consistent with the S_N2 mechanism through which products having the trans configuration result. The study of acid-catalyzed hydrolysis of 1-arylcyclohexene oxides has shown that the transition state leading to the cis diol has a higher degree of carbocationic character.[16] Furthermore, it has been demonstrated[17a] that the gauche conformer is more stable than the trans conformer in certain highly electronegatively substituted systems (gauche effect). Hence, it is reasonable to suggest that the reaction proceeds via an α-stabilized cationic intermediate **8** which may have a longer lifetime, thus allowing the attack of water from an energetically favorable direction to yield the cis diol. The favorable gauche interaction in this system is in agreement with the proposed mechanism for the stereospecific formation of *cis