

Hydrolysis of α,α,α -Trichlorotoluene. α,α,α -Trichlorotoluene (4.1 g, 21 mmol) was stirred magnetically with 30 ml of 20% aqueous NaOH at 80°. Runs catalyzed by surfactant contained either 0.11 g (0.30 mmol) of cetyltrimethylammonium bromide or 0.20 g (0.17 mmol) of Brij 35. All organic reagents were purchased from Aldrich. The work-up of product consisted of acidifying with HCl, cooling in ice, filtering, washing the collected solid with cold water, and drying the solid. The unpurified benzoic acid melted at 119–121°.

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Registry No.—Piperonal, 120-57-0; piperonylic acid, 94-53-1; α,α,α -trichlorotoluene, 98-07-7; benzoic acid, 65-85-0; cetyltrimethylammonium bromide, 57-09-0; Brij 35, 9002-92-0; tetrabutylammonium bromide, 1643-19-2.

References and Notes

- Recipient of a Camille and Henry Dreyfus Foundation Teacher-Scholar Grant and a National Institutes of Health Research Career Development Award.
- A large number of examples may be found in "Organic Syntheses".
- D. Martin, A. Weise, and H.-J. Niclas, *Angew. Chem., Int. Ed. Engl.*, **6**, 318 (1967).
- C. L. Liotta and H. P. Harris, *J. Am. Chem. Soc.*, **96**, 2250 (1974); D. J. Sam and H. E. Simmons, *ibid.*, **96**, 2252 (1974).
- E. V. Dehmlow, *Angew. Chem., Int. Ed. Engl.*, **13**, 170 (1974); J. Dockx, *Synthesis*, 441 (1973).
- E. H. Cordes, Ed., "Reaction Kinetics in Micelles", Plenum Press, New York, N.Y., 1973.
- Polymerization in the presence of an emulsifying agent is a well-known industrial process: W. D. Harkins, "The Physical Chemistry of Surface Films", Reinhold, New York, N.Y., 1952. For specific examples see E. B. Berkowitz and H. T. Hanson, *Chem. Abstr.*, **71**, P81886 (1969); R. Lanthier, *ibid.*, **68**, P22368 (1968).
- R. L. Shriner and E. C. Kleiderer, "Organic Syntheses", Collect. Vol. II, Wiley, New York, N.Y., 1943, p 538, report a >80% yield for the same reaction carried out on a much larger scale and at a higher temperature. This does not negate the potential usefulness of the fact that under the experimental conditions described in Table I the surfactant substantially improves the yields.
- M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *J. Am. Chem. Soc.*, **87**, 266 (1965); C. A. Bunton and L. Robinson, *J. Org. Chem.*, **34**, 773 (1969); F. M. Menger and C. E. Portnoy, *J. Am. Chem. Soc.*, **89**, 4698 (1967).
- However, most phase transfer catalysts possess *N*-alkyl groups larger than methyl because solubility in the organic phase is necessary for activity.
- A. W. Herriott and D. Picker, *J. Am. Chem. Soc.*, **97**, 2345 (1975).
- M. Makosza, *Tetrahedron Lett.*, 5489 (1966); A. Brandstrom and U. Junggren, *Acta Chem. Scand.*, **23**, 2204 (1969).
- It is not clear whether the small activity of tetramethylammonium bromide in Table II results from phase transfer catalysis or from the surface activity of the salt. See E. M. Arnett, M. Ho, and L. L. Schaleger, *J. Am. Chem. Soc.*, **92**, 7039 (1970), Figure 3.
- C. M. Starks, *J. Am. Chem. Soc.*, **93**, 195 (1971).
- H. E. Zaugg and R. T. Rapala, "Organic Syntheses", Collect. Vol. III, Wiley, New York, N.Y., 1955, p 820.
- H. L. Vaughn and M. D. Robbins, *J. Org. Chem.*, **40**, 1187 (1975).
- An ideal surfactant forms only unstable emulsions. Cetyltrimethylammonium bromide (although commercially available and cheap) leaves something to be desired in this regard. Further work is required to improve the technology.

