THE ORIGIN OF ELECTROLYTE EFFECTS IN ELECTROOXIDATIVE SUBSTITUTION REACTIONS

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Abstract— The electrooxidation of alkylbenzenes in wet acetonitrile can give rise to either alcohols ($ArCH_2OH$) or acetamides ($ArCH_2NHCOCH_3$). It has been proposed previously that the ratio $ArCH_2OH/ArCH_2NHCOCH_3$ reflects a kinetic competition for $ArCH_2^+$. The oxidation of hexamethylbenzene at a platinum anode was reinvestigated using several different electrolytes and reaction conditions. It was found that in many cases this product ratio is not kinetically controlled. Acid was concomitantly produced during oxidation and catalyzed the conversion of the alcohol to the acetamide. Conversion of pentamethylbenzylacetate to pentamethylbenzyl acetamide formed during oxidation of hexamethylbenzene in acetic acid-acetonitrile was also studied.

SEVERAL intriguing results have been reported concerning the anodic oxidation of alkylbenzenes. Eberson and Olofsson[1] found that the oxidation of toluene, xylene. durene and hexamethylbenzene in aqueous acetonitrile, sodium perchlorate at a platinum electrode, produced the corresponding benzylic acetamides and alcohols. The predominant product was the amide and in going from toluene to hexamethylbenzene, the relative yield of amide was found to increase. Even with 5% aqueous acetonitrile, the amide was still the predominant product. Benzylic carbonium ions seem well established as reactive intermediates in these oxidations and nucleophilic trapping by water or acetonitrile yields the products. The major anomaly is the increased nucleophilic trapping by acetonitrile of the more highly substituted benzylic cations. It was expected that the more substituted, more stable, carbonium ions would react more selectively. Since water is a stronger nucleophile than acetonitrile, these carbonium ions would then react predominantly with water and produce more alcohol than amide. In order to explain this anomalous result, it has been tentatively proposed that the composition of the solution at the electrode surface is different than that of the bulk of the solution.

We have performed several control experiments which show that in these oxidations unbuffered acid is generated which can convert benzylic alcohols to the corresponding amides. Therefore, in some cases, the products are thermodynamically, not kinetically, controlled. A critical experiment is the oxidation of hexamethylbenzene **1** in aqueous acetonitrile. An undivided cell which held 50 ml acetonitrile and 0·2 ml water was utilized. The cathode was a platinum sheet, 2 in², and the anode a platinum

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cylinder, 5 in^2. Hexamethylbenzene (0·81 g, 0·005 mole) and sodium perchlorate (1·2 g, 0·01 mole) were added, the oxidation was carried out at 1·05 V (vs Ag/0·1 N AgNO$_3$) for 25 min and 1·1 mFaradays of charge was passed. After electrolysis, the solution was divided into two equal parts. Part 1 was immediately worked up by adding water and extracting with chloroform. Gas chromatographic analysis showed that pentamethylbenzyl acetamide 2 and pentamethylbenzyl alcohol 3 were present in the molar ratio 95:5. Part 2 was purposely contaminated with 30 mg (0·16 mmole) of pentamethylbenzyl alcohol and after standing for 25 min was worked up identically. Gas chromatographic analysis showed that the added alcohol had been converted to 0·15 mmole of amide. The 2:3 ratio was 94:6. This, of course, indicates that *the alcohol would not survive if formed.*

$$ArCH_2OH + CH_3CN \xrightarrow{H^+} ArCH_2NHCOCH_3$$
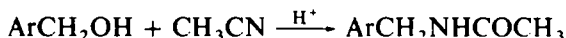
The same results were obtained with lithium perchlorate or using a divided cell with sodium or lithium perchlorate, as shown in Table 1.

TABLE 1. OXIDATION OF HEXAMETHYLBENZENE IN AQUEOUS ACETONITRILE[a]

