

Anodic Aromatic Substitution

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Unfortunately, electrons cannot be stored in bottles for instant use in reductions, nor can positive holes be made similarly available for oxidations. However, electrons can be supplied or withdrawn at interfaces between electrodes and solution by use of the electric current in an electrolytic cell. Organic electrochemistry¹ deals with the application of this method to organic systems.

Even if Lord Bowden's classical statement² "An art may become a science if it is concerned with less than about seven variables" would seem to classify organic electrochemistry as a typical borderline case, we think that achievements during recent years have definitely moved it into the domain of science. The development of several successful industrial processes,³ of which the Baizer process⁴ for the electrohydrodimerization of acrylonitrile to adiponitrile is outstanding, and many promising laboratory synthetic methods⁵ shows that electrochemistry is becoming of significant importance in the practice of organic chemistry. The many challenging theoretical problems that still remain to be solved will here be exemplified by phenomena in the area of anodic substitution reactions.

General Principles

Let us first consider the principles of electrolysis and the problems associated with their application to organic systems. One wishes simply to carry out an electron transfer⁶ between a metal or semiconductor electrode and some *electroactive* species (the *substrate*) dissolved in a suitable solvent. Such a process obviously cannot take place continuously at an isolated electrode, since the electroneutrality principle would then be violated; hence an electrolysis cell must always have at least two electrodes, one *anode* at which electrons flow from the solution to the electrode (anodic oxidation) and one *cathode* at which electrons flow in the opposite direction (cathodic reduction). Since the medium defined above normally is an insulator it must be rendered conducting by adding a *supporting electrolyte*—a strong acid or base, or a salt—to the solution.

The electron transfer takes place in a layer of solution, 10–15 Å thick, at the interface between the electrode and the solution. In order for an electron to

transfer between the electrode metal and the electroactive species, the energy level of the electrode orbitals (the Fermi level) and the highest occupied or lowest empty orbital, respectively, of the substrate molecule must match each other exactly. Only then can a radiationless transfer of one electron take place.⁷

One achieves the desired matching of the energy levels by changing the energy of the Fermi level, which is done practically by changing the *electrode potential*, *i.e.*, the potential applied across the electrode-solution interface. Thus, in an anodic oxidation one raises the anode potential until electron transfer from substrate to electrode becomes possible. The domain of anodic potentials⁸ extends up to +3.5 V (*vs.* the hydrogen electrode) and of cathodic ones down to -3.5 V. A potential difference of 1.0 V is equivalent to an energy difference of 23 kcal; thus, it is easily realized that electrolysis provides a very powerful means of oxidation or reduction. At one extreme it allows for oxidation of C-H bonds in saturated hydrocarbons⁹ and at the other for the generation of solvated electrons.¹⁰

(1) The missionary zeal of practitioners in this field has resulted in a large number of recent reviews and textbooks: (a) N. L. Weinberg and H. R. Weinberg, *Chem. Rev.*, **68**, 449 (1968); (b) R. N. Adams, *Accounts Chem. Res.*, **2**, 175 (1969); (c) R. N. Adams, "Electrochemistry at Solid Electrodes," Marcel Dekker, New York, N. Y., 1969; (d) C. K. Mann and K. K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, New York, N. Y., 1970; (e) *Progr. Electrochem. Org. Comp.*, **1**, 1971; (f) L. Eberson and H. Schäfer, *Fortschr. Chem. Forsch.*, **21**, 1 (1971); (g) "Organic Electrochemistry," M. M. Baizer, Ed., Marcel Dekker, New York, N. Y., in press; (h) "Technique of Electro-Organic Synthesis," N. L. Weinberg and A. Weissberger, Ed., Wiley-Interscience, New York, N. Y., in press; (i) A. J. Fry, "Synthetic Organic Electrochemistry," Harper and Row, New York, N. Y., in press.

(2) B. V. Bowden, "Proposals for the Development of the Manchester College of Science and Technology," The College, Manchester, 1956, p 48.

(3) C. Jackson and A. T. Kuhn, in "Industrial Electrochemical Processes," A. T. Kuhn, Ed., Elsevier, Amsterdam, 1971, Chapter 13.

(4) For a review of this reaction, see ref 1g, Chapter XIX.

(5) (a) S. Wawzonek, *Synthesis*, 285 (1971); (b) J. Chang, R. F. Large, and G. Popp in "Physical Methods of Chemistry," Part IIB, A. Weissberger and B. W. Rossiter, Ed., Wiley-Interscience, New York, N. Y., 1971, Chapter X.

(6) For some reason, the concept of electron-transfer processes has never come to occupy a permanent place in organic chemistry; see K. A. Bilevich and O. Yu. Okhlobystin, *Russ. Chem. Rev.*, **37**, 1 (1968); P. J. Andrusis, M. J. S. Dewar, R. Dietz, and L. Hunt, *J. Amer. Chem. Soc.*, **88**, 5473 (1966).

(7) It is an important postulate of electrochemistry that electrons are always transferred one by one: N. N. Semenov, "Some Problems in Chemical Kinetics and Reactivity," Vol. 1, Princeton University Press, Princeton, N. J., 1958, p 198.

(8) The concept of *electrode potential* should not be confused with that of *applied potential*, which is the potential applied between anode and cathode and, apart from the two electrode potentials, contains a term for the potential drop due to the ohmic resistance of the cell. The applied potential is of no theoretical interest whatsoever.

