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## Anodic Hydroxylation of Aromatic Compounds

*Sir:*

We report the first unequivocal evidence for anodic hydroxylation of aromatic compounds under voltammetric conditions. These hydroxylations take place at low potentials in aqueous solutions. The reaction details can be examined by quantitative electrochemical techniques and can provide valuable comparisons with hydroxylations of physiological significance.

To best illustrate the style of reaction, Figure 1A shows the cyclic voltammetry for the oxidation of 1,5-dihydroxynaphthalene in 2 *M* perchloric acid at a carbon paste electrode. (The electrochemical techniques and electrodes used are all conventional and have been described.[1] The initial oxidation peak N is at +0.54 V *vs.* sce, but there is practically no reversible reduction current for the corresponding quinone. Instead, a rapid follow-up chemical reaction has occurred and new reduction product is seen at peak J. On the second and subsequent scans, the new, reversible redox system (peaks J, J′) is well defined. This new redox system is readily identified as that of juglone–hydrojuglone (5-hydroxy-1,4-naphthoquinone–1,4,5-trihydroxynaphthalene). A controlled potential oxidation of 1,5-dihydroxynaphthalene at a potential corresponding to peak N yields a quinone whose nmr, ir, and uv spectra are identical with those of authentic juglone. Raising the pH of such a solution to about 12 gives an epr spectrum identical with that of the juglone semiquinone. Finally, the cyclic voltammetry of authentic 1,4,5-trihydroxynaphthalene (Figure 1B) matches perfectly that of the follow-up couple, J, J′. Clearly, in the over-all oxidation of 1,5-dihydroxynaphthalene, a hydroxyl group is inserted in position 4 of the naphthalene ring. The resulting 1,4,5-trihydroxynaphthalene is more easily oxidized than the starting material and first appears in the cyclic voltammetry as a reduction peak of juglone.

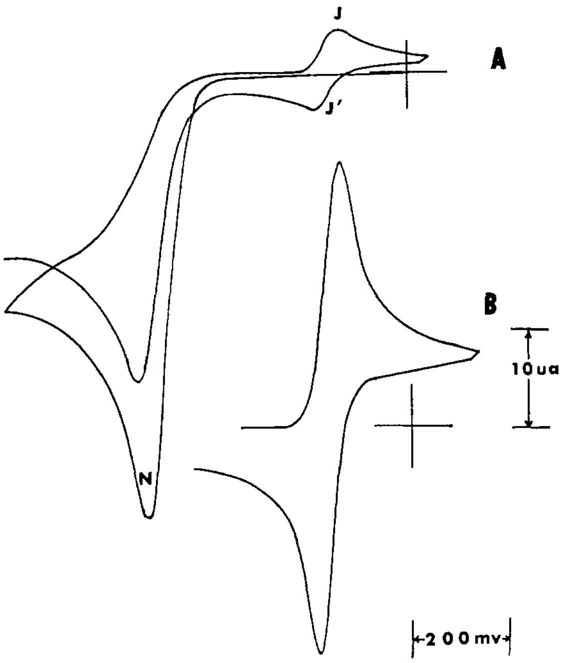
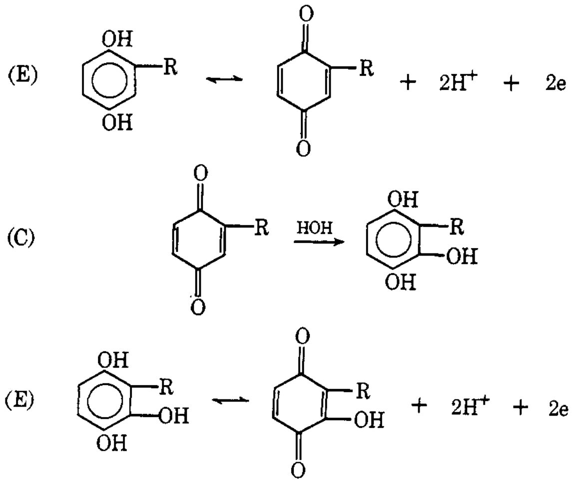


Figure 1. Cyclic voltammetry of anodic hydroxylation of 1,5-dihydroxynaphthalene: (A) cyclic polarogram of 1,5-dihydroxynaphthalene in 2 *M* $HClO_4$; (B) cyclic polarogram for oxidation of 1,4,5-trihydroxynaphthalene, same conditions.

