Ph   R
  \   /
   C=C
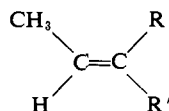 /   \
 H   R'

V, R = H; R' = COOH
VIII, R = Cu; R' = COOCu
XI, R = COOH; R' = CH₃
XIV, R = COOCH₃; R' = H

I, R = Br; R' = COOH
III, R = CH₃; R' = COOH
VI, R = H; R' = COOCH₃
IX, R = COOH; R' = Br
XII, R = COOCH₃; R' = CH₃
XV, R = COOH; R' = D

II, R = Br; R' = COOCH₃
IV, R = CH₃; R' = COOCH₃
VII, R = D; R' = COOH
X, R = COOCH₃; R' = Br
XIII, R = COOH; R' = H
XVI, R = COOZ; R' = Cu

CH₃   R
  \   /
   C=C
  /   \
 H   R'

XXI, R = COOH; R' = Br
XXIV, R = COOCH₃; R' = H

XVII, R = Br; R' = COOH
XIX, R = H; R' = COOH
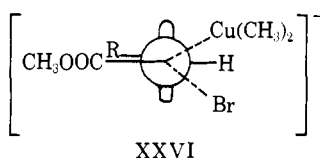XXII, R = COOCH₃; R' = Br
XXV, R = D; R' = COOCH₃

XVIII, R = Br; R' = COOCH₃
XX, R = H; R' = COOCH₃
XXIII, R = COOH; R' = H

smaller ratio of dimethylcopper lithium to X. In this case only the cis ester XIV was obtained. The ester XVI (Z = CH₃) is apparently more prone than the acid copper derivative XVI (Z = Cu) to isomerization by the reagent, or possibly by methyllithium that is in equilibrium with the copper compound.

trans-α-Bromocrotonic acid (XVII) and its methyl ester XVIII gave, with dimethylcopper lithium, replacement of the halogen with copper and finally crotonic acid (XIX) and its ester XX, respectively. The cis isomers XXI and XXII yielded a mixture of cis and trans crotonic acids and esters, respectively.

Nucleophilic vinylic substitution has been reviewed[17-21] several times and it is assumed generally that these reactions consist of two steps. Only an addition–elimination sequence could apply in our case, since elimination–addition with both I and IX would give *cis*-β-methylcinnamic acid.[9] On the other hand, addition as the first step should occur by attack of the nucleophile at the carbon β and not α to the carboxyl. The reaction of *trans*-α-bromocrotonic acid and its ester with phenylmagnesium bromide gave 2-bromo-3-phenylbutyric acid[16] by a 1,4 addition. The stereoselectivity of the reaction eliminates also the possibility of a radical reaction by electron transfer.[22]

It seems to us that our reaction and many other nucleophilic vinylic substitutions proceed by an SN2 mechanism with retention of configuration with a transition state depicted by XXVI. The nucleophile approaches perpendicularly to the plane of the molecule, then begins to rotate together with the leaving group in such a manner that there is a continuous partial overlap of the orbitals of both the forming and breaking bonds with the p orbital of the β-trigonal carbon, until bromine leaves perpendicularly to the plane of the molecule. Other accepted explanations involving differences of

angles of rotation in two directions before the second step (elimination) occurs,[23-26] or fast inversion–rotation,[20] cannot explain the regiospecificity and the steric course of our reaction. It is not the angle of rotation which should determine the ease of rotation in a particular direction, but rather the height of the potential barrier to the rotation in each direction. Consideration of the reactions of the isomeric bromo acids shows that no correlation can be found between reasonable barriers and the stereochemistry of the reaction.

The retention of configuration in vinylic nucleophilic substitution is in agreement with the rules[27,28] for concerted reactions with the participation of six electrons (including those of the double bond). A four-electron reaction with retention is also possible[28] in the case of a π-type electron donor. However, inversion of configuration in the reaction with saturated alkyl halides[5] supports the six-electron reaction course.

