Electroorganic Synthesis. 1. Electrode-Catalyzed Synthesis of a Dioxetane

E. L. Clennan,* W. Simmons, and C. W. Almgren

Department of Chemistry, University of Wyoming
Laramie, Wyoming 82071
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Successful synthesis of a 1,2-dioxetane was not accomplished until 1968 when the synthesis of trimethyl-1,2-dioxetane was reported.[1] Since that time many 1,2-dioxetanes have been synthesized and characterized.[2] Four synthetic methods have been utilized in their production: (1) closure of a β-halohydroperoxide with base, (2) addition of singlet oxygen to enol ethers, enamines, and alkenes with unreactive allylic hydrogens, (3) assisted closure of a β-halohydroperoxide with silver ion, and (4) 9,10-dicyanoanthracene (DCA) photooxidations.[3]

We now report a fifth method which we have used for the synthesis of adamantylideneadamantane dioxetane. A solution consisting of 50 mL of methylene chloride, 1.71 g of tetra-*n*-butyl ammonium perchlorate, and 104.5 mg of adamantylideneadamantane (**1**) was subjected to a constant potential electrolysis (1.6 V vs. SCE) at a platinum gauze electrode. The electrolysis was conducted while the solution was continually agitated by bubbling oxygen vigorously through the cell and until current passage through the cell ceased. The methylene chloride was then removed from the electrolysis mixture and the residue chromatographed on silica gel to give a 85% yield of adamantylideneadamantane dioxetane which was identified by comparison to an authentic sample.[4]

The constant potential electrolysis was conducted sufficiently anodic of the reversible oxidation potential (E^0 = 1.45 V vs. SCE)[5] of **1** to produce the radical cation $\mathbf{1}^{+\cdot}$ as shown in step A of Scheme I. Reaction of $\mathbf{1}^{+\cdot}$ with molecular oxygen produces the peroxy radical cation $\mathbf{2}^{+\cdot}$ as shown in step B. Reactions of oxygen with diene[5] and acetylene[7] radical cations have been reported to produce similar peroxy radical cations. Steps C and D in the mechanism produce the peroxy diradical **2** by the reduction of the peroxy radical cation $\mathbf{2}^{+\cdot}$ with **1** (step C) or the electrode (step D). The peroxy diradical subsequently closes to form the dioxetane.

The mechanism in Scheme I is supported by several experimental observations: (1) isolation of good yields (75–90%) of adamantylideneadamantane dioxetane, (2) exhaustive electrolysis of **1** under an argon atmosphere results in passage of 1.04 F/mol while under an oxygen atmosphere only 0.04 F/mol is observed, and (3) a decrease in the concentration of **1** or oxygen results in a decrease in the average chain length of the reaction (see Table I).

The cyclic voltammetric behavior of **1** in oxygen-saturated solution is also significantly different from its behavior in an argon-saturated solution and reflects the chain-like character of the reaction (see Figure 1). In oxygen-saturated solutions, a small amount of Faradaic current is observed, but it peaks quickly and then falls as **1** is depleted by the chain reaction near the electrode.

Foote[8] has proposed and observed olefin radical cations in 9,10-dicyanoanthracene (DCA) photooxidations. Reaction of these radical cations with superoxide ($O_2^{-\cdot}$) produced the oxidation products. The potential of our electrolysis (+1.6 V vs. SCE) is more than 2.4 V anodic of the potential necessary to electrogenerate superoxide,[9] and its involvement in this reaction is precluded.