(9) (a) M. Fleischmann and D. Pletcher, *Tetrahedron Lett.*, 6255 (1968); (b) *Chem.-Ing.-Tech.*, **44**, 187 (1962); (c) D. Clark, M. Fleischmann, and D. Pletcher, *J. Electroanal. Chem.*, **36**, 137 (1972).

(10) E. J. Hart and M. Anbar, "The Hydrated Electron," Wiley-Interscience, New York, N. Y., 1970, p 6.

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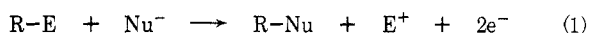
Klas Nyberg received his Ph.D. from the University of Lund in 1971 and is Assistant Professor there.

The layer at the interface between electrode and solution is commonly called the *electric double layer*. A more modern and descriptive term is the *electrically modified interface* (EI). The EI is considered to have a rigidly ordered structure, composed of ions and solvent and substrate molecules. This composition is in turn determined by the adsorption properties of the components present in the solution.¹¹

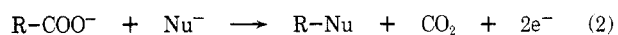
It is in the EI where the most important mechanistic problems of electrochemistry appear: Does the molecule have to be oriented in a special way for electron transfer to occur? Does it have to be adsorbed before electron transfer can occur? Does the composition of the EI differ from that of the bulk of the solution and does this difference influence the product distribution? How does the nature of the electrode material exert its influence on the electrochemical reaction? What is the chain of events following electron transfer and where do these take place with respect to the EI? These questions are not yet fully answered, and here we can only point to experimental approaches to some of the problems.

Definitions

An anodic substitution process is defined by eq 1,



in which E^+ and Nu^- denote an electrophile and nucleophile, respectively. Nu^- can be chosen from a large list of nucleophiles, both neutral and charged: OH^- , RO^- , $RCOO^-$, NO_3^- , NO_2^- , N_3^- , OCN^- , SCN^- , $SeCN^-$, halide ion, CN^- , H_2O , ROH , $RCOOH$, CH_3CN , pyridine, and $R-E$ ¹² itself. E^+ in most cases is H^+ , but can also represent a carbonium, halonium, or alkoxonium ion. When E^+ is equal to CO_2 (*i.e.*, $R-E = R-COO^-$) we have the familiar case of the carbonium ion pathway of the Kolbe reaction¹³ (eq 2).



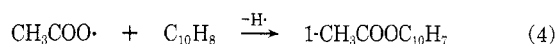
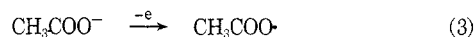
Substitution Processes

Acetoxylation. Before tackling the mechanistic problems outlined above, one must first solve a few "trivial" problems of mechanism. The first and simplest problem is to find which component of the electrolyte is the electroactive species. Here one distinguishes between *direct* mechanisms, in which the compound to undergo substitution ($R-E$ of eq 1) is the electroactive species, and *indirect* ones, in which a solvent molecule or, most commonly, the anion of the supporting electrolyte is the electroactive species. The second problem—often much more difficult—is to find out the sequence of events succeeding the initial electron transfer.

Ten years ago, when we embarked on a study of anodic substitution processes, practically all such reactions were viewed as indirect ones.¹⁴ Thus, an-

odic halogenation, except fluorination, in electrolytes containing substrate, halide ion, and an aqueous-organic solvent, was formulated as an oxidation of halide ion to the corresponding halogen, which would attack the substrate in a homogeneous reaction.¹⁵ Fluorination (in liquid $HF-KF$ at Ni anodes) was similarly viewed as a reaction of anodically generated NiF_3 , a possibility that has been substantiated by recent work.¹⁶

However, the mechanistic interpretation of some other processes as indirect ones was in apparent violation of available evidence. One of these reactions was anodic acetoxylation, first discovered by Linstead, *et al.*,¹⁷ in the course of an investigation of the Kolbe acetate oxidation. In this study, naphthalene was added to an electrolyzing mixture of $HOAc-NaOAc$ whereupon a 24% yield of 1-naphthyl acetate could be isolated. This was taken as evidence¹⁸ (quite logical at that time) for a mechanism involving formation of an acetoxy radical (eq 3), which would attack a naphthalene molecule in a radical substitution process (eq 4). Data suggesting that this



mechanism was improbable¹⁹ included the short lifetime (estimated²⁰ to be 10^{-9} sec) of the acetoxy radical, much too short to allow for the fairly good yield of acetoxy compound obtained.²¹ Secondly, it had long been known that the Kolbe reaction requires a very high anode potential,¹³ >2.3 V. Thirdly, a pioneering polarographic investigation by Lund²² had shown that aromatic hydrocarbons, including naphthalene, are oxidized at lower potentials in $CH_3CN-NaClO_4$. Experimental verification that the same situation prevails in $HOAc-NaOAc$ was obtained by polarographic studies on a large number of compounds.²³

Controlled potential electrolyses, conducted at a potential where practically only the substrate is electroactive, confirmed that acetoxylation products were formed *via* a direct mechanism.²⁴ At first, this

(14) This view permeated the classical textbooks of organic electrochemistry: F. Fichter "Organische Electrochemie," T. Steinkopf, Dresden and Leipzig, 1942; M. J. Allen, "Organic Electrode Processes," Chapman and Hall, London, 1958.

