (dl/-meso 7.9 by the peak-height method). The crude product was crystallized from n-hexane to give white crystals which were recrystallized from n-hexane (0.572g), m.p. 119-121°C. Examination by nmr spectroscopy (100M Hz) showed that this material contained very little of the meso-isomer.

General procedure for the preparative electrolyses of acetophenone and 3-methylcinnamonitrile. - The composition of the solution and the conditions of electrolysis are given in Tables 8-11. In general, 50ml of solvent was used with a catholyte volume of 38ml and the depolariser concentration was approximately 0.1M. The electrolyses were carried out under a nitrogen atmosphere. It often proved difficult to determine when the electrolysis was complete due to a residual current which was observed in most cases and, consequently, coulometric measurements were difficult to carry out. The electrolyses were discontinued when the current had dropped to a constant value, which could sometimes be as high as 40mA, and an excess of aqueous ammonium chloride solution was added to the catholyte mixture to protonate any remaining anions. The internal standards for glc analysis (benzonitrile or benzophenone) and hplc

analysis (m-nitroacetanilide) were added at this point and the mixture was extracted with either ether or methylene chloride (2 x 100ml). The organic extracts were combined, washed with water (2 x 100ml), dried ($MgSO_4$) and the solvent was removed by rotary evaporation keeping the temperature of the water bath below 50°C. The concentrated mixtures were then analysed by glc and hplc, the product distributions being calculated by the use of molar response factors which had previously been measured from mixtures of pure samples.

The work-up procedure was tested by subjecting a mixture of pure product samples to the work-up process and then comparing the ratios of the product peak-areas to the standard peak-area before and after work-up. It was found that the procedure was satisfactory for the glc analysis when either ether or methylene chloride were used for the extraction of the catholyte mixture, the differences in the ratios being less than the experimental error. However, it was found in the hplc analysis that, if ether was used for the extraction process, the ratio of products to standard increased, indicating the preferential loss of standard. This situation presumably arose due to the poor solubility of m-nitroacetanilide in ether. Fortunately, the situation was corrected by the use of methylene chloride for extraction. The hplc analyses listed in Table 9 were affected by this error.

The accuracy of the analyses varied depending upon the compounds being analysed. All of the compounds analysed by glc, with the exception of 3-methyl-3-phenylglutaronitrile, had reasonable retention times ($\leqslant$15 min) and, consequently, could be estimated with reasonable accuracy ($\pm$5%). However, 3-methyl-3-phenylglutaronitrile had a long retention time (ca. 30 min, depending on the temperature program employed) and, consequently, exhibited a broad peak. The area of such a broad peak was difficult to estimate accurately since it was much more subject to

base-line drift variations than the more rapidly eluted peaks, especially if the area was small. For such conditions the accuracy of estimation of 3-methyl-3-phenylglutaronitrile was ca. ±10%. Of the two compounds analysed by hplc, the acetophenone pinacol proved to be extremely difficult to estimate due to its low ultraviolet absorption. In fact, the molar response ratio of this compound was of the order of 0.01, thus magnifying any error in the peak-area estimation by a factor of 100. Furthermore, any traces of UV-active compounds eluted at the same time as the pinacol would cause a very large error. Under such conditions the accuracy of estimation of the pinacol was ±20%. Since the hydrodimer of 3-methylcinnamonitrile exhibited greater sensitivity, the molar response ratio being ca. 0.8, it could be much more accurately estimated (±5%).

During the electrolyses, it was noted that the actual potential of the working electrodes (measured by means of a voltameter connected across the working and reference terminals) was in many cases, less than that which had been set on the potentiostat. This was due to the resistance of the cell solution. In most cases, the potentiostat was capable of adequately controlling the potential for most of the duration of the electrolysis. However, very often towards the end of the electrolysis, when the cell current was small, the potentiostat was unable to maintain the set potential. However, it was also noted that the potentiostat was sometimes unable to maintain its set potential in cases of high current at the beginning of an electrolysis.

The current was recorded during the course of several electrolyses and it was observed that the current increased from the initial value in the majority of cases before decaying exponentially. However, it was also observed that the temperature of the cell solution increased markedly, initially, and the increases in current were probably due to this. It was notable that when the cell was cooled to -28°C no such increase in

current was observed. Similarly, no current increase was observed when an electrolysis was carried out at reflux temperature.