Electrolyte	Electrolysis time (min)	Time before work up (min)	Added alcohol 3[b] (mmol)	Molar ratio 3:2
LiClO$_4$	25	0	0	5:95
LiClO$_4$	25	25	0·16	8:92
NaClO$_4$	25	0	0	5:95
NaClO$_4$	25	25	0·16	6:94
(C$_4$H$_9$)$_4$NClO$_4$	25	0	0	77:23
(C$_4$H$_9$)$_4$NClO$_4$	25	25	0	70:30
NaBF$_4$	25	0	0	60:40
NaBF$_4$	25	25	0	43:57
(CH$_3$)$_4$NBF$_4$	25	0	0	67:33
(CH$_3$)$_4$NBF$_4$	25	25	0	50:50
(C$_4$H$_9$)$_4$NBF$_4$	25	0	0	82·18
(C$_4$H$_9$)$_4$NBF$_4$	25	25	0	83:17
NaClO$_4$[c]	25	0	0	15:85
NaClO$_4$[c]	25	25	0	10:90
(C$_4$H$_9$)$_4$NBF$_4$[c]	25	0	0	5:95
(C$_4$H$_9$)$_4$NBF$_4$[c]	25	25	0	1:99

[a] Results from electrolysis in an undivided cell with 50 ml acetonitrile, 0·2 ml water and 0·01 mole of electrolyte. The anode potential was 1·05 V vs Ag/Ag$^+$.

[b] These figures refer to experiments in which a portion of the anolyte was contaminated with 3 after electrolysis.

[c] Experiments in a divided cell. The anolyte was 50 ml of acetonitrile, 0·2 ml water and 0·01 mole of electrolyte.

It should be noted that this acid catalyzed product interconversion explains the high yield of amide[1,2] in wet acetonitrile. It also explains the fact that the compounds producing the most stable cations gave a higher proportion of amide[1] since the initial alcohol product is more susceptible to acid catalyzed conversion to the amide. The most sensitive compound would, of course, be 1. We find, furthermore, that benzyl alcohol from the oxidation of toluene is converted to benzyl acetamide only slowly

in sodium perchlorate medium if the reaction is limited to 10% conversion as in the reported experiments.

Nyberg has reported on the oxidation of **1** in aqueous acetonitrile utilizing tetra-butylammonium tetrafluoroborate and a platinum electrode.[2] The ratio **2**:**3** was 5:95 instead of the 95:5 found when sodium perchlorate was used. Since the electrolyte did not oxidize at 1·0 V, it was necessary to postulate that the tetrafluoroborate
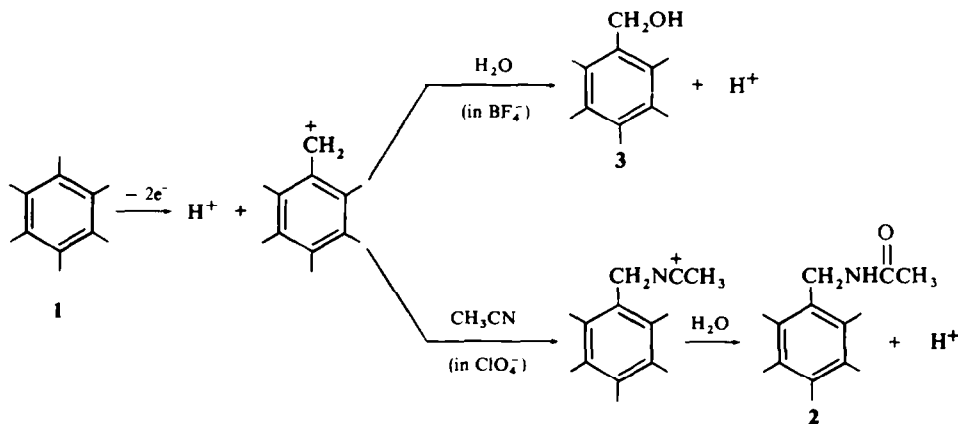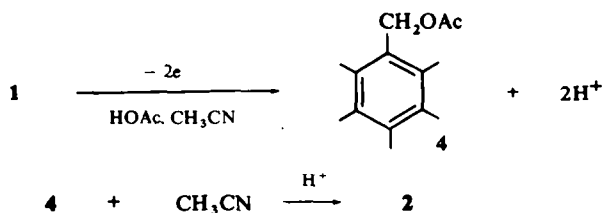

anion preferentially brought water into the double layer giving high alcohol yields. Again, in an identical control experiment, the ratio of **2**:**3** was 20:80 for both part 1 and 2. No pentamethylbenzyl alcohol was added since the conversion to the amide could be easily detected. It is apparent that the tetrabutylammonium fluoroborate medium is a less effective catalytic solution. The high yield of **3** is not extraordinary since this is what is expected, based upon the nucleophilicities of water and aceto-nitrile.