(15) Direct chlorination and bromination reactions have actually been observed recently: G. Fanta, M. Fleischmann, and D. Pletcher, *J. Electroanal. Chem.*, **25**, 455 (1970); J. P. Millington, *J. Chem. Soc. B*, 982 (1969).

(16) J. Burdon, I. W. Parsons, and J. C. Tatlow, *Tetrahedron*, **28**, 43 (1972). However, see also I. N. Rozhkov, A. V. Bukhtiarov, E. G. Gal'pern, and I. L. Knunyants, *Proc. Acad. Sci. USSR*, **199**, 598 (1971).

(17) R. P. Linstead, J. C. Bunt, B. C. L. Weedon, and B. R. Shephard, *J. Chem. Soc.*, 3624 (1952).

(18) C. L. Wilson and W. T. Lippincott, *J. Amer. Chem. Soc.*, **78**, 4291 (1956).

(19) L. Ebersson, *Acta Chem. Scand.*, **17**, 2004 (1963).

(20) W. Braun, L. Rajkenbach, and F. R. Eirich, *J. Phys. Chem.*, **66**, 1591 (1962).

(21) The possibility of substitution by an adsorbed and hence stabilized acetoxy radical was neglected at that time but was later advocated: A. K. Vijn and B. E. Conway, *Chem. Rev.*, **67**, 623 (1967); L. Ebersson, *Electrochim. Acta*, **12**, 1473 (1967). Cf. also ref 1g and 13.

(22) H. Lund, *Acta Chem. Scand.*, **11**, 1323 (1957).

(23) L. Ebersson and K. Nyberg, *Acta Chem. Scand.*, **18**, 1568 (1964); *J. Amer. Chem. Soc.*, **88**, 1686 (1966).

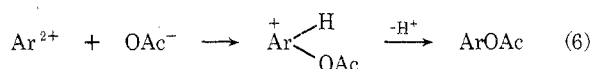
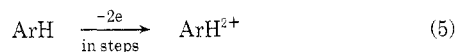
(24) Similar conclusions were reached independently by two other groups: M. Leung, J. Herz, and H. W. Salzberg, *J. Org. Chem.*, **30**, 310 (1965); S. D. Ross, M. Finkelstein, and R. C. Petersen, *J. Amer. Chem. Soc.*, **86**, 4139 (1964).

(11) J. O'M. Bockris and A.K.N. Reddy, "Modern Electrochemistry," Vol. 2, Plenum Press, New York, N. Y., 1970.

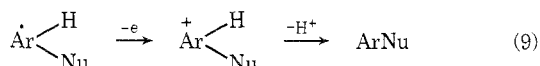
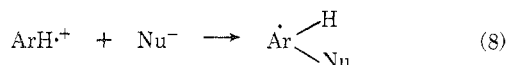
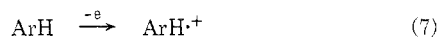
(12) In this case we are dealing with a dehydrodimerization process, which we have chosen to classify as a substitution reaction.

(13) For a review, see L. Ebersson in "The Chemistry of Carboxylic Acids and Esters," S. Patai, Ed., Interscience, New York, N. Y., 1969, Chapter 2, and ref 1g, Chapter 13.

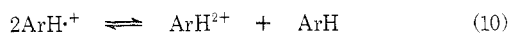
was formulated as a two-electron oxidation of the substrate to form a dication (eq 5), followed by its reaction with acetate ion. The resulting intermediate was thought to lose a proton rapidly to form product (eq 6). This mechanism in the electrochemists' jargon is an EECC process (Electrochemical-Electrochemical-Chemical-Chemical step).



The dication postulate initiated a lively discussion. An alternative mechanism, of the ECEC type, involves an initial one-electron transfer to give a cation radical, followed by reaction with a nucleophile to give a neutral radical. This radical is oxidized in a second one-electron step (eq 7-9) to give the same intermediate as in eq 6.



The ECEC mechanism was at one time postulated to be valid for all direct anodic substitution reactions,²⁵ but this was soon disputed. In the intervening time, cation-radical chemistry in homogeneous solution had been developed into a thriving area of research, primarily through work by Shine²⁶ and Ledwith²⁷ and their coworkers. Kinetic studies in homogeneous solution^{26a} suggested that the nucleophilic reactions of certain cation radicals proceed through the dication *via* a fast disproportionation equilibrium (eq 10). Thus, the whole problem was



open for discussion again.²⁸ Since this discussion is of limited importance for the *practical* applications of anodic oxidations, we shall not dwell upon it further but shall assume that the cation radical is the species that undergoes the nucleophilic follow-up reactions in anodic substitution.²⁹

A variation of the ECEC mechanism was proposed by one of us³⁰ in order to account for some interesting features of anodic aromatic acetoxylation. It was discovered that a benzylic hydrogen could be

(25) G. Manning, V. D. Parker, and R. N. Adams, *J. Amer. Chem. Soc.*, **91**, 4584 (1969).

(26) (a) Y. Murata and H. J. Shine, *J. Org. Chem.*, **34**, 3368 (1969); (b) J. J. Silber and H. J. Shine, *ibid.*, **36**, 2923 (1971); (c) C. V. Ristagno and H. J. Shine, *ibid.*, **36**, 4050 (1971).