The Tables listing the product distributions are arranged such that all the reactions in one Table were carried out with the same batch of acetonitrile. The experiments are listed in chronological order so that the experiments at the top of each Table were carried out with freshly purified solvent whereas those at the foot of the Tables were carried out with solvent which could have been stored for up to two months. The acetonitrile used in the experiments listed in Tables 8 and 9 was not treated with sodium hydride during purification. This resulted in some residual acrylonitrile remaining in the solvent which was removed electrolytically be pre-electrolysing the blank solution at -2.95V before the addition of the depolariser. The solvent used for the experiments listed in Tables 10 and 11 was treated with sodium hydride and, consequently, no pre-electrolysis was carried out for those experiments.

Since such a pre-electrolysis was probably producing cyanomethyl anions, a check was carried out on this procedure by sampling the solution after the addition of acetophenone and before the main electrolysis was begun for the case where such a procedure was in use and also for the case where no pre-electrolysis was carried out. The solvent in both cases had not been treated with sodium hydride. Samples (5ml) were withdrawn from the solution by means of a syringe and these were then worked-up in the normal manner described for the electrolyses above. Analysis by glc (10% ApL) of the pre-electrolysed solution gave the following product distribution: acetophenone 1.9%, 3-phenylbutanenitrile 0.3%, 3-methylcinnamonitrile 0.25%, 3-hydroxy-3-phenylbutanenitrile 4.3%. Analysis of the sample from the control experiment where no pre-electrolysis was carried out showed the presence of only one compound, acetophenone (28%). No nitrile compounds were observed.

Sampling of the catholyte solution during the course of the electrolysis of acetophenone in dry acetonitrile. - A solution of 0.1M $TEABF_4$ in dry acetonitrile (200ml) which had not been treated with sodium hydride during its purification, was placed in the flange-flask type cell (Figure 30) together with a mercury pool cathode. The solution was de-aerated by flushing with nitrogen and was pre-electrolysed for 2h at -2.95V. After this time, the background current was 0.8mA and 20 coulombs had been passed. Acetophenone (1.636g, 1.362×10^{-2} mol) was added to the catholyte 15 min before the electrolysis was commenced. A sample (5ml) of the catholyte solution was withdrawn 10 min later by means of a syringe as above. The sample was worked up and analysed by glc; the analysis confirmed the result found in the pretreatment check described above. The main electrolysis was carried out at -2.95V and samples (5ml) of the catholyte solution were withdrawn at intervals. Work-up of these samples and analysis by glc and hplc gave the product distributions which are listed in Table 12 together with the current- and coulomb-time behaviour. The product concentrations were plotted against the number of coulombs passed and the result is shown in Figure 14.

Isolation of products from an electrolysis of acetophenone in dry acetonitrile. - Acetophenone (1.53g, 1.28×10^{-2} mol) was reduced at a mercury pool electrode in a solution of 0.1M $TEABF_4$ in dry acetonitrile (150ml). The working-electrode potential was -2.95V vs. Ag/0.1M $AgNO_3$ and the initial current was 73mA, which rose to a maximum of 140mA before decaying to the background current. After 6h the number of coulombs passed was 1792 ($n = 1.44$ F mol^{-1}) and the electrolysis was terminated. The catholyte was worked-up in the normal way except that the chromatographic internal standards were not added. The crude product was chromatographed on a 20" x 1" 10% deactivated alumina dry column with ether as the eluent. The fractions which separated were extracted with ether

from the alumina, the solvent was removed and the residues were examined by glc analysis and nmr spectroscopy: fraction (i) (0.488g) was shown to be almost entirely 3-phenylbutanenitrile; fraction (ii) (0.101g) was 3-methyl-3-phenylglutaronitrile; fraction (iii) (0.039g) contained acetophenone pinacol; fraction (iv) (0.050g) contained acetophenone pinacol and 3-hydroxy-3-phenylbutanenitrile.

Co-electrolysis of acetophenone with azobenzene. -

(i) Azobenzene (0.61g, 3.35×10^{-3} mol) and acetophenone (0.40g, 3.31×10^{-3} mol) were added to the catholyte compartment of a cell which had been set up in the normal way and which contained 0.1M $TEABF_4$-CH_3CN (50 ml). Electrolysis was carried out at a mercury pool electrode at -2.2V vs. Ag/0.1M $AgNO_3$ for 16h, after which the solution was worked up in the manner described previously for glc and hplc analysis. Analysis by glc showed the presence of 3-phenylbutanenitrile (0.4%), 3-methylcinnamonitrile (2.3%), 3-hydroxy-3-phenylbutanenitrile (2.1%) and 3-methyl-3-phenylglutaronitrile (2.5%). No trace of acetophenone was found and, unfortunately, the products of the reduction of the azobenzene masked the acetophenone-pinacol peak in the liquid chromatogram.