Schaap[3] has reported that radical cations of type **3** generated by treatment with tris(*p*-bromophenyl)ammoniumyl tetrafluoroborate react very slowly with molecular oxygen. We have examined tetraphenyl-*p*-dioxin[10] (**4**) and report results consistent

Scheme I

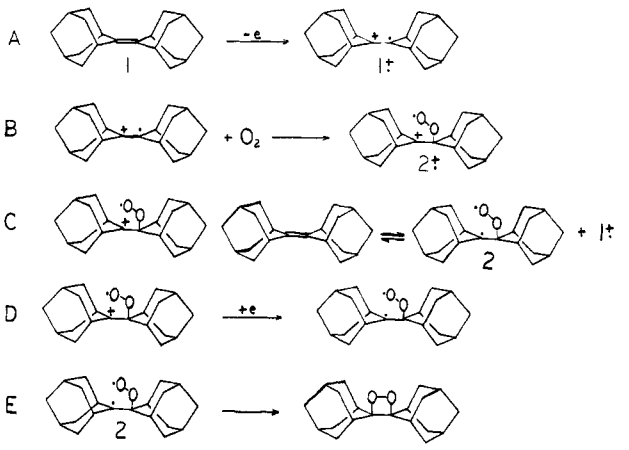


Table I. Coulometric Data for the Oxidation of 1

[1], mol/L × 10^3 [a]	purging gas	coulombs	average chain length[c]
7.8	O_2	1.50	24.1
7.8	O_2	1.57	22.9
7.8	Ar	39.14	
7.8	air	2.72	12.8
2	Ar	9.94	
2[b]	O_2	1.06	8.1

[a] 50 mL of 1 M solution in Bu_4NClO_4 in methylene chloride. [b] Average of five runs. [c] Chain length = (theoretical coulombs for a $1e^-$ process/coulombs passed) − 1.

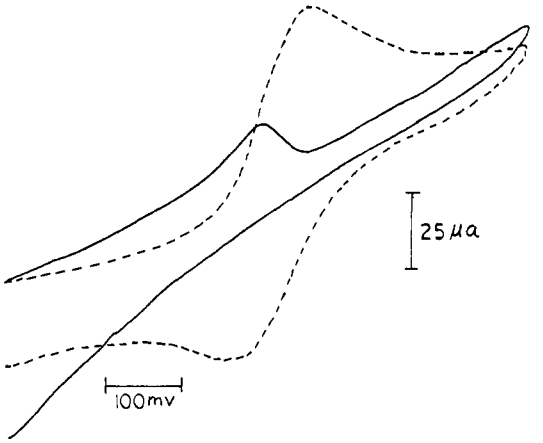
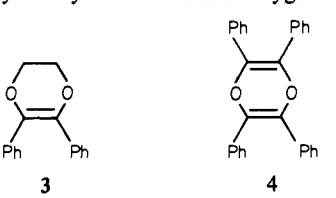


Figure 1. Cyclic voltammograms of **1** in oxygen-saturated (—) and argon-saturated solutions (– – –).



3 **4**

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with Schaap's observations. Exhaustive electrolysis of **4** at 0.93 V vs. SCE ($E^{0'}$ = +0.89 V vs. SCE)[11] in an argon- or oxygen-saturated solution produced a deep green-colored solution with passage of 1 F/mol. The deep green solution persisted for several hours in argon-saturated solution but faded in 20 min in an oxygen atmosphere to form a colorless solution. An ESR signal was observed for the green solution but disappeared as soon as the color faded. The slow reaction of these radical cations with oxygen reflects the extensive delocalization of the odd electron density in $3^{+\cdot}$ and $4^{+\cdot}$.

This reaction is an example of a continually increasing class of reactions[12] in which a chemical reaction is accelerated in the presence of an electrode. The successful isolation of the dioxetane is based upon the enhanced reactivity of an oxidized state of the substrate with molecular oxygen. This reaction provides a counter example to the $S_{RN}1$ electrode-catalyzed reaction[13] which owes its success to enhanced reactivity of a reduced state of the starting material.

We are continuing our study of the electrode-catalyzed oxidations of organic molecules to determine the generality of this reaction and we anticipate the communication of additional results in the near future.