(27) A. Ledwith, *Accounts Chem. Res.*, **5**, 133 (1972).

(28) V. D. Parker and L. Eberson, *J. Amer. Chem. Soc.*, **92**, 7488 (1970); L. Marcoux, *ibid.*, **93**, 537 (1971); O. Hammerich and V. D. Parker, *J. Electroanal. Chem.*, **36**, 11A (1972); **38**, 9A (1972).

(29) It is pertinent to note that an analogous problem exists for anion radicals in their reactions with electrophiles, both in homogeneous systems and at electrodes: S. Bank and B. Bockrath, *J. Amer. Chem. Soc.*, **93**, 430 (1971); G. Levin and M. Szwarc, *Chem. Commun.*, 1029 (1971); M. Szwarc, *Accounts Chem. Res.*, **5**, 169 (1972); M. Peover in "Electroanalytical Chemistry," Vol. 2, A. J. Bard, Ed., Marcel Dekker, New York, N. Y., 1967, Chapter 1, and in "Reactions of Molecules at Electrodes," N. S. Hush, Ed., Wiley-Interscience, London, 1971, Chapter 5.

(30) L. Eberson, *J. Amer. Chem. Soc.*, **89**, 4669 (1967).

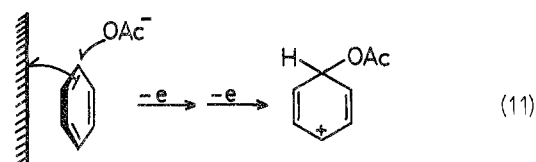
Table I
Distribution between Nuclear and α Cyanation and Acetoxylation^{30,32,33b}

Compound	Anodic cyanation, ^a %		Anodic acetoxylation, ^b %	
	Nuclear	α	Nuclear	α
Toluene	99.5	0.5 ^c	71	29
Ethylbenzene	100	0	49	51
Mesitylene	100	0.1 ^c	72	28

^a In CH₃OH-NaCN. ^b In HOAc-NaOAc. ^c Limit of detection.

substituted by an acetoxy group. Thus, α acetoxylation competes with nuclear acetoxylation in HOAc-NaOAc. A major difference between α and nuclear acetoxylation is, however, that the nuclear process is dependent on the presence of AcO⁻ in the electrolyte, whereas α acetoxylation occurs in the presence of other ions too, such as ClO₄⁻ or tosylate ion.

Since it appeared likely that a cation radical would react rapidly with HOAc, it was suggested that in the nuclear process AcO⁻ assists the electron transfer from an adsorbed substrate molecule (eq 11) with direct formation of a neutral radical, followed by the usual EC steps.³¹



Cyanation. Thus, nuclear substitution seems to require a fairly strong nucleophile, assisting the electron transfer from an adsorbed substrate molecule, whereas α substitution occurs without any such assistance. According to this reasoning, a stronger nucleophile than AcO⁻ should direct substitution preferentially to the ring, which was confirmed by a study³² of the cyanation process taking place upon anodic oxidation of aromatic compounds in, *e.g.*, CH₃OH-NaCN.³³ This reaction proceeds *via* a direct mechanism^{32,34} and gives no α substitution (see Table I). Another consequence of the higher nucleophilicity of CN⁻ ion as compared to AcO⁻ in the concerted mechanism (eq 11) should be a higher selectivity with respect to the (ortho + para)/meta ratio. Again this prediction fits with experimental data (Table II).

Anodic Acetamidation. Having established that carbonium ions generated *via* anodic oxidation of carboxylate ions (RCOO⁻ \rightarrow R⁺ + CO₂ + 2e⁻) react with acetonitrile to form *N*-alkylacetamides in an electrochemical Ritter reaction,^{35,36} we looked for

(31) Cf. also R. Dietz, *Discuss. Faraday Soc.*, **45**, 269 (1968).

(32) L. Eberson and S. Nilsson, *Discuss. Faraday Soc.*, **45**, 242 (1968).

(33) (a) K. Koyama, T. Susuki, and S. Tsutsumi, *Tetrahedron Lett.*, 627 (1965); (b) *Discuss. Faraday Soc.*, **45**, 247 (1968).

(34) (a) V. D. Parker and B. E. Burgert, *Tetrahedron Lett.*, 4065 (1965); (b) S. Andreaes and E. W. Zahnov, *J. Amer. Chem. Soc.*, **91**, 4181 (1969).

(35) L. Eberson and K. Nyberg, *Acta Chem. Scand.*, **18**, 1567 (1964).

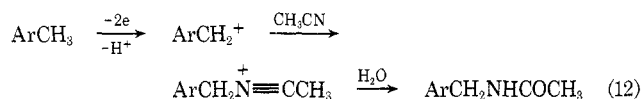
(36) For further work on this reaction, see (a) J.-M. Kornprobst, A. Laurent, and E. Laurent-Dieuzéide, *Bull. Soc. Chim. Fr.*, 3657 (1968); 1490 (1970); (b) D. L. Muck and E. R. Wilson, *J. Electrochem. Soc.*, **117**, 1358 (1970).

