

ANODIC ORGANIC CHEMISTRY

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Abstract - Anodic organic reactions in solvents acetonitrile, trifluoroacetic acid, sulfur dioxide, methylene chloride and the molten salt from ethylpyridinium bromide and aluminum chloride are discussed. The importance for solvent/electrolyte systems of a high conductivity, a wide anodic range and solvent nucleophilicity are emphasized.

Modern organic electrochemistry relies almost exclusively on non-aqueous solvents. This paper describes some general aspects of solvent utility and limitations as they pertain to anodic chemistry. In this context the utility of any solvent/electrolyte system depends on its conductivity, oxidizability and nucleophilicity.

Preparative electrochemistry is of special interest here and because high currents are necessary, highly conducting solvent/electrolyte mixtures are especially important. Low conductivity escalates power requirements and will make industrial scale processes unfeasible. Laboratory experiments are also susceptible to this problem. A typical preparative set-up involves three electrodes (reference, working and auxiliary) and a cell divider (ion exchange membrane or porous glass disc). The potential of the working electrode can then be controlled and monitored with a potentiostat to maximize the selectivity of the reaction and the interpretability of the data. Also the catholyte and anolyte solutions are usually separated. This is often crucial since it is usually desired to oxidize the reactant, but not reduce either the reactant or its oxidation products, but the separation adds to the *ir* problem. Since a "high power" potentiostat typically has a voltage limitation of 100 V at 1 A, poorly conducting solutions will exceed the voltage limit at very low currents. These restrictions then force one to use polar solvent/electrolyte combinations of which the most popular are methanol, acetonitrile and trifluoroacetic acid. This paper primarily reviews work from the laboratory of the author and artificially de-emphasizes important results obtained using alcohol solvents (1). Less polar alternatives are methylene chloride and sulfur dioxide. Both of these must be used with tetrabutylammonium salts for solubility and even then the conductivity is marginal. Although less polar organics have been used, for example, with crown ethers to promote dissociation of the electrolyte, these have not proven very satisfactory either in terms of conductivity, cost or work-up.

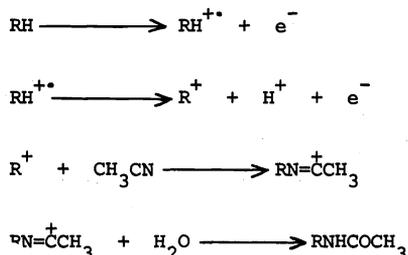
A second solvent characteristic of prime importance for anodic chemistry is the potential at which the solvent/electrolyte oxidizes. There are two useful situations. In one, the solvent/electrolyte is electroinactive over a wide range and redox reactions involve electron transfer from organic substrate to the electrode. In the second the solvent, or more generally, the electrolyte anion is oxidized, producing a reactive intermediate which attacks the substrate.

Let us consider the first of these approaches more thoroughly. In essence one desires a non-oxidizable electrode, solvent and electrolyte. Platinum electrodes have proven most useful and if an electroinactive electrolyte anion like fluoroborate is chosen, the anodic potential window can be very wide and allows the direct oxidation of many compounds. A medium with an admirable anodic range is fluorosulfonic acid/sodium fluorosulfonate. As shown by Pletcher and Fleischmann, one can directly oxidize even aliphatic hydrocarbons in this solution (2). Fluorosulfonic acid is, however, a very reactive chemical and it destroys many organic compounds before they can be oxidized.