The wider scope of such reactions is shown by a series of 2-substituted hydroquinones. If the 2 substituent is electron withdrawing like COOH, CHO, $NO_2$, hydroxylation occurs in an over-all process



For 2-nitrohydroquinone, after controlled potential electrolysis, a carbon–hydrogen analysis and mass spectrum of the 2,4-dinitrophenylhydrazine derivative of the quinone formed shows unquestionable proof of OH insertion. No hydroxylation occurs if the 2 substituent is Cl, $CH_3$, OH, or H. In this case the reaction only involves a two-electron oxidation to the ordinary benzoquinone (whereas a total of four electrons are found in the controlled potential coulometry of the COOH, CHO, and $NO_2$ derivatives). In acetonitrile all derivatives give a simple two-electron oxidation (if water is added to the acetonitrile, hydroxylation reappears for the above three compounds).

These reactions are typical 1,4-nucleophilic additions to quinones, but they have never been seen previously under these mild electrochemical conditions. We have not proven unequivocally that the hydroxyl group enters position 3 of the substituted hydroquinones. The nmr spectra of the products are not definitive enough for this proof. However, for the hydroquinone-2-carboxylic acid the cyclic voltammetry of the follow-up product is identical with that of authentic 2,3,6-trihydroxybenzoic acid. Molecular orbital calculations also show the 3 position to be that of highest positive charge, and hence the most reactive site for nucleophilic attack. The 1,4 addition of thiols to similar 2-substituted benzoquinones was shown to occur in the 3 position.[2]

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[1] For typical applications of the electrochemical techniques to anodic oxidations, see Z. Galus, H. Y. Lee, and R. N. Adams, *J. Electroanal. Chem.*, **5**, 17 (1963).

[2] H. S. Wilgus, E. Frauenglass, E. T. Jones, R. F. Porter, and J. W. Gates, *J. Org. Chem.*, **29**, 594 (1964).

We have found similar hydroxylations in the voltammetry of dimethoxybenzenes, methoxyphenols, and catechols. Sivaramaih and Krishnan have recently postulated a follow-up hydroxylation in the prolonged coulometric oxidation of catechol in sulfuric acid.[3]

Most of the hydroxylations of biological significance appear to involve molecular oxygen and hydroxyl or perhydroxyl radicals,[4] but nucleophilic reactions are not excluded and have been definitely established in some cases.[5] The exact pathways of hydroxylation in the biosynthesis of plant phenolics are particularly not well understood,[6] and the electrochemical studies may have particular relevance here. We are currently investigating the full range of these anodic hydroxylations including the kinetics and pH dependence.

**Acknowledgment.** The support of this work by the National Institutes of Health through Grant GM-13791 is gratefully acknowledged.

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(5) A. L. Hunt, D. E. Hughes, and H. M. Lowenstein, *Biochem. J.*, **66,** 2P (1957).

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## Amide Tautomerism. Evidence for the Iminol Form of Trimethylacetamide in a Platinum Complex

*Sir:*

Several claims for amide tautomerism have been made in the past, based on solvent effects on the ORD spectra of optically active N-substituted benzamides,[1] the uv spectra of amides of trichloroacetic and benzoic acids,[2] and the infrared spectrum of urea.[3] The evidence which has been presented is far from conclusive and the nmr studies of Skulski, Palmer, and Calvin[4] have shown that, in at least the first case, the results are better explained in terms other than amide–iminol equilibrium. In the course of a study of the constitution of platinum blue[5] and its analogs, we have isolated a material which we believe does contain an amide in its tautomeric, iminol form.