Table II
Isomer Distribution in Nuclear Anodic Cyanation and Acetoxylation of Aromatic Compounds

Compound	Anodic cyanation, ^a %			Anodic acetoxylation, ^b %		
	Ortho or 11	Meta or 2-	Para	Ortho or 1-	Meta or 2-	Para
Anisole	53; 51	0.1; 0	47; 49	67	4	29
Toluene	40; 32	8; 3	52; 65	43	11	46
Ethylbenzene	33	10	57	44	10	46
Isopropylbenzene				44	17	39
tert-Butylbenzene				35	22	43
Diphenylmethane				43	12	45
Fluorobenzene				34	8	58
Chlorobenzene	50	0.5	50	37	5	58
Bromobenzene				30	3	67
Iodobenzene				17	4	79
Biphenyl	24; 30	0.4; 0	70; 75	31	1	68
Naphthalene	90	10		96	4	

^a The first number refers to cyanation in $\text{CH}_3\text{OH}-\text{NaCN}$.^{32,33b} The second to cyanation in $\text{CH}_3\text{CN}-\text{Et}_4\text{NCN}$.^{34b} ^b In $\text{HOAc}-\text{NaOAc}$.³⁰

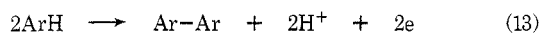
a similar course in the oxidation of alkylaromatic hydrocarbons in $\text{CH}_3\text{CN}-\text{NaClO}_4$ (eq 12), provided the



mechanism really involved the formation of benzylic cations as postulated for α acetoxylation. Indeed this reaction gives predominantly *N*-benzylacetamides from methylaromatic hydrocarbons *via* a direct mechanism.³⁷ Interesting effects were observed with regard to the nucleophilicity order between acetonitrile and water (see below).

Coupling. According to the definition given in eq 1, the substrate R-E can function both as electroactive species and nucleophile. In order to achieve a coupling reaction, the nucleophilicity of other species present must be low, or otherwise normal substitution takes place.

When R-E is an alkylbenzene, two types of coupling products, biphenyls and diphenylmethanes (eq 13 and 14), are generally formed.³⁸ Although in both



cases high substrate concentrations favored the formation of dehydro dimers, biphenyl coupling was less sensitive to the nucleophilicity of the medium than diphenylmethane coupling. Thus, anodic oxidation of mesitylene produced bimesityl (2,2',4,4',6,6'-hexamethylbiphenyl) in high yield in $\text{Bu}_4\text{NBF}_4-\text{CH}_3\text{COOH}$,³⁹ $\text{Bu}_4\text{NBF}_4-\text{CH}_3\text{CN}$,⁴⁰ and $\text{Bu}_4\text{NBF}_4-\text{CH}_2\text{Cl}_2$,³⁸ whereas anodic oxidation of durene in the same media produced the acetate (2,4,5-trimethyl-

benzyl acetate), the acetamide [*N*-(2,4,5-trimethylbenzyl)acetamide], and the coupling product (2,2',3',4,5,5',6'-heptamethyldiphenylmethane), respectively.

Several other methylbenzenes were investigated in media of low nucleophilicity.⁴¹ Biaryl coupling was generally the major reaction mode for anodic oxidation of 1,3,5-trialkylbenzenes,⁴² mesitylene being converted to bimesityl in almost 50% yield on a preparative scale.⁴³

Mixed coupling takes place under certain reaction conditions.⁴⁴ Anodic oxidation of naphthalene in $\text{Bu}_4\text{NBF}_4-\text{CH}_3\text{CN}-\text{CH}_3\text{COOH}$ in the presence of alkylbenzenes produced 1-aryl-substituted naphthalenes, the yield being dependent on the nucleophilicity of the alkylbenzene and increasing in the order *m*-xylene < 1,2,4-trimethylbenzene < durene < mesitylene < isodurene < pentamethylbenzene. Large-scale oxidation of naphthalene in the presence of isodurene produced 1-(2,3,4,6-tetramethylphenyl)naphthalene in 42% yield, and in the presence of pentamethylbenzene, 1-(pentamethylphenyl)naphthalene in 56% yield.⁴⁵

These results suggest that the dehydro dimers are formed *via* electrophilic pathways. The primary species, the cation radical, either reacts with a substrate molecule (biphenyl formation) or in the case of a methylbenzene loses an α proton to form a benzyl radical that is further oxidized to a benzyl cation that reacts with a substrate molecule (diphenylmethane formation). In support of this mechanism, the yield of bimesityl from oxidation of mesitylene increased when the concentration of mesitylene was increased, whereas varying the current density had no effect.

Other Direct Processes. A number of other types of anodic substitutions involving direct mechanisms are known. Among these are anodic methoxylation,⁴⁶ hydroxylation⁴⁷ (anodic hydroxylation of benzo[*a*]pyrene^{47a} and simple phenols^{47b} has been thoroughly investigated as a model for biological hydroxylation), pyridination,⁴⁸ and cyanation.⁴⁹

Influence of Adsorption

The structure and composition of the EI are dependent on the adsorbability^{50,51} of the electrolyte

(41) K. Nyberg, *Acta Chem. Scand.*, **25**, 2499 (1971).

(42) K. Nyberg, *Acta Chem. Scand.*, **25**, 2983 (1971).

(43) Diphenylmethane coupling was the predominant reaction for *p*-xylene, durene, and pentamethylbenzene. 1,2,4-Trimethylbenzene and isodurene gave a mixture of biphenyls and diphenylmethanes. The yield of products was always higher from polysubstituted benzenes than from mono- and disubstituted ones since the latter types give products that are easier to oxidize than the starting materials. Thus one ends up with a lot of polymers.