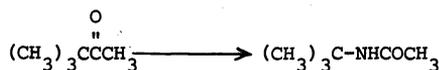
A less reactive solvent which is also quite electroinactive is acetonitrile and this has proven to be one of the most popular solvents for anodic chemistry. Its anodic window extends to 2.9V using a perchlorate electrolyte and to 3.2V using fluoroborate. This means that redox reactions some 70 kcal/mol more endothermic than the reference reaction can be performed and that extraordinarily energetic species can be produced. Within this range one can usually assume that anodic reactions are initiated by electron transfer from the substrate to the electrode. This process has analogy with gas phase ionization and, indeed, there is a broad correlation between ionization potentials and half wave oxidation potentials (3). This is somewhat surprising when it is considered that the oxidation potentials are

generally kinetically, not thermodynamically, controlled and that there are many possibilities for differential solvation. Speaking in broad terms, however, there is also little evidence for the importance of adsorption in organic anodic reactions in non-aqueous solutions. This contrasts sharply with aqueous electrochemistry.

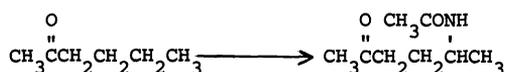
The overall anodic reactions observed in acetonitrile are of primary interest here and illustrate the final important solvent characteristic, nucleophilicity. The oxidation of most alkanes produces acetamides as major products (4,5) and these are postulated to result from carbonium ion intermediates, e.g.,



In this text then, nucleophilicity means the ability to scavenge cations or cation radicals and convert them to substitution products. Many solvents, e.g., methylene chloride, are not effective in this regard and tend to give polymeric products. Acetonitrile seems especially effective because in the absence of much water it leads from RH to a more difficultly oxidized and, therefore, stable product, $\text{RN}=\overset{+}{\text{C}}\text{CH}_3$. Many other anodic acetamidations have been discovered including aromatic acetamidation (6). Specifically required are aromatic compounds with very positive oxidation potentials and correspondingly reactive cation radicals. Examples are nitrobenzene and benzoic acid. If electroinactive solvents like acetonitrile are used comparisons of mass spectrometry and anodic electrochemistry might also be expected to reveal similarities in reaction pathways. In each case the process is initiated by electron loss, forming a cation radical. In general, cation radicals formed in the presence of a nucleophilic solvent/electrolyte behave quite differently from those formed at 10^{-5} Torr. In particular the rather indiscriminate fragmentations observed mass spectroscopically are not seen in solution. The anodic chemistry of ketones at platinum in acetonitrile is, however, an exception. Two pathways are extant, fragmentation and remote substitution. The former is found for ketones with tertiary carbons α to the carbonyl, like *t*-butyl methyl ketone (7). It is similarly favorable in the mass spectrum.

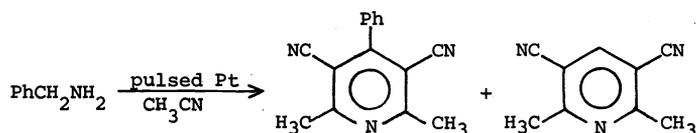


The latter reactions is exemplified by the reaction of 2-hexanone (8).

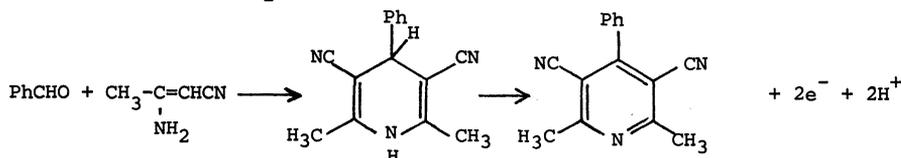
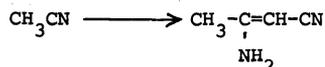


Substitution is in this case specific for the γ -position and in all cases avoids the α - and the β -position. A mechanism based upon the mass spectral analogy (McLatterty rearrangement) involves remote hydrogen abstraction by a ketone cation radical. There are in these ketone reactions also some interesting unexplained effects of "adventitious" water (7,8). Thus, acetamides cannot be isolated from either type of ketone reaction unless some water is present. The water has some small effects on the voltammetry as well. Water is most likely involved as a nucleophile or base. Indeed, the absence of buffering in these non-aqueous media is a crucial problem. As a preparative oxidation proceeds the anolyte becomes progressively more acidic and this can cause undesirable side reactions. Furthermore, there is a concentration gradient near the electrode surface and the acidity near the electrode can be very high. One crude electroinactive buffer we have employed for anodic reactions is sodium bicarbonate. If the acetonitrile contains 1% water this is soluble enough to alleviate some acidity problems. As shown by Kolthoff small amounts of water have large effects on acidity in acetonitrile (9).