In order to account for the different catalytic activities of the sodium perchlorate and tetrabutylammonium fluoroborate media, we postulate that they have differing acidities. The hydrogen ion activity was measured in reaction mixtures from runs in the undivided cell using *m*-nitroaniline as an indicator.[3] The decrease in absorbance at 380 nm was measured for a standard solution of perchloric acid in acetonitrile and then for the perchlorate and fluoroborate oxidation mixtures. The pH of the perchlorate mixture was 2·19 and 3·93 for the fluoroborate. Both mixtures were oxidized for 25 min; so it can be seen that the fluoroborate mixture is less acidic. *A priori*, this difference could arise from two factors. The first factor is that tetra-fluoroboric acid is a weaker acid than perchloric acid in acetonitrile. This was tested by preparing a standard solution of tetrafluoroboric acid in acetonitrile and measuring the hydrogen ion activity with *m*-nitroaniline. It was found that tetrafluoroboric acid had approximately the same activity as perchloric acid and therefore effects due to different anions were small. In accordance with this hypothesis, both tetrabutyl-ammonium perchlorate and tetrafluoroborate yield **3** as the major product in an undivided cell. The second factor considered was that perhaps the cation was affecting the acidity. We propose that the cathodic process is responsible for this behavior. With sodium or lithium perchlorates, the initial primary cathodic process is the reduc-tion of the alkali metal and the cathode rapidly becomes coated and, therefore, the

solution is unbuffered. This decrease in acid reduction is supported by results obtained from the divided cell experiments. For lithium and sodium perchlorate in a divided cell, similar results to those found in an undivided cell were obtained because the acid reduction is nominal because the cathode is physically removed from the anolyte. With tetrabutylammonium perchlorate and tetrafluoroborate, the initial primary cathodic process is, presumably, reduction of the tetrabutylammonium cation to produce a soluble base. As the acid concentration increases with time, its reduction will become more important. In effect, the solution becomes buffered and both electrolytes yield 3 as the major product. This is again supported by results obtained with a divided cell. When either of these electrolytes is used in a divided cell, 2 is the major product, indicating acid catalysis is occurring. For sodium or tetramethyl-ammonium tetrafluoroborate, the product ratios lie between the two extremes for 2 and 3. This may be due to partial buffering. Both of these electrolytes are only slightly soluble in acetonitrile. It should also be pointed out that current efficiencies may have a minor effect since they are different for different electrolytes. The differences are not great enough, however, to account for an approximately 100 fold difference in acid concentration for sodium perchlorate and tetrabutylammonium tetrafluoroborate.

It is apparent that the presence or absence of acid is very critical in determining the yield and types of products obtained. From a synthetic viewpoint, it is important to determine product stability towards acid catalysis if a reasonable yield is desired. Once this stability has been determined, suitable conditions may then be employed to optimize the yield of the desired product. An illustration of this technique is the preparative electrolytic conversion of 1 to yield 3. 3 is known to undergo acid catalysis so that if it is to be isolated in any quantitative yield, this acid catalysis must be abrogated. Indeed, when a divided cell with lithium perchlorate and anhydrous sodium carbonate added to the anolyte was utilized, a 50% yield of 3 (based on added reactant) was realized.

Nyberg also reported on the ratio of pentamethylbenzyl acetate 4 to 2 using acetic acid in acetonitrile and sodium perchlorate.[2] Using these conditions, 2 was found to be the major product. Since the ratio of 4:3 was comparable to the ratio of 2:3, this was taken as evidence for preferential solvation theory. Utilizing various electrolytes, these oxidations were found to be independent of the cation used. We were, unfortunately, unable to reproduce these results. Several undivided cell geometries were employed. These had some effect ($\pm 10\%$) on the 4:3 ratio but the results were essentially as indicated in Table 2. If, for example, 1 was oxidized under conditions as similar as possible to Nyberg's, using 1% acetic acid in acetonitrile and sodium perchlorate, the major product was 4. No conversion of 4 → 3 was taking place. Although we cannot explain his results, the data from this study are easily rationalized. In an undivided cell reduction of acetic acid would lead to the formation of acetate,

$$1 \quad \xrightarrow[\text{HOAc. CH}_3\text{CN}]{-\,2e} \quad \overset{\text{CH}_2\text{OAc}}{\underset{4}{\bighexagon}} \quad + \quad 2\text{H}^+$$

$$4 \quad + \quad \text{CH}_3\text{CN} \quad \xrightarrow{\text{H}^+} \quad 2$$

a buffer. Thus, the acid catalyzed process is slowed down, compared to that in aqueous acetonitrile. Employing the usual control experiment, it was found that the acetate underwent conversion to the amide in an undivided cell only if lithium perchlorate was used. Lithium is deposited on the cathode. In a divided cell, **4 → 2** is more rapid since acid builds up.