(44) K. Nyberg, *Acta Chem. Scand.*, **25**, 3770 (1971).

(45) K. Nyberg, *Acta Chem. Scand.*, in press.

(46) N. L. Weinberg and E. A. Brown, *J. Org. Chem.*, **31**, 4058 (1966); N. L. Weinberg and T. B. Reddy, *J. Amer. Chem. Soc.*, **90**, 91 (1968); N. L. Weinberg, *J. Org. Chem.*, **33**, 4326 (1968).

(47) (a) L. Jęftic and R. N. Adams, *J. Amer. Chem. Soc.*, **92**, 1332 (1970); (b) A. Nilsson and A. Ronlán, *J. Chem. Soc., Perkin Trans. 1*, in press.

(48) (a) V. D. Parker and L. Ebersson, *Chem. Commun.*, 973 (1969); (b) M. Sainsbury, *J. Chem. Soc. C*, 2888 (1971).

(49) V. D. Parker and B. E. Burgert, *Tetrahedron Lett.*, 3341 (1968).

(50) (a) B. B. Damaskin, O. A. Petrii, and V. V. Batrakov, "Adsorption of Organic Compounds on Electrodes," Plenum Press, New York, N. Y., 1971; (b) "Electrosorption," E. Gileadi, Ed., Plenum Press, New York, N. Y., 1967.

(37) (a) L. Ebersson and K. Nyberg, *Tetrahedron Lett.*, 2389 (1966); (b) V. D. Parker and B. E. Burgert, *ibid.*, 2411 (1968); (c) L. Ebersson and B. Olofsson, *Acta Chem. Scand.*, **23**, 2355 (1969); (d) K. Nyberg, *Chem. Commun.*, 774 (1969).

(38) K. Nyberg, *Acta Chem. Scand.*, **24**, 1609 (1970).

(39) K. Nyberg, *Chem. Scr.*, **1**, 57 (1971).

(40) K. Nyberg, *Acta Chem. Scand.*, **25**, 534 (1971).

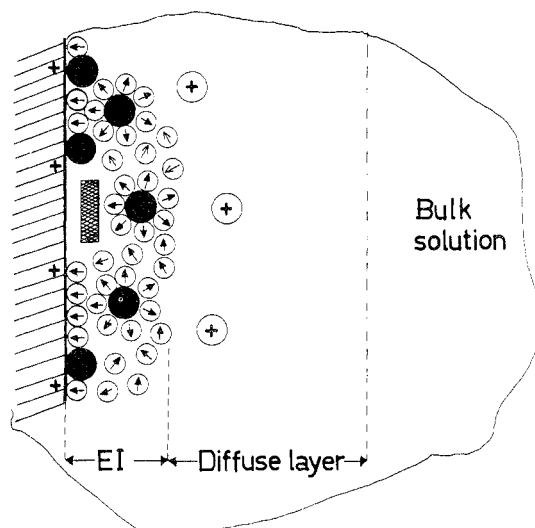
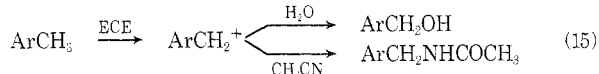


Figure 1. Schematic representation of the anode EI (for explanation of symbols, see text). The *diffuse layer* is the region separating the EI and the bulk electrolyte and is between 50 and 100 Å thick.

components. A crude model⁵² of the anode EI is depicted in Figure 1. Filled circles represent negative ions, either specifically adsorbed through some kind of weak bonding to the electrode or nonspecifically adsorbed through electrostatic forces in an outer layer. The small circles are solvent molecules, the arrow indicating the direction of their dipole. Outside the second layer some cations are shown. The last feature of Figure 1 is a schematic representation of an aromatic hydrocarbon, considered to be adsorbed with the ring plane parallel to the electrode plane *via* a bond closely related to the π bond of π -donor-acceptor complexes.⁵³ This is admittedly a crude qualitative model, which at present cannot be extended into a quantitative one.

Nucleophilicity. Anodic acetamidation exhibited some unusual features upon closer study.^{37c,d} When water was added to the electrolyte there was a competition between capture of an anodically generated benzyl cation by H_2O and CH_3CN , respectively (eq 15). However, for a series of benzyl cations the *less*



reactive ones were selective toward the *weaker* nucleophile, acetonitrile, contrary to predictions based on concepts from homogeneous solution chemistry. Moreover, in a certain region of water concentrations the competition ratio between the two processes was constant for each substrate, indicating that the composition of the EI is independent of that of the bulk electrolyte. A similar phenomenon was encountered when water was exchanged for acetic acid; in this case the anion of the supporting electrolyte turned out to have a strong influence in that BF_4^- favors

(51) Adsorption of anions on metal electrodes can be qualitatively treated as a soft-soft coordination reaction in terms of Pearson's HSAB principle. See: D. J. Barclay and J. Caja, *Croatica Chim. Acta*, **43**, 221 (1971).