XXVI structure: [CH₃OOC—C(R)=C(Cu(CH₃)₂)(H)(Br)]⁻

XXVI

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Electrochemical Irreducibility of the Cyclooctatetraene Radical Anion

Sir:

We have recently reexamined the electrochemical behavior of two benzo-fused derivatives of cyclooctatetraene, and found that the radical anion product of electron addition to the neutral hydrocarbon is not electroreducible in water-free ($<10^{-5}$ M H_2O) tetrahydrofuran (THF) solutions.[1] This implies that it is considerably more difficult to form the dianion species in these cases than had been reported previously.[2] On the basis of this evidence, we therefore turned to a study

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Table I. Polarographic Characteristics of COT in Various Solvent Media

Solvent	Background electrolyte	$-E_{1/2}{}^a$ waves 1	2	3	$I(\eta)^{1/2}{}^b$ waves 1	2	3^c
AN^d	0.16 M TBAHFP	-1.80	-1.97	-2.60	2.6	2.4	1.5
AN^e	0.1 M TMAHFP	-1.87		-2.65	2.5		0.3
AN^e (10^{-4} M H$_2$O)	0.1 M TMAHFP	-1.81		-2.62	4.6		1.4
THF^f	0.19 M TBAHFP	-1.96	-2.16	-2.78	3.0	1.5	0.6

^{a} V $vs.$ sce. ^{b} Diffusion current constant times square root of viscosity, μA mM^{-1} mg$^{-2/3}$ sec$^{1/2}$ cP$^{1/2}$. ^{c} Based on COT concentration. ^{d} 0.15 mM COT. ^{e} 0.16 mM COT. ^{f} 0.24 mM COT.

of the electrochemistry of the unsubstituted hydrocarbon, COT, under rigorously aprotic conditions.

Figure 1A illustrates the typical behavior of COT in acetonitrile, AN, solutions containing 0.16 M tetrabutylammonium hexafluorophosphate (TBAHFP).
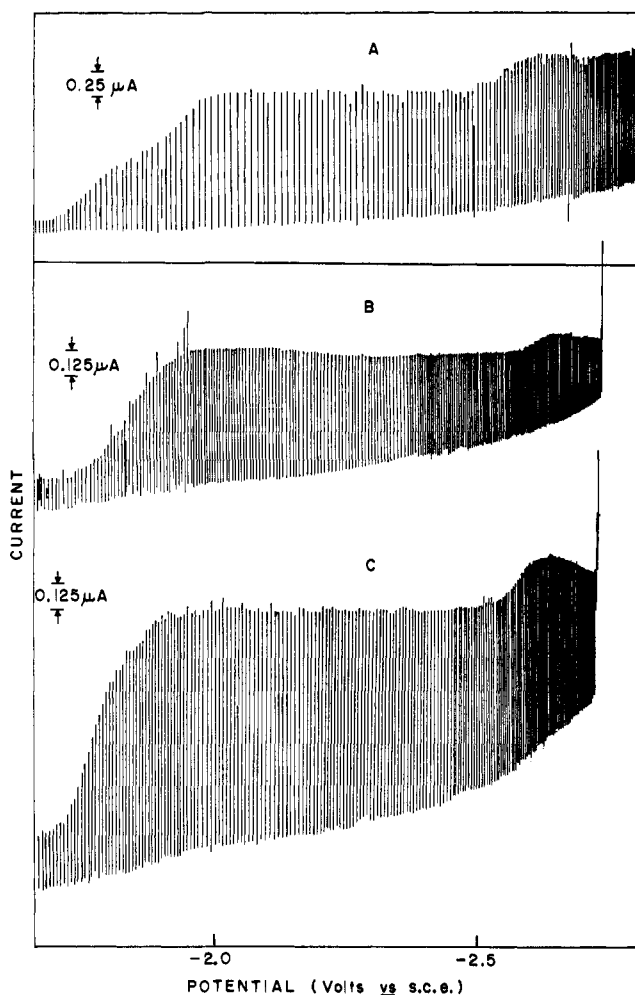

Figure 1. Polarography of cyclooctatetraene in AN solvent: (A) 1.5 $\times$ 10^{-4} M COT with 0.16 M TBAHFP; (B) 1.6 $\times$ 10^{-4} M COT with 0.1 M TMAHFP; (C) same as B plus 2.1 $\times$ 10^{-4} M H$_2$O added (traced from original data).