TABLE 2. OXIDATION OF HEXAMETHYLBENZENE IN 1 % ACETIC ACID, ACETONITRILE[a]

Electrolyte	Electrolysis time (min)	Time before work up (min)[b]	Molar ratio 2:4
LiClO$_4$	5	0	100 : < 1
(CH$_3$)$_4$NBF$_4$	5	0	25 : 75
(CH$_3$)$_4$NBF$_4$	5	10	40 : 60
LiClO$_4$[c]	5	0	80 : 20
LiClO$_4$[c]	5	5	95 : 5
(CH$_3$)$_4$NBF$_4$[c]	5	0	35 : 65
(CH$_3$)$_4$NBF$_4$[c]	5	5	35 : 65
NaClO$_4$[c]	10	0	25 : 75
NaClO$_4$[c]	10	10	25 : 75

[a] Results from electrolysis in a divided cell using 75 ml acetonitrile with 0·6 ml acetic acid and 0·01 mole of electrolyte

[b] See footnote b, Table 1.

[c] Experiments in an undivided cell. Solution was 50 ml of acetonitrile and 0·6 ml acetic acid and 0·01 mole of electrolyte.

The above results seem to resolve the anomalous selectivity-reactivity observed[1] for side-chain substitution in aqueous acetonitrile-sodium perchlorate. The proposition that fluoroborate preferentially draws water and acetic acid into the double layer, thus discriminating against amide formation, must remain an open question. There is no evidence for it in aqueous acetonitrile (compare Bu$_4$N,ClO$_4$ and Bu$_4$N,BF$_4$ results in Table 1). Nyberg's results using acetic acid/acetonitrile are internally consistent and agree with ours with the important exception of sodium perchlorate solutions. We believe the above hypothesis concerning electrolyte effects is still viable, but needs to be tested.

It should be emphasized that if mechanistic conclusions are based on product ratios, then these products must not be interconverting. This is particularly critical if a divided cell is employed. A case in point is the work of Parker and Adams in which p-methoxytoluene was oxidized in aqueous acetonitrile.[4] The formation of only side-chain amide was taken as evidence for an EEC mechanism involving dications instead of an ECE process involving cation radicals. A control experiment demonstrating product stability was not, however, reported. In this case it is, furthermore, not clear how the eventual products could differentiate two mechanisms, ECE and EEC, which involve the same product forming steps via the benzylic cation.[5]

EXPERIMENTAL

A modified "H" cell was employed as a divided electrochemical cell. The anode compartment was separated from the cathode by a 1½″ diameter glass frit and from the reference by a ¼″ diameter glass frit. The porosity of the frits was fine. A beaker was utilized for an undivided cell. The reference compartment was a glass tube with a glass frit at one end which was then immersed into the soln. In both the divided

and undivided cell, 0·1 N AgNO₃ in acetonitrile with a Ag wire was utilized as the reference electrode. The anode was a cylindrical platinum electrode, 5 in², and the cathode a Pt sheet, 2 in². A model 61RS or 70 HV 1/90 Wenking potentiostat was employed for controlled potential electrolysis. Products were analyzed by GLC with a F and M Research Chromatograph Model 5750 equipped with a programmed temp unit and hydrogen flame detector An 8' × ¼" 5% S.E. 30 Chromosorb W column was used. A temp program of 8°/min from 150° to 230° was used. Peak areas were compared with those from standard solns.

Hexamethylbenzene was used without purification. Pentamethylbenzyl alcohol, amide and acetate were isolated from electrooxidations, identified by NMR and purified for use as GLC standards. Tetrabutylammonium fluoroborate was prepared from tetrabutylammonium bromide and fluoroboric acid. All other electrolytes were commercial samples recrystallized and dried in a vacuum oven. Except for lithium perchlorate, their infrared spectra indicated no residual water. Acetonitrile (Eastman, anhydrous) was distilled from phosphorous pentoxide and stored over molecular sieves.

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