Recent studies by M. Pasternak (10) have revealed a further possibility for involvement of the solvent acetonitrile. He has shown that the oxidation of benzyl amine at 2.0 V in a divided cell gives primarily benzaldehyde and benzyl acetamide. However, when the platinum electrode potential is regularly pulsed to 0.0 V (for 1 sec after 5 sec at 2.0 V) these products are replaced by two completely unexpected pyridine derivatives.



It is known that acetonitrile can reductively produce crotonitrile and it is hypothesized that this compound is an intermediate in the reaction. In the case of the phenyl derivative a pathway might be:



It is known that crotonitrile will readily condense with aldehydes to give dihydropyridines and, indeed, oxidation of a mixture of benzaldehyde and crotonitrile gave the expected cyanopyridine. There are, however many aspects of this reaction which remain obscure.

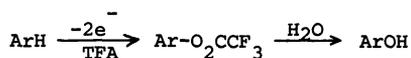
The electrolyte can also be oxidized and thus play a direct role in anodic organic chemistry. Of preparative interest are indirect aliphatic substitutions initiated by oxidation of perchlorate in acetonitrile.



In this way electroinactive compounds like methylbutyrate can be acetamidated (11). Further study of this process was initiated using tetraethylammonium fluoroborate as electrolyte and a smaller amount of perchlorate as a reagent. Cyclic voltammetry on this solution gave a peak for perchlorate oxidation at 2.9 V which was unaffected by addition of methyl butyrate. This system was effective in substitution. Interestingly, one can also start with chlorine dioxide, chloride or even fluoroborate and achieve exactly the same result (12). This seems to indicate that a solvent derived radical is responsible for the initial attack on methyl butyrate.

An even more useful and selective halide derived reagent can be generated by oxidation of iodine in acetonitrile. After passage of 2F/mol of I₂ a clear solution containing an iodine species in the plus one oxidation state is produced. This reagent, presumably N-iodoacetonitrilium ion, rapidly and cleanly iodinate aromatic compounds (13).

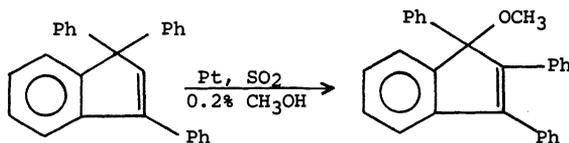
A second solvent with considerable utility is trifluoroacetic acid (TFA). It has been used with sodium trifluoroacetate or with tetraalkylammonium salts and also with cosolvents like methylene chloride or nitromethane. The characteristics of TFA/trifluoroacetate are an anodic window to about 2.5 V, conductivity comparable to acetonitrile/tetraethylammonium fluoroborate and low nucleophilicity. Utility of TFA can be illustrated by a method for aromatic hydroxylation. It is of synthetic importance to perform monohydroxylation, e.g., benzene to phenol. Under most conditions the phenol produced is more reactive than benzene and polyhydroxylation, oxidation takes place. This problem can be overcome by electrochemical oxidation in TFA producing the aryltrifluoroacetate (14,15). This is not readily oxidized but can be readily hydrolyzed to the phenol upon completion of the reaction.