(ii) The experiment was repeated using similar concentrations to (i) and a working potential of -2.1V vs. Ag/0.1M $AgNO_3$. The products found by glc analysis were: 3-phenylbutanenitrile (0.4%), 3-methylcinnamonitrile (2.8%), 3-hydroxy-3-phenylbutanenitrile (0.5%) and 3-methyl-3-phenylglutaronitrile (2.5%). No trace of acetophenone was found.

(iii) The experiment was repeated once more using a working potential of -2.0V vs. Ag/0.1M $AgNO_3$. The products found by glc analysis were acetophenone (20%) and 3-methylcinnamonitrile (39%).

(iv) Azobenzene (0.59g, 3.24×10^{-3} mol) was reduced at -2.5V vs. Ag/-0.1M $AgNO_3$ at a mercury pool in 0.1M $TEABF_4$-CH_3CH (50ml). When the

current had fallen to zero, the cell was disconnected and acetophenone (0.40g, 3,37 x 10^{-3} mol) was added to the catholyte. The solution was stirred for 16h, after which it was worked up as described above for glc analysis. The products found were acetophenone (60%), 3-methylcinnamonitrile (3%) and 3-hydroxy-3-phenylbutanenitrile (2%).

Co-electrolysis of acetophenone pinacol with azobenzene. - Although acetophenone pinacol is not electro-active itself in acetonitrile, it is possible that in very basic conditions it might decompose to the constituent radical-anions in very basic media, which may either recombine or disproportionate to give pinacol or alcohol. In order to check this, azobenzene (0.531g, 2.91 x 10^{-3} mol) and acetophenone pinacol (0.311g, 1.34 x 10^{-3} mol) were electrolysed together at -2.95V vs. Ag/0.1M $AgNO_3$. Analysis of the product by glc and hplc showed only the presence of pinacol and no 1-phenylethanol or nitrile products were formed. Examination of the product by nmr spectroscopy showed that the dl/meso ratio of the pinacol remained unchanged.

Preparation of trans-pent-3-en-2-ol.[148] - Dry, freshly distilled crotonaldehyde (71.1g, 1.012 mol) in anhydrous ether (150ml) was added dropwise to an ice-cold, vigorously stirred solution of methylmagnesium chloride in anhydrous ether (850ml), prepared from magnesium (30.99g) and methyl chloride. The reaction mixture was allowed to stand at room temperature for 1h and was then cooled to 0°C and was decomposed by the dropwise addition of saturated, aqueous ammonium chloride solution (218 ml), forming a dense, off-white precipitate. After the mixture had stood at room temperature for 1h, the ether solution was decanted off and the precipitate was washed by decantation with ether (4 x 100ml). The combined ether solutions were dried ($MgSO_4$) and the solvent was removed by distillation.

Distillation of the residue through a 30cm Vigreux column gave three fractions: fraction (i) (3.94g), b.p. 100-115°C contained the expected trans-pent-3-en-2-ol but was not completely pure; fraction (ii) (53.56g), b.p. 120-1°C consisted of trans-pent-3-en-2-ol which contained less than 0.5% impurity by glc analysis (15% PEGA, 70°C). The spectral data confirmed the structure of the product: ν_{max}(film) 3360 (s), 1680cm^{-1} (w), identical with the literature spectrum;[169] nmr spectrum (100M Hz): δ 1.20 (d, 3H, J = 6.5Hz; $C\underline{H}_3$ α to CHOH), 1.64 (d of d, 3H, J = 1.0 and 5.0Hz, $C\underline{H}_3C$ = C), 2.70 (s, 1H, which disappeared on shaking with D_2O,OH), 4.20 (m, 1H; H(2)), 5.56 (m, 2H; $H_{(3)}$ and $H_{(4)}$).

Attempted preparation of trans-1-(2-methylcyclopropyl)ethanol. - The Simmons-Smith procedure as modified by Perraud and Arnaud[147] was employed using trans-pent-3-en-2-ol.