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Direct Evidence from Multiple ^{13}C Labeling and Homonuclear Decoupling for the Labeling Pattern by Glucose of the *m*-Aminobenzoyl (C_7N) Unit of Pactamycin

Kenneth L. Rinehart, Jr.,* Maria Potgieter, and Dana L. Delaware

Roger Adams Laboratory, University of Illinois Urbana, Illinois 61801

Haruo Seto

Institute of Applied Microbiology, The University of Tokyo Tokyo, Japan

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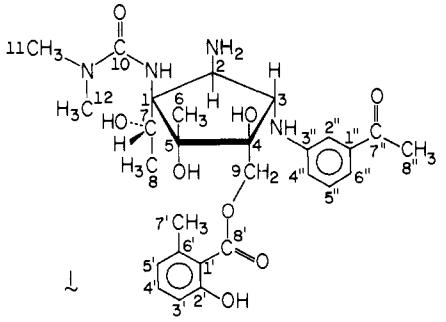
A number of structurally interesting and clinically important antibiotics contain a "C_7N" unit whose biosynthesis is believed to be related to the shikimate pathway.[1] The simplest of these C_7N units is the *m*-aminobenzoyl unit found in pactamycin (**1**).[1,2]



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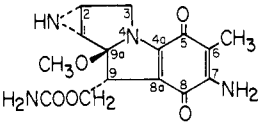
The aminobenzoquinonoid portions of mitomycin C (**2**, C-4a through C-8a, 6-methyl, N-4),[3] geldanamycin,[4] and the nearly



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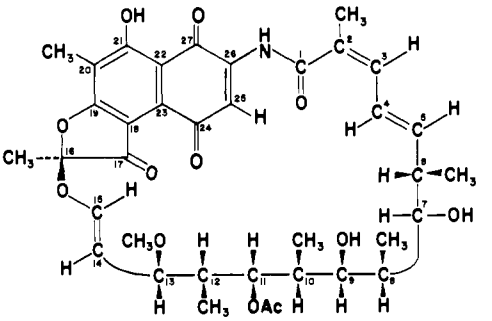
identical herbimycin[5] and asukamycin[6] are of intermediate complexity, while modified C_7N units are built into the aminonaphthoquinonoid portions of rifamycin S (**3**, C-21 through C-27)[7,8] and streptovaricin D.[9]



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In each of these antibiotics, studies thus far have shown C-6 of glucose to label the C_7N unit at both carbons ortho to the carbon bearing the exocyclic carbon,[10] in agreement with a shikimate-type pathway,[11] involving condensation of phosphoenol pyruvate and erythrose 4-phosphate to 3-deoxy-D-*arabino*-heptulosonic acid 7-phosphate (DAHP) and the latter's cyclization to 5-dehydroquinic acid (DHQ). An attractive possibility for introduction of the amino group into the C_7N unit would involve transamination of the keto group of DHQ or dehydroshikimic acid (DHS), as shown in path A (Scheme I). This pathway requires that erythrose 4-phosphate provide C-2″ through C-5″ of the *m*-aminobenzoyl portion of **1** and phosphoenol pyruvate provide C-1″, C-6″, and C-7″. Path A was suggested by our earlier observation of the relatively greater labeling of C-2″ than C-6″ by [6-^{13}C]-glucose and the opposite ratio (C-6″ > C-2″) by [1-^{13}C]glucose,[1,2] a direct analogy to the relative labeling patterns in the original shikimate pathway study of Srinivasan et al.[11] Hornemann has recently suggested that the alternative path B is operative in mitomycin biosynthesis, on the basis of chemical degradation of mitomycin labeled by D-[4-^{14}C]erythrose and [3-^{14}C]pyruvate.[3] Path B, if operative in pactamycin biosynthesis, would require that erythrose 4-phosphate provide C-3″ through C-6″ of the *m*-aminobenzoyl group and phosphoenol pyruvate provide C-1″, C-2″, and C-7″.

A third possibility, combining elements of paths A and B, was suggested by White and Martinelli,[7] who argued for a DHS intermediate but for amination at C-3 of DHS, which would give

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