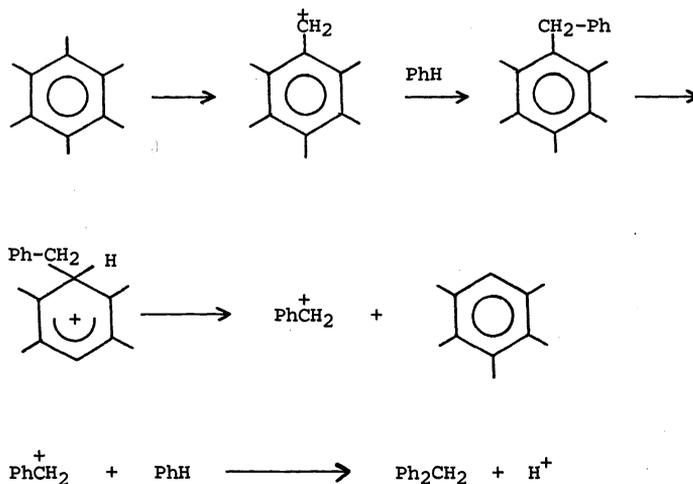
TFA is preferable to acetic acid in most cases because acetate products are rather easy to oxidize (16) and because acetate oxidizes at about 1.8 V precluding good yields for benzene or deactivated aromatics. It is of further interest in this regard that trifluoroacetoxylation is successful with deactivated aromatics like methyl benzoate, but lower yields are obtained with compounds like anisole where bimolecular coupling takes over.

The weak nucleophilicity of TFA makes it possible to observe rather unstable cation radicals using electrochemical techniques. Thus species which rapidly react with other solvents can be detected by cyclic voltammetry in TFA. This has been most fully exploited by V.D. Parker, who has demonstrated that "unadventitious" nucleophilic impurities control the rate of disappearance of many cation radicals. These species can be scavenged by trifluoroacetic anhydride or very efficaciously by adding dry alumina to the cell (17). In certain cases even aromatic dications can be detected using this approach (17,18).

The possibility of electrochemically detecting rather unstable cation radicals has been accomplished with other non-nucleophilic solvents. Methylene chloride, for example, can be used at -70° in order to slow down the reactions which destroy these cations (19). Other solvents with low melting points which have been used for analytical scale anodic chemistry are butyronitrile and sulfur dioxide. Sulfur dioxide is quite non-nucleophilic. This property has been used to permit an unusual cation radical rearrangement. Thus, 1,1-diphenyl indene oxidized at platinum in methanol gives a dimethoxy derivative from addition across the double bond. Oxidation in SO_2 containing 0.2% methanol at -25° however, gives a product resulting from phenyl migration.



A final intriguing possibility is the use of low melting organic molten salts as solvents. Our studies in this area have been done in conjunction with Professor R. Osteryoung. The solvent of interest here is produced by mixing N-ethyl pyridinium bromide and aluminum chloride. A "50:50 melt" is, therefore, primarily N-ethylpyridinium bromotrichloroaluminate. The acidity (pCl) of the solvent can be varied by controlling the ratio of AlCl_3 and pyridinium salt. Using a 67:33 mole % AlCl_3 /pyridinium bromide melt at 25° , a tungsten anode and an aluminum wire reference electrode both preparative and analytical scale electrochemistry has been studied (21). The anodic window extends to about 1.8 V and within this range, compounds like adamantane and benzene can be oxidized. The "2:1 melt" is rather viscous at room temperature and the virtual absence of nucleophiles tends to give polymeric products in preparative experiments. Addition of benzene to this melt alleviates both these problems. Thus the viscosity drops, the conductivity rises and benzene acts as a nucleophilic trap. The oxidation of hexamethylbenzene has been mostly thoroughly studied. It is found that pentamethylbenzene and diphenylmethane are the major oxidation products. These are postulated to arise from the following mechanism.



Cyclic voltammetry at rapid sweep rates detected the hexamethyl benzene cation radical and these data plus data from rotating ring-disc voltammetry elucidated some mechanistic aspects of the early stages of this reaction.

In summary then the utility of polar, non-aqueous anolytes depends to a large extent on their nucleophilicity. If cation traps are not present, little of synthetic significance is accomplished. If, on the other hand, the goal is detection of unstable cation radicals then anodic oxidation in non-nucleophilic media provides an attractive approach.

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