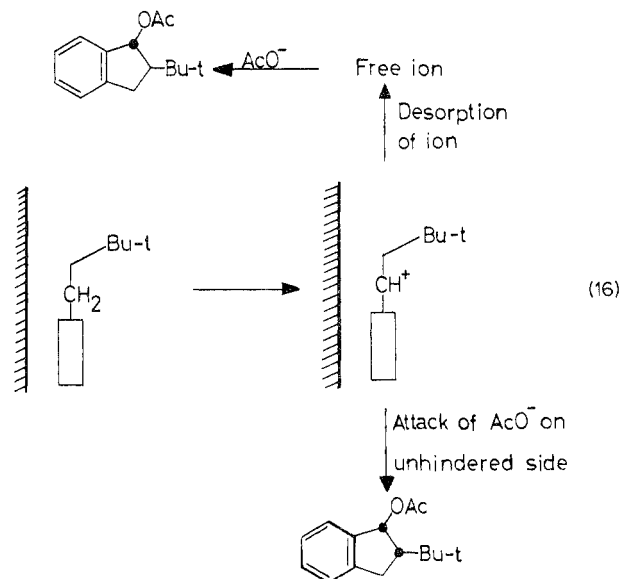
(52) Based on the models discussed in ref 11.

(53) (a) H. Dahms and M. Green, *J. Electrochem. Soc.*, **110**, 1075 (1963); (b) J. O'M. Bockris, M. Green, and D. A. J. Swinkels, *ibid.*, **111**, 743 (1964); (c) X. de Hemptinne, *Ann. Soc. Sci. Bruxelles*, **80**, 140 (1966).

acetate formation strongly as compared to ClO_4^- , perhaps because the more strongly hydrogen-bonding BF_4^- brings more acetic acid into the EI than ClO_4^- .⁵⁴

Anomalous results of this type are not confined to the system described above.⁵⁵ One finds the same puzzling phenomenon for Kolbe-generated carbonium ions (eq 2) in their reactions with water and acetonitrile.^{36b} It takes more than 25% water to produce any alcohol, and besides very few cations are captured by the carboxylate ion present. Also pyridine and water show an inverse nucleophilicity order in the presence of Kolbe-generated carbonium ions.^{13,56}

Stereochemistry. The concept of a π -type adsorption complex between an aromatic hydrocarbon and the electrode surface immediately suggests that the electrode might sterically control the anodic process. As an example, one could make one face of the aromatic compound sterically hindered for approach toward the surface and thus favor adsorption *via* the unhindered side. We have explored this idea on two compounds, 2-*tert*-butylindan and 1-*tert*-butylacetonaphthene (1 and 2), in which a *tert*-butyl group provides the necessary steric hindrance. If the reasoning is correct, one might expect an abnormally high *cis/trans* ratio in α acetoxylation, provided the initial substrate-electrode configuration is kept during the whole ECEC sequence (as exemplified by 1 in eq 16).



If on the other hand the cation is desorbed before being trapped by AcO^- , the result would be the same as if the cation was generated in a homogeneous medium.

(54) It has been suggested (E. A. Mayeda and L. L. Miller, *Tetrahedron*, **28**, 3375 (1972)) that these phenomena might be explained on the basis of the electrolyte becoming acidic during electrolysis, thus creating conditions to convert a benzyl alcohol or acetate into the thermodynamically favored *N*-benzylacetamide. We have checked this possibility but find that the electrolytes remain neutral during the runs. It cannot be dismissed, however, that a *locally* high $[\text{H}^+]$ near the electrode surface (*cf.* eq 12) might cause these phenomena.

(55) In *cathode* reactions, inverse *electrophilicity* orders are similarly observed. Thus, in certain cases Et_4N^+ appears to be a more efficient proton donor than H_2O , PhOH , or HOAc (*cf.* A. J. Fry and R. G. Reed, *J. Amer. Chem. Soc.*, **93**, 553 (1971)).

(56) A good example of this behavior is found in P. G. Gassman and F. V. Zalar, *J. Amer. Chem. Soc.*, **88**, 2252 (1966).

For 1, the *cis/trans* ratio of 1-acetoxy-2-*tert*-butylindan is indeed abnormally high when the reaction is conducted at a Pt anode in HOAc-NaOAc. The ratio is 0.19, which is about ten times larger than that observed (0.01-0.02) when the 2-*tert*-butyl-1-indanyl cation is generated by a solvolysis reaction under similar conditions;⁵⁷ at a C anode the ratio is 0.05, in line with the order of adsorptivity between these two electrode materials.

For 2, the Pt *vs.* C behavior was the same as for 1, but it was not possible to obtain reliable data regarding the behavior of a homogeneously generated 1-*tert*-butyl-2-acenaphthyl cation. The most unusual feature here is that 2 substitution is favored over 1 substitution by a factor of 35, in spite of the fact that 1 substitution proceeds *via* a tertiary carbonium ion. This indicates that removal of the 1-proton by base is strongly hindered, exactly as expected for a substrate-electrode complex in which the *tert*-butyl group points away from the electrode.⁵⁸

Effect on Orientation in Aromatic Substitution. While studying the feasibility of using competition experiments⁵⁹ for studying electrode processes, we noticed that anodic acetoxylation of anisole alone gave a different isomer distribution from that observed in the presence of an equimolar amount of naphthalene,⁶⁰ the ortho/para ratio changing from 2.2 to 1.0. This phenomenon was dependent on [naphthalene]/[anisole] in a way characteristic of adsorption processes and was caused by a variety of aromatic molecules (Table III). Significantly, strong π donors (*e.g.*, naphthalene and pentamethylbenzene) caused greater changes in the ortho/para ratio than weak ones (*e.g.*, biphenyl and *tert*-butylbenzene), thus supporting the π -donor-acceptor model of aromatic adsorption. Although the effect is rather small, it is of general interest in connection with preparative work. Suppose we could find additives which, added in small amounts to an electrolyte, would change the product distribution significantly. If these additives in themselves are electroinactive, we would have truly catalytic processes at hand.⁶¹