Anodic Acetoxylation of Dimethoxybenzenes

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Many of the electrochemical oxidations of aromatic compounds are considered to proceed via cation radical intermediates.¹ Dimethoxybenzenes produce the quinone diketals in methanolic potassium hydroxide² and form methoxybenzonitriles in acetonitrile solution of tetraethylammonium cyanide³ or in methanol containing sodium cy-

anide.⁴ These products arise from the attack of nucleophiles on the highest positive center of cation radical, a carbon atom bearing a methoxy substituent. When a bulky nucleophile such as pyridine or substrate itself is used, the attacking point changes; the anodic pyridination⁵ and the anodic coupling⁶ of *o*-dimethoxybenzene¹⁰ occur on the carbon atom with an aromatic hydrogen.

On the other hand, the electron transfer reaction of dimethoxybenzenes by lead tetraacetate in acetic acid produces dimethoxyphenyl acetates.¹¹ In this case, the acetoxylation position is the carbon atom with an aromatic hydrogen. Data on anodic acetoxylation are indispensable to clarify which is the cause of an apparent contradiction of attacking points, the different oxidant or the nature of nucleophile. Anodic acetoxylation of dimethoxybenzenes has been described only in the case of the para isomer. The reported product is 2,5-dimethoxyphenyl acetate; however, details are not clear.¹²

Results

Methoxybenzenes were electrolyzed in a one-compartment cell under a nitrogen atmosphere using platinum foil anode in glacial acetic acid containing sodium acetate with a constant current of 0.1 A. The results of these studies are summarized in Table I.

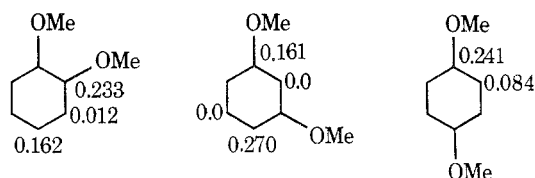
Anodic oxidation of *p*-dimethoxybenzene produced a 68% yield of 2,5-dimethoxyphenyl acetate as the sole organic product, except for a very small amount of a brownish substance.

The electrochemical oxidation of *m*-dimethoxybenzene gave a 2.5% yield of a 16:1 mixture of 2,4- and 2,6-dimethoxyphenyl acetate, respectively, together with a considerable amount of tarry product.

Under identical conditions, *o*-dimethoxybenzene produced a 8.9% yield of a mixture of 2,3- and 3,4-dimethoxyphenyl acetate in the proportions 1:90, along with a significant amount of tarry residue.

Discussion

The primary step of anodic acetoxylation is attributed to a direct discharge of the aromatic at the anode to a cation radical intermediate.^{1,13} The second stage is the combination reaction of the cation radical intermediate with nucleophile. Observed orientations in the aromatic cyanation of methoxybenzenes are in accord with the spin density distributions calculated from ESR spectra of the cation radicals.^{3,14,15} In each case, the methoxyl displacement by



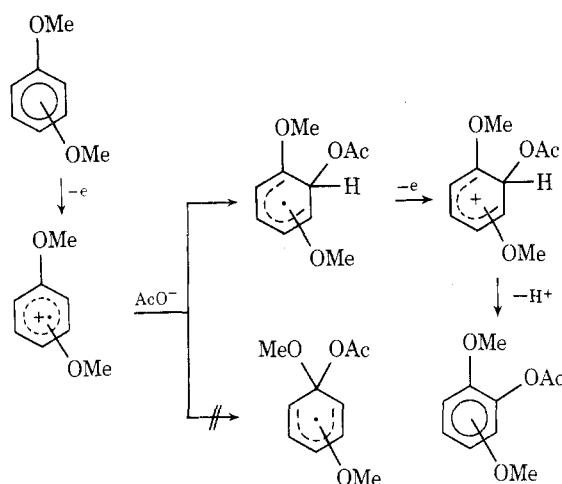
cyanide ion occurs at the position of highest spin density. This can also account for the position of attack by methoxide ion.² In contrast, the acetoxylation by a metal ion oxidant¹¹ and the present electrode process does not occur at these positions. This would be ascribable to the instability of an acylal type intermediate, because acetate ion is a better leaving group than methoxide ion.²⁰ Bonding between the oxygen atom of the cation radical and acetate ion, followed by rearrangement,²¹ is also improbable, because *o*-dimethoxybenzene does not produce 2,3-dimethoxyphenyl acetate predominantly (see Table I). The mechanism shown in Scheme I would, therefore, be reasonable to account for the anodic acetoxylation of dimethoxybenzenes.