A mixture of trans-pent-3-en-2-ol (2.08g, 0.024 mol), anhydrous ether (20ml) and Zn/Cu couple[170] (3.20g, 0.05 mol) under nitrogen was warmed to reflux with vigorous stirring and methylene iodide (13.18g, 0.049 mol) was added slowly. The reaction mixture was refluxed for 4h

and then hydrolysed with saturated, aqueous ammonium chloride solution. The solid residue was broken up, filtered off and then washed with ether (4 x 10ml). The combined filtrates were dried ($MgSO_4$) and the solvent was removed by distillation. Distillation of the residue gave the product (1.514g), b.p. 137-8°C, which was shown by glc analysis (15% PEGA, 70°C) to contain small amounts of unchanged reactants. Examination by nmr spectroscopy showed the presence of methylene iodide and small amounts of unchanged pentenol. The spectral properties of the main product agreed with those quoted for trans-1-(2-methylcyclopropyl)ethanol in the literature;[171] nmr spectrum (100M Hz): δ 3.09 (m, 1H; C<u>H</u>OH), 2.19 (s, 1H, which disappeared on shaking with D_2O, O<u>H</u>), 1.21 and 1.00 (m, 6H, d of d at 1.21, J = 6 and 2Hz, at 1.00 d of d, J = 7 and 1Hz, 2C<u>H</u>$_3$), 0.52 and 0.22 (2m, 4H, cyclopropyl H).

The preparation was repeated on a larger scale using Zn/Cu couple (31.66g), trans-pent-3-en-2-ol (20.98g, 0.247 mol) and methylene iodide (126.63g, 0.472 mol) which were treated as described above. Distillation of the residue left after work-up gave three fractions: fraction (i) (2.52g), b.p. 100-115°C contained CH_2I_2 and pentenol; fraction (ii) (10.39g) b.p. 115-123°C contained starting material and some of the desired cyclopropyl compound (30% by glc analysis); fraction (iii) (2.35g), b.p. 125-140°C was similar to fraction (ii).

Chromic acid oxidation of trans-1-(2-methylcyclopropyl)ethanol. - An ice-cold solution of fairly pure trans-1-(2-methylcyclopropyl)ethanol (0.499g, 0.005 mol), prepared as described above, in ether (10ml) was treated dropwise with 6N chromic acid (2ml). After stirring for 2h, examination by glc analysis (15% PEGA, 70°C) indicated the presence of some unchanged carbinol. Addition of a further 2ml of 6N chromic acid and stirring for a further 2h completed the oxidation, as shown by glc analysis. The aqueous layer was separated off and extracted with ether

(2 x 25ml). The combined ether extracts were washed with water (20ml), saturated, aqueous sodium bicarbonate solution (20ml) and water (20ml), and finally dried ($MgSO_4$). Removal of the solvent gave the crude product (0.242g) which was shown by infrared spectroscopy to contain the desired ketone.

The oxidation was repeated with the carbinol (0.302g, 0.003 mol) and 6N chromic acid (4ml) to give the crude product (0.112g). The two crude products were combined and distilled to give a colourless liquid (0.153g), b.p. 114-6°C which contained 5% of impurities (by glc analysis). This colourless liquid had spectral values almost identical with those published for trans-1-acetyl-2-methylcyclopropane [146]: ν_{max}(film) 1700 cm^{-1} (s); nmr spectrum (100M Hz): δ 0.70 (m, 1H; $H_{(3)}$ trans to acetyl), 1.09 (d, 3H; J = 5Hz; CH_3 at $C_{(2)}$), 1.26 (m, 2H; $H_{(2)}$ and $H_{(3)}$, cis to acetyl), 1.65 (m, 1H; $H_{(1)}$) and 2.19 (s, 3H; acetyl).

Preparation of trans-pent-3-en-2-one. - (i) Wittig reaction.[149] A solution of triphenylphosphine (112.5g, 0.475 mol) and freshly distilled chloroacetone (37.26g, 0.403 mol) in chloroform (300ml) was refluxed for 45 min. The solution was filtered into anhydrous ether (1l) and the precipitated acetonyltriphenylphosphonium chloride was filtered off and dried in vacuo. The yield was 94.8g, m.p. 231-236°C (lit[172] m.p. 234-237°C).

Acetonyltriphenylphosphonium chloride (94.8g) was shaken with an excess of 10% aqueous sodium carbonate solution for 8h and the acetylmethylenetriphenylphosphorane formed was filtered off and dried. The yield was 72.0g, m.p. 193-5°C (lit.[172] m.p. 199-202°C).

Acetylmethylenetriphenylphosphorane (72.0g) in methylene chloride (200ml) was treated with freshly distilled acetaldehyde (20.0g) in methylene chloride (300ml). After refluxing for 6h and then standing at room temperature for 6h, the solvent was distilled off through a 30cm

Vigreux column and the residue was diluted with pentane (200ml). The precipitated triphenylphosphine oxide was filtered off and washed until colourless with pentane. The organic filtrates were combined and the solvent was distilled off through the vigreux column. Distillation of the residue yielded trans-pent-3-en-2-one (3.76g), b.p. 117-120°C (lit[173] b.p. 120°C), which contained 5% of combined impurities (by glc analysis, 15% PEGA, 70°C).