Synthetic Applications of Anodic Substitution Reactions

Although the major part of the work on anodic substitution reactions in the last decades has been concerned with mechanistic problems, the hope of practical applications has been a strong motivation. As is evident from eq 1, anodic substitution offers a unique way of introducing functional groups into cheap starting materials, such as hydrocarbons. Our own main interest has been directed toward the possible use of anodic acetoxylation, acetamidation, cyanation, and dehydrodimerization reactions (eq 1,

Table III
Influence of Additives upon the Ortho/Para Ratio in the Acetoxylation of Anisole in HOAc-1.0 M NaOAc (Pt Anode)

Additive	[Additive]/ [Anisole]	Ortho/Para ratio
None		2.2
Naphthalene	1.00	1.0
Pentamethylbenzene	1.00	1.0
<i>tert</i> -Butylbenzene	1.00	1.0
Biphenyl	1.00	2.7
Pyrene	0.100	1.3
Anthracene	0.050	1.6
Coronene	0.0050	4.2
Hexahelicene	0.0050	4.0

Nu⁻ = OAc⁻, CH₃CN, CN⁻, and R-E) for the synthesis of aromatic compounds of different types. The possibility of unidirectional selectivity in the acetoxylation of alkylaromatics had led to a synthetic procedure for preparing benzylic acetates in good yield using HOAc-Bu₄NBF₄ as supporting electrolyte. Thus *p*-xylene and durene have been converted to 4-methylbenzyl and 2,4,5-trimethylbenzyl acetate, respectively, in over 50% yield on a large laboratory scale (2-5 mol/run).⁶²

The preparation of aryl acetates in good yields is hampered by the problem of low selectivity in the case of alkylaromatics, and of further oxidation of initially formed product in the general case. The anode material seems to have some effect on the aryl acetate/ α acetate ratio, being larger on graphite or lead dioxide than on platinum or gold.⁶³

It should be mentioned that acetoxylation works with certain types of aliphatic substrates too, such as olefins⁶⁴ and *N,N*-dialkylamides.⁶⁵ In the latter case, excellent yields of *N*-(α -acetoxyalkyl)-*N*-alkylamides are obtained.

A carbon-nitrogen bond is formed in the acetamidation of the α position in alkylaromatics or the allylic position of simple olefins. At least in the case of alkylaromatics, the reaction gives good yields for substitution into methyl groups only.

The synthesis of aromatic nitriles by anodic cyanation of aromatics is an attractive possibility, but has so far not been developed on a large scale due to the difficulty in finding a good solvent-supporting electrolyte system. NaCN-MeOH gives appreciable amounts of by-products (methoxylation), whereas Et₄N⁺CN⁻-CH₃CN is far too expensive.

There are few methods for preparing biaryls and diphenylmethanes through a short reaction sequence starting from aromatic hydrocarbons, and therefore the anodic dehydrodimerization reaction should find use in selected cases. Limitations of the method are: (1) mono- and disubstituted benzenes do not work well due to polymerization reactions, and (2) the

(57) L. Ebersson and H. Sternerup, *Acta Chem. Scand.*, **26**, 1431 (1972).

(58) L. Ebersson and J. P. Dirlam, *Acta Chem. Scand.*, **26**, 1454 (1972).

(59) Cf. L. Ebersson, *J. Amer. Chem. Soc.*, **91**, 2402 (1969).

(60) L. Ebersson and R. G. Wilkinson, *Acta Chem. Scand.*, **26**, 1671 (1972).

(61) One possible case of catalytic stereoselective electrolyses is the cathodic reduction of certain compounds in the presence of optically active cations. Here asymmetric induction (up to 20%) is observed and the cations are electroinactive: R. N. Gourley, J. Grimshaw, and P. G. Miller, *J. Chem. Soc. C*, 2318 (1970); L. Horner, D. Degner, and D. Skaletz, *Chem.-Ing.-Tech.*, **44**, 209 (1972).

(62) We have recently developed a very simple flow cell which allows for passage of up to 50 A through organic electrolytes at applied potentials in the range of 10-50 V (L. Ebersson, K. Nyberg, and H. Sternerup, *Chem. Scr.*, **3**, 12 (1973)).

(63) U. S. Patent 1021908 (1964); U. S. Patent, 3347758 (1967); V. D. Parker, *Chem. Commun.*, 1164 (1968).

(64) P. Courbis and A. Guillemonat, *C. R. Acad. Sci. Ser. C*, **262**, 1435 (1966).

(65) S. D. Ross, M. Finkelstein, and P. C. Petersen, *J. Amer. Chem. Soc.*, **86**, 2745 (1964); **88**, 4657 (1966); *J. Org. Chem.*, **31**, 128 (1966).

nucleophilicity of the aromatic hydrocarbon is sometimes too low for reaction with a cation radical to occur. On the other hand, the anodic coupling of polysubstituted benzenes appears to be a superior way of preparing certain biaryls in quantities.⁶² The preparation of mixed biaryls is also an example of the usefulness of anodic synthesis.⁶²

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