Table I
Anodic and Lead Tetraacetate Oxidation of Dimethoxybenzenes

Reactant ^d	Faradays	Conversion, %	Product ^e	Yield, ^b %	Product distribution	
					Anodic	Lead tetraacetate
<i>p</i> -Dimethoxybenzene	0.183	93.1	2,5-Dimethoxyphenyl acetate	68.0	100	100
<i>m</i> -Dimethoxybenzene ^a	0.072	34.5	2,4-Dimethoxyphenyl acetate	2.3	94	95
			2,6-Dimethoxyphenyl acetate	0.2	6	5
			2,3-Dimethoxyphenyl acetate	0.1	1	1
<i>o</i> -Dimethoxybenzene ^a	0.074	13.8	3,4-Dimethoxyphenyl acetate	8.8	99	99

^a Considerable amounts of tarry substance were produced. ^b Based on dimethoxybenzene consumed. ^c Data from ref 11. ^d Registry no. are, respectively, 150-78-7, 151-10-0, 91-16-7. ^e Registry no. are, respectively, 27257-06-3, 27257-07-4, 944-99-0, 27257-08-5, 7203-46-5.

Scheme I



Isomer distributions from anodic acetoxylation are also shown in Table I, together with the corresponding data from lead tetraacetate oxidation. A comparison between anodic and lead tetraacetate oxidations demonstrates the fundamental similarity between these two reactions; the cation radical intermediates produced from the different sources show the analogous preference for aromatic acetoxylation.

An alternative mechanism for aromatic substitution involves an aromatic proton release,^{22,23} followed by further anodic oxidation and attack by acetate ion (or solvent acetic acid), thus leading to the aromatic acetoxylation products. However, this mechanism cannot elucidate the isomer distribution observed.

Experimental Section

The spectroscopic instrumentation was as previously described.¹⁷

Materials. Analytical grade acetic acid and sodium acetate were used directly. *o*- and *m*-dimethoxybenzene were shaken with aqueous sodium hydroxide and purified by distillation. *p*-Dimethoxybenzene was recrystallized from ethanol.

The following reference materials were prepared according to the literature: *o*-, *m*-, and *p*-methoxyphenyl acetate,¹¹ 2,3-,^{11,24} 2,4-,²⁵ 2,5-,²⁶ 2,6-,²⁴ 3,4-,²⁷ and 3,5-dimethoxyphenyl acetate,^{26,28} and *o*-methoxyphenoxymethyl acetate.²⁶

Electrolysis. The preparative experiments were run according to the following standard procedure. The electrolyte was made up of 0.09 mol of the organic compound, 0.15 mol of anhydrous sodi-

um acetate, and 150 ml of glacial acetic acid. The electrolysis was conducted at the terminal voltage of about 20 V to maintain the current of 0.1 A in an undivided cell under a nitrogen atmosphere. Platinum foils having an area of 8 cm² were used as electrodes. During the electrolysis, the solution was stirred magnetically and cooled externally with water. The electrolyzed solution was poured into a vigorously stirred slurry of sodium bicarbonate in water. The ether extract was washed with sodium bicarbonate, dried over sodium sulfate, filtered, and stripped on a rotary evaporator. A crude product was then analyzed by GLC using AGL and PEG 6000 columns. Each product was separated in pure form by preparative VPC and characterized by ir and NMR spectra.