(ii) Chromic acid oxidation of trans-pent-3-en-2-ol. trans-Pent-3-en-2-ol (0.454g, 0.005 mol) was stirred in ether (10ml) with 6N chromic acid (4ml) for 4h. The aqueous layer was separated, extracted with ether (2 x 25ml) and the combined ether extracts were washed with water (20ml), saturated, aqueous sodium bicarbonate solution (20ml) and water (20ml). The extracts were dried ($MgSO_4$) and the solvent was removed by distillation to yield a crude product (0.122g) which had a long retention time upon examination by glc analysis (15% PEGA, 70°C), different from that of the starting carbinol. Examination of this product by nmr and infrared spectroscopy showed it to have the same spectral data as trans-pent-3-en-2-one.

(iii) Oxidation of trans-pent-3-en-2-ol with pyridinium chlorochromate.[150] - Chromium trioxide (100g, 1 mol) was rapidly added to 6N hydrochloric acid (184ml, 1.1 mol) with vigorous stirring. After 5 min the solution was cooled to 0°C and pyridine (79.1g, 1 mol) was carefully added over 10 min. Re-cooling to 0°C gave a yellow-orange solid which was collected on a sintered-glass funnel and dried in vacuo (149.9g).

Pyridinium chlorochromate (97.79g, 0.46 mol) was dissolved in methylene chloride (500ml) with stirring, trans-pent-3-en-2-ol (21.62g, 0.26 mol) was rapidly added and the solution was stirred at room temperature for 90 min. The solvent was then decanted off and the residual black solid was washed with ether (200ml). The washings were combined

with the decanted solvent, filtered and the solvent was removed by distillation. Distillation of the residue through a 30cm Vigreux column gave trans-pent-3-en-2-one (11.45g, 0.138 mole; 54% yield) which contained less than 0.5% impurity by glc analysis (15% PEGA, 70°C): nmr spectrum (100M Hz): δ 1.90 (d of d, 3H, J = 1.5 and 6.5Hz; $CH_3C=C$), 2.19 (s, 3H; acetyl), 6.10 (m, 1H, consisting of a doublet, J = 15.5Hz, each peak of which was split into a quarter, J = 1.5Hz; $H_{(3)}$) and 6.82 (m, 1H, consisting of a doublet, J = 15.5Hz, each peak of which was split into a quartet, J = 6.5Hz, $H_{(4)}$).

Preparation of trans-1-acetyl-2-methylcyclopropane.[146] - Sodium hydride (6.233g, 0.25 mol) and powdered trimethylsulphoxonium iodide[174] (55g) were stirred together under nitrogen while dimethylsulphoxide (362.5ml) was slowly added, ensuring that the temperature of the solution remained below 0°C. trans-Pent-3-en-2-one (21.29g, 0.256 mol) was added dropwise over 10 min and stirring was continued for 3h at room temperature. The mixture was left to stand for 12h after which time it was poured onto crushed ice (500g). Pentane (200ml) was added and, after all the ice had melted, the aqueous layer was separated and extracted with pentane (2 x 100ml). The combined organic extracts were washed with water (2 x 100ml), saturated, aqueous sodium chloride solution (2 x 100ml) and dried ($MgSO_4$). The solvent was removed by distillation through a 30cm Vigreux column and the residue was distilled. The first fraction (3.178g), b.p. 87-94°C/20mm was shown to be trans-1-acetyl-2-methylcyclopropane by nmr spectroscopy and glc analysis (10% ApL and 15% Carbowax 20M) but it contained about 5% of an impurity. The second fraction, (5.575g), b.p. 94°C/20mm, consisted of trans-1-acetyl-2-methylcyclopropane which contained less that 1% impurity by glc analysis.