Solid dichlorobis(acetonitrile)platinum(II) and trimethylacetamide were ground together, and the dry mixture was gently heated until its pale yellow color had turned to deep green. After extracting the reaction mixture with ether and evaporating the blue ether solution to dryness, the unreacted amide was sublimed from the mixture. Solution of the remaining solid in ether and slow evaporation of this solution yielded several crops of blue-green, spear-shaped needles (I), mp 157–159° dec. *Anal.* Calcd for $PtCl_2[(CH_3)_3CCONH_2]_2$: Pt, 41.66; O, 6.83; N, 5.98; C, 25.65; H, 4.74. Found: Pt, 41.92; O, 6.85; N, 6.15; C, 25.72; H, 4.58.

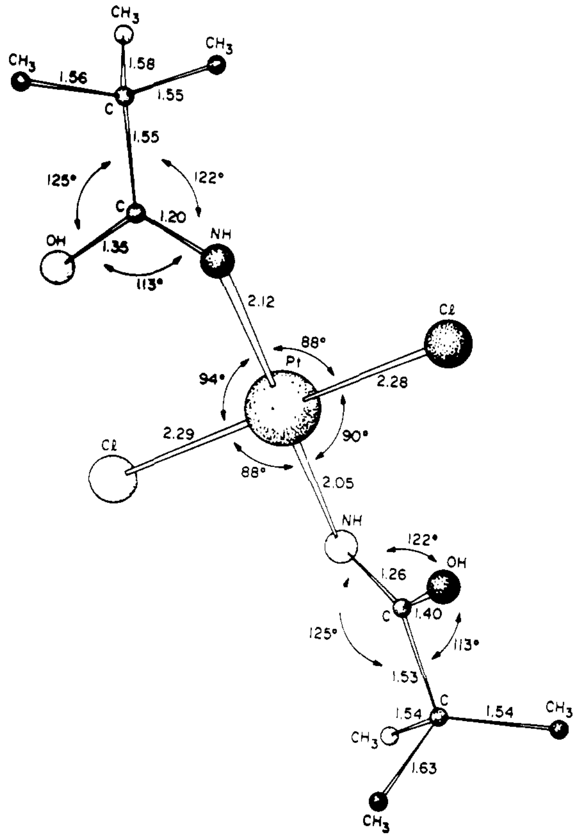

Figure 1. The molecular structure of dichlorobis(trimethylacetamide)platinum(II).

Chromatography of I on a silica gel column yielded three fractions. The first, eluted with $CHCl_3$, gave yellow crystals (II) in 70% yield, mp 173–176° dec. *Anal.* Calcd for $PtCl_2[(CH_3)_3CCONH_2]_2$: mol wt, 468. Found: Pt, 41.44; O, 6.58; N, 5.88; C, 25.77; H, 4.59; mol wt (in $CHCl_3$), 440. Continued elution with $CHCl_3$ led to the collection of a second yellow material (III) in 20% yield, and, finally, elution with ether gave a deep blue, amorphous powder (IV). Compounds III and IV had analyses identical with those of I and II, and, moreover, the yellow needles II and III appear to be isostructural with the original blue-green needles I, as demonstrated by X-ray powder patterns. Thus was it demonstrated that the apparently homogeneous needles I are really mixed crystals of the three components, II, III, and IV.

The crystal structure of I has been solved in large part[6] and showed that its major component, II, has the molecular structure pictured in Figure 1. The analysis, however, was not nearly good enough to allow us to locate the hydrogens in the amide group or to distinguish the oxygen and nitrogen atoms, though it is usually assumed that the amide has its normal form and is bonded to the metal through its oxygen atom. Nonetheless, the proton nmr spectra of I and II in $CDCl_3$ suggest that the proton configurations within their amide groups is not that usually assumed for this ligand.

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