References and Notes

- (1) N. L. Weinberg, Ed., "Technique of Electroorganic Synthesis", Part 1, A. Weissberger, Ed., in "Techniques of Chemistry Series", Wiley, New York, N.Y., 1974.
- (2) N. L. Weinberg and B. Belleau, *Tetrahedron*, **29**, 279 (1973).
- (3) S. Andreades and E. W. Zahnow, *J. Am. Chem. Soc.*, **91**, 4181 (1969).
- (4) N. L. Weinberg, D. H. Marr, and C. N. Wu, *J. Am. Chem. Soc.*, **97**, 1499 (1975).
- (5) M. Sainsbury, *J. Chem. Soc. C*, 2888 (1971).
- (6) Cation radical pairing has been postulated as the mechanism for anodic coupling of aromatic compounds.^{7,8} Recently, a mechanism has been proposed for the coupling of aromatic hydrocarbons which involves the attack of anodically generated cation radicals on the aromatic substrate.⁹ Since methoxy aromatic compounds are far more nucleophilic than hydrocarbons, the latter mechanism would appear to be even more plausible for these substrates.
- (7) R. N. Adams, *Acc. Chem. Res.*, **2**, 175 (1969).
- (8) A. Ronl an, O. Hammerich, and V. D. Parker, *J. Am. Chem. Soc.*, **95**, 7132 (1973), and references cited therein.
- (9) K. Nyberg, *Acta Chem. Scand.*, **25**, 3770 (1971).
- (10) F. Fichter and W. Dietrich, *Helv. Chim. Acta*, **7**, 131 (1924).
- (11) R. O. C. Norman and C. B. Thomas, *J. Chem. Soc. B*, 421 (1970).
- (12) N. L. Weinberg, unpublished work; *Chem. Rev.*, **68**, 466 (1968).
- (13) L. Eberson and K. Nyberg, *Acc. Chem. Res.*, **6**, 106 (1973).
- (14) A. Zweig, W. G. Hodgson, and W. H. Jura, *J. Am. Chem. Soc.*, **86**, 4124 (1964).
- (15) There are two independent affinities to unite the cation radical with nucleophiles; one is the ability of radicals to combine with nucleophiles,¹⁶ and we can select the spin density as a measure, and the other is the positive charge in cation radicals.¹⁷⁻¹⁹ In almost all substrates, the spin density distributions coincide with the positive charge distributions.
- (16) D. Y. Myers, G. G. Stroebel, B. R. Ortiz de Montellano, and P. D. Gardner, *J. Am. Chem. Soc.*, **95**, 5832 (1973); **96**, 1981 (1974).
- (17) K. Yoshida and T. Fueno, *J. Org. Chem.*, **36**, 1523 (1971).
- (18) K. Yoshida, T. Saeki, and T. Fueno, *J. Org. Chem.*, **36**, 3673 (1971).
- (19) K. Yoshida, M. Shigi, and T. Fueno, *J. Org. Chem.*, **40**, 63 (1975).
- (20) R. T. Morrison and R. N. Boyd, "Organic Chemistry", 2nd ed, Allyn and Bacon, Boston, Mass., 1966, p 663.
- (21) The primary attack on the oxygen atom of anisole by benzyloxy radical could account for ortho substitution preponderance: B. M. Lynch and R. B. Moore, *Can. J. Chem.*, **40**, 1461 (1962).
- (22) T. Osa, A. Yildiz, and T. Kuwana, *J. Am. Chem. Soc.*, **91**, 3994 (1969).
- (23) G. Neubert and K. B. Prater, *J. Electrochem. Soc.*, **121**, 745 (1974).
- (24) F. Weygand, H. Weber, and E. Maekawa, *Chem. Ber.*, **90**, 1879 (1957).
- (25) J. S. Bradshaw, E. L. Loveridge, and L. White, *J. Org. Chem.*, **33**, 4127 (1968).
- (26) C. A. Bartran, D. A. Batty, and C. R. Worthing, *J. Chem. Soc.*, 4691 (1963).
- (27) D. G. Orphanos and A. Taurins, *Can. J. Chem.*, **44**, 1875 (1966).
- (28) K. Nakazawa and S. Matsuura, *J. Pharm. Soc. Jpn.*, **73**, 751 (1953).