Preparation of 1-acetyl-2,2-dimethylcyclopropane.[146] - To sodium hydride

(5.392g, 0.224 mol), powdered trimethylsulphoxonium iodide (45.3g) and dimethylsulphoxide (314ml) which were mixed together as described above, was added freshly distilled mesityl oxide (20.95g, 0.214 mol). The mixture was treated as described above and distillation of the residue through a 10cm Vigreux column gave 1-acetyl-2,2-dimethylcyclopropane (9.547g), b.p. 120°C/80mm, which contained less that 1% impurity by glc analysis (10% ApL and 15% Carbowax 20M). The spectral data were in agreement with literature values[146]; ν_{max}(film) 1690cm^{-1} (s); nmr spectrum (60M Hz, $CDCl_3$): δ 0.78 (m, 1H; $H_{(3)}$ trans to acetyl), 1.07 (s, 3H; methyl cis to acetyl) 1.18 (s, 3H; methyl trans to acetyl) 1.10 (m, 1H; $H_{(3)}$ cis to acetyl), 1.82 (m, 1H; $H_{(1)}$) and 2.20 (s, 3H; acetyl). A smaller fraction (2.800g), b.p. 100-110°C/80mm was also collected and shown to be mainly 1-acetyl-2,2-dimethylcyclopropane but contained about 10% of an impurity by glc analysis (10% ApL and 15% Carbowax).

General procedure for the Knoevenagel condensation reaction.[145] - Malononitrile (0.05 mol), ketone (0.05 mol), ammonium acetate (0.005 mol) and glacial acetic acid (0.001 mol) were heated(reflux)in dry benzene (50ml). The water which separated from the azeotrope was removed by a modified Dean and Stark trap. The mixture was refluxed until no more water separated (usually 4 to 5h). Ether (50ml) was added to the cooled mixture and this solution was then washed with saturated, aqueous sodium bicarbonate solution (100ml), water (100ml), saturated, aqueous sodium chloride solution (100ml) and dried ($MgSO_4$). The solvent was removed by rotary evaporation and the residue was distilled or recrystallized to give a product of the general structure $Me(R)C{:}C(CN)_2$. The group (R) was varied by the choice of ketone and the yields of these products are listed below together with their characteristic infrared absorption bands and their boiling points. In most cases the nmr spectrum was essentially the same as that for the initial ketone save for small changes

in the chemical shifts. All the compounds were colourless when purified and where liquid, attained a dark colour upon standing.

Compound	R	b.p.	Yield / %	ν_{max}(film) / cm^{-1}
a	Propyl	96-7°C/4mm	84	2210(s), 1606(s)
b	Butyl	140-1°C/20mm	86	2250(s), 1610(s)
c	2-Methyl-propyl	119°C/9mm	46	2210(s), 1605(s)
d	3-Methyl-butyl	159°C/30mm	71	2212(s), 1598(s)
e	2,2-Dimethyl-propyl	100°C/3.5mm	41	2212(s), 1589(s)
f	cyclo-propyl	m.p. 64-5°C*	57	2220(s), 1595(s) (CCl_4)
g	2,2-dimethyl cyclopropyl	100-1°C/2.5mm	38	2210(s), 1570(s)
h	trans-2-methyl-cyclopropyl	120°C/5.5mm	14	2211(s), 1569(s)

*, recrystallized from an ethanol-water mixture whose temperature was kept below 60°C

Compound g, 2-cyano-3-(2,2-dimethylcyclopropyl)but-2-enenitrile, showed the following absorptions in the nmr spectrum (100M Hz): δ 1.10 (s, 3H; $C\underline{H}_3$ cis to vinyl group), 1.15 (m, 1H; $H_{(3)}$, cyclopropyl H trans to vinyl group), 1.30 (s, 3H, $C\underline{H}_3$ trans to vinyl group), 1.90 (m, 2H; $H_{(3)}$ cis to vinyl group and $H_{(1)}$) and 2.16 (s, 3H; $C\underline{H}_3C$). The mass spectrum exhibited a highest mass peak at m/e 160. A smaller mass peak (60%) was observed at m/e 159 and other peaks were observed at m/e 145 and 118. An accurate mass analysis of m/e 160 showed a deviation of less than 2ppm from the calculated mass. Elemental analysis of this compound showed the percentage composition to be (i) 65.98% C, 6.63% H, 18.01% N; (ii) 71.78% C, 7.04% H, 20.75% N (calculated, 75.0% C, 7.54% H, 17.5% N).

Compound h, 2-cyano-3-(trans-2-methylcyclopropyl)-but-2-enenitrile, showed the following absorptions in its nmr spectrum (100 M Hz): δ 1.14 (m, 3H; cyclopropyl hydrogens), 1.22 (d, 3H, J = 5.0Hz; $C\underline{H}_3$ at $C_{(2)}$), 1.89 (s, 3H; $C\underline{H}_3C$) and 2.05 (m, 1H, $H_{(1)}$). The mass spectrum exhibited a highest mass peak at m/e 146, a slightly larger peak at m/e 145 and further peaks at m/e 131 and 104. An accurate mass analysis of m/e 160 showed a deviation of less that 6ppm from the calculated mass. Elemental analysis of this compound showed the percentage composition to be (i) 72.20% C, 7.09% H, 18.30% N; (ii) 74.14% C, 7.21% H, 18.85% N (calculated, 73.9% C, 6.89% H, 19.19% N).