Two characteristics of this polarogram are common to all reported electrochemical studies, whether performed in THF, AN, or dimethylformamide. (1) Two waves are observed whose diffusion currents are in the approximate ratio of 1.2:0.8, and this ratio is not strongly dependent on the addition of small amounts of proton donors (e.g., mM H$_2$O). (2) The third (and sometimes a fourth) wave is always present, even under rigorously water-free conditions in THF.[1] These results imply

that some chemical reaction is coupled to the initial electron transfer to the parent hydrocarbon, and the most likely reactive species is the tetrabutylammonium ion of the background electrolyte, which is in great molar excess. Quaternary ammonium ions are known to undergo Hofmann elimination by basic anionic species[3] to form the corresponding trialkylamine, olefin, and protonated hydrocarbon.

This hypothesis was tested by carrying out the electrochemical reduction using tetramethylammonium hexafluorophosphate (TMAHFP) as the background electrolyte in carefully dried AN.[4] The tetramethylammonium ion does not undergo Hofmann elimination, although radical substitution reactions may occur. Figure 1B shows the polarographic behavior under these conditions. A single wave is observed in the region of the previously described double wave in Figure 1A, and the diffusion current constant (Table I) indicates that only one electron is transferred. No other electrochemical activity is observed until -2.7 V $vs.$ sce, where reduction of the diprotonation product, cyclooctatriene, occurs (indicating approximately 2 $\times$ 10^5 M residual protic impurity in the solution). Successive additions of water to these solutions results in proportionate increases in the height of both the wave at -1.9 and that at -2.7 V (Table I). Raising the water concentration to values approximately equimolar to the COT concentration results in nearly doubling the height of the wave at -1.9 V as well as significantly increasing the height of the triene wave (Figure 1C).

We conclude from these results that the electrochemistry of COT is limited in the accessible potential region, to the following single reduction in the absence of coupled chemical reactions

$$COT + e^- \Longleftrightarrow COT\cdot^-$$ (1)
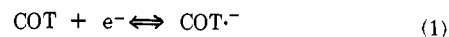
In the presence of quaternary ammonium ions active to Hofmann elimination, this primary reduction product is apparently protonated and reduced at a potential slightly more negative than the original hydrocarbon.

$$COT\cdot^- + TBA^+ \longrightarrow HCOT\cdot + TBA + butene$$ (2)

$$HCOT\cdot + e^- \Longleftrightarrow HCOT^-$$ (3)
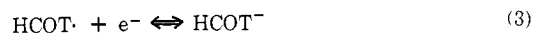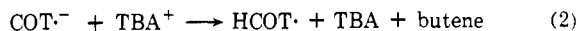
The anion thus formed is apparently less active in the elimination reaction with TBA$^+$ ion and thus the wave at -2.9 V for the triene, H$_2$COT, does not increase proportionately.

Added water, on the other hand, freely protonates the anion products of both reactions 1 and 3 producing

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the triene in proportionate yield. We have employed this reaction as a highly sensitive method of determining water concentrations in the submillimolar region. In the absence of active quaternary ammonium ions, either wave will serve to quantitatively indicate the presence of protic impurities in the solution. In the presence of TBA⁺, however, the triene wave alone is quantitatively responsive to protons from water donors.

Of fundamental importance to studies of aromaticity is the lack of any observable electrochemical reduction of the radical anion product of reaction 1. There is no evidence that the Hückel aromatic 10π-electron dianion can be formed in the solvent–electrolyte system studied here. Guidance in interpretation of this result may be found in recent theoretical calculations of the heat of formation of the COT dianion,[5] which is estimated to require approximately 80 kcal/mol more than formation of either the planar or puckered radical anion. Thus, in the absence of extremely strong preferential interactions between the dianion and components of the condensed phase (i.e., existence of large organizational entropy terms favoring formation of the dianion plus parent over two radical anions), the predicted difference between the reduction potentials of COT and COT·⁻ would be 3 V. Clearly the aromatic dianion is very difficult to attain by electrochemical reduction.