Catalytic hydrogenation of 2-Cyano-3-methylhex-2-enenitrile. - The conditions employed by Baldwin et al.[166] were employed. 2-cyano-3-methylhex-2-enenitrile (0.676g, 0.005 mol) was hydrogenated in the presence of 10% palladium on charcoal (0.0585g) in a mixture of ethyl acetate (15ml) and glacial acetic acid (1ml) at 1 atmosphere pressure of hydrogen. After the uptake of hydrogen had ceased (1 mole-equivalent), the mixture was heated, filtered and poured into ether (150ml). The mixture was

washed with saturated, aqueous sodium bicarbonate solution (100ml), water (100ml) and dried ($MgSO_4$). Removal of the solvent and distillation of the residue gave a colourless liquid (0.471g), b.p. 80°C/2mm, which exhibited the following spectral data; nmr spectrum (60M Hz): δ 0.70 to 1.6 (m, 7H; $C_3\underline{H}_7$), 1.19 (d, 3H, J = 7Hz; $C\underline{H}_3$), 2.15 (m, 1H; tertiary H) and 3.79 (d, 1H, J = 4.5Hz; $C\underline{H}(CN)_2$); ν_{max}(film) 2250cm^{-1} (s). No sign of an olefinic absorption band was observed. The highest mass peak in the mass spectrum was m/e 134. Examination by glc analysis (10% ApL and 15% Carbowax 20M) showed only one peak which had a different retention time from that of the starting compound (a). The properties of the product were consistent with the structure being 2-cyano-3-methylhexanenitrile.

Reduction of 2-cyano-3-methylhex-2-enenitrile (a) with tetraethylammonium formate (TEAF). - The method of Nanjo et al.[175] was employed. TEAF was prepared by the addition of triethylamine to ice-cold formic acid (98-100%) until the solution became basic. The mixture was then concentrated by rotary evaporation and the residue was distilled to give TEAF, b.p. 80°C/3.5mm.

2-Cyano-3-methylhex-2-enenitrile (2.605g, 0.02 mol) was added to a solution of TEAF (5.40g) in DMF (40ml) and the mixture was stirred overnight at room temperature. Ether (100ml) and water (100ml) were added and the organic layer was separated, washed with water (3 x 100ml) and dried ($MgSO_4$). The solvent was removed and the residue was examined by glc analysis (10% ApL) which showed the presence of the unsaturated nitrile, a, plus a smaller amount of another compound which had the same retention time as 2-cyano-3-methylhexanenitrile. The residue was added to another solution of TEAF (5.40g) in DMF (40ml) and the mixture was refluxed for 6h, followed by work-up as described above. Examination of the residue by glc analysis showed no starting material to be present and

distillation of this material gave a clear liquid (0.802g), b.p. 100-120°C/3mm. This liquid was shown by nmr spectroscopy and glc analysis to be contaminated with DMF. In an attempt to remove this contaminant, the product was dissolved in ether (50ml) and the ethereal solution was washed with water (5 x 100ml), dried ($MgSO_4$) and concentrated. However, the residue was still contaminated with DMF.

To avoid the above contamination the reaction was repeated using acetonitrile as solvent. The substrate (0.02 mol) was refluxed with TEAF (5.40g) in acetonitrile (40ml) until glc analysis of samples (0.5 l) of the solution showed that all the substrate had disappeared. Two days were required for this, presumably due to the lower reaction temperature. Work-up as above and distillation of the residue gave 2-cyano-3-methylhexanenitrile (1.499g), b.p. 97-99°C/5.5mm which showed only one peak on examination by glc analysis (10% ApL and Carbowax 20M).

Compounds b, c, d and e were all reduced similarly with TEAF in acetonitrile. Heating was continued until no more substrate could be detected by glc analysis and the solutions were then worked-up and distilled to give the following products:

2-Cyano-3-methylheptanenitrile, b.p. 99°C/3mm, was formed in 74% yield from compound b and was found to be pure on examination by glc analysis (10% ApL). Infrared spectroscopy showed an absorption band at 2250cm^{-1} (s) characteristic of the nitrile groups and showed the absence of the olefinic absorption; nmr spectrum (60M Hz): δ 0.6 to 1.8 (m, 9H; $CH_3(CH_2)_3$-), 1.26 (d, 3H, J = 7Hz; CH_3), 2.12 (m, 1H: tertiary H) and 3.71 (d, 1H, J = 5Hz; $C\underline{H}(CN)_2$).

2-Cyano-3,5-dimethylhexanenitrile, b.p. 90-1°C/2.7mm was formed in 70% yield from compound c, was pure by glc analysis (10% ApL) and possessed the following spectral data - ν_{max}(film) 2250cm^{-1} (s, CN): nmr spectrum (60M Hz): δ 0.91 (d of d, 6H, J = 6Hz and 2Hz; $(C\underline{H}_3)_2CH$), 1.21 (d, 3H,

J = 6.5Hz; $C\underline{H}_3CH\text{-}CH(CN)_2$) 1.0 to 1.8 (m, 3H; $C\underline{H}_2\text{-}C\underline{H}(CH_3)_2$), 2.25 (m, 1H; $CH_3C\underline{H}\text{-}CH(CN)_2$) and 3.69 (d, 1H, J = 4.5Hz; $-C\underline{H}(CN)_2$).

2-Cyano-3,6-dimethylheptanenitrile, b.p. 101-3°C/2mm, was formed from d in 55% yield and exhibited only one peak on examination by glc analysis (10% ApL). The spectral details of this compound were: ν_{max}(film) 2250 cm^{-1} (m); nmr spectrum (60M Hz); δ 0.6 to 1.8 (m, 5H; $-C\underline{H}_2\text{-}C\underline{H}_2\text{-}C\underline{H}(CH_3)_2$), 0.89 (d, 6H, J = 6Hz; $(C\underline{H}_3)_2CH$-), 1.26 (d, 3H, J = 7Hz: $C\underline{H}_3C\text{-}CH(CN)_2$), 2.05 (m, 1H, $C\underline{H}\text{-}CH(CN)_2$) and 3.69 (d, 1H, J = 5Hz, $-C\underline{H}(CN)_2$).

2-Cyano-3,5,5-trimethylhexanenitrile, b.p. 98-100°C/1.5mm was formed in 42% yield from compound e and exhibited only one peak on examination by glc analysis (10% ApL). The spectral details of this compound were: ν_{max}(film) 2250cm^{-1} (m); nmr spectrum (60M Hz, $CDCl_3$): δ 0.99 (s, 9H; $(C\underline{H}_3)_3C$-), 1.31 (d, 3H, J = 7Hz, $CH_3CH\text{-}CH(CN)_2$), 1.48 (d, 2H, J = 4Hz; $(CH_3)_3C\text{-}C\underline{H}_2$-), 2.25 (m, 1H, $CH_3C\underline{H}\text{-}CH(CN)_2$) and 2.71 (d, 1H, J = 5Hz, $-C\underline{H}(CN)_2$).

General procedure for preparative electrolyses of alkylidenemalononitriles e, f, g and h.

The cell used was the same as that used for reduction of acetophenone and 3-methylcinnamonitrile; 50ml of solution was employed and the various conditions used are set out in Tables 14 and 15. In general, the initial current was about 200mA but it fell rapidly to about 10mA within 10 min. Strong agitation of the mercury surface was usually required to maintain the current at this level.

Usually, the electrolysis was terminated after 1h when the current was 1-2mA and ca. 1.5 F mol^{-1} had passed. An excess of aqueous ammonium chloride solution was added to the catholyte together with the glc internal standard (benzonitrile). This mixture was then extracted with ether (2 x 100ml) and the extracts were dried ($MgSO_4$) and concentrated for glc analysis.

Reduction of the substituted 1-cyclopropylalkylidenemalononitriles g and h, by lithium-ammonia solutions. - Liquid ammonia (50ml) was condensed in a tube immersed in liquid nitrogen. The ammonia was then distilled through a drying tube packed with calcium oxide into a three-necked flask (100ml) equipped with a dry-ice condenser. Lithium (0.110g) was added to the ammonia and the resulting blue solution was stirred magnetically for 30 min to ensure complete dissolution of the metal. The cyclopropyl compound (0.1g) was added, by means of a syringe, directly into the solution. Stirring was continued for 2h and then the mixture was quenched by the careful addition of an excess of solid ammonium chloride. Ether (50ml) was added before the ammonia was allowed to evaporate. The glc internal standard (benzonitrile) was added followed by water (10ml). The ether layer was separated and the aqueous layer was extracted with more ether (2 x 25ml). The combined extracts were dried ($MgSO_4$) and concentrated for glc analysis.

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