Lastly, these results call into serious question the generality of a basic assumption made extensively in interpretation of successive electrochemical reductions. The difference in half-wave potentials between the addition of the first and second electron to fused polycyclic aromatics is reported to be approximately −0.4 V.[6] Most of the data on which these conclusions are based were obtained in 95% dioxane–water solutions, where protonation reactions are known to be extremely rapid. Substitution of aprotic solvents for the dioxane–water has usually been accompanied (for reasons of solubility) by introduction of alkylammonium ions in the background electrolyte, which must themselves be suspected of rapid reaction with radical anion products. The results described here indicate that before valid correlations may be made between observed half-wave potentials and quantum mechanical properties of olefinic and aromatic systems, it is necessary to unequivocally establish the mechanism of each reaction under consideration.

The data presented here virtually rule out the possibility that the dianion of COT may be achieved through electrochemical reduction in these media. They do not explain the apparent existence of the dianion as a product of the alkali metal reduction of COT. Indeed, considering the ready reducibility of alkali metal ions at the dropping mercury electrode in the vicinity of −2.5 V vs. sce, we are currently pursuing studies of structure and properties of the product of reaction of 2 equiv of alkali metal with COT.

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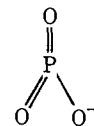D. R. Thielen, L. B. Anderson*

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Oxygen-18 Isotope Effect in the Hydrolysis of 2,4-Dinitrophenyl Phosphate. A Monomeric Metaphosphate Mechanism

Sir:

The role of the monomeric metaphosphate ion intermediate, 1, in the unimolecular decomposition of phos-

1

phate monoesters has been the subject of much investigation. Numerous studies on such esters as methyl phosphate,[1] acetyl phosphate,[2] and aryl phosphates[3,4] have attempted to use pH–rate profile data, entropy of activation comparisons, solvent effects, etc., to confirm the metaphosphate hypothesis. While a substantial body of data now exists[5] which appears consistent only with the metaphosphate mechanism, as suggested by Jencks,[2] no one piece of evidence is conclusive in itself, and support for this mechanism must rest upon the accumulation of a sufficient number of reasonable arguments. We now wish to report the ester–oxygen ¹⁸O-isotope effect for the hydrolysis of the dianion of a monoaryl phosphate ester (ArO*PO₃²⁻). We believe this represents the most convincing evidence yet given for this mechanism.

Heavy-atom isotope effects have been shown to be a powerful investigative tool of the mechanistic chemist.[6] Large (2–4%) ¹³C and ¹⁵N isotope effects have been demonstrated (and theoretically justified[7]) to indicate substantial bond breaking or bond order change in the transition state.[6,8] Although ¹⁸O-isotope effects have been used only rarely,[9] they should be just as useful as the other heavy-atom effects in delineating reaction mechanisms.

We have chosen to measure the isotope effect by a direct kinetic approach,[10] comparing the rate of hydrolysis of the aryl ¹⁸O-2,4-dinitrophenyl phosphate to that of the ¹⁶O ester. The mono-2,6-lutidinium salts of the phosphate esters were prepared from the appropriate phenol oxygen labeled, 2,4-dinitrophenol by the method of Kirby and Varvoglis.[4] The ¹⁸O-labeled phenol was prepared by the reaction of redistilled 2,4-

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(10) Schowen has demonstrated quite nicely the feasibility of this method: C. G. Mitton and R. L. Schowen, Tetrahedron Lett., 5803 (1968). While heavy-atom isotope effects have been traditionally studied by a competitive method using isotope-ratio mass spectrometry,[6] the direct kinetic approach should be an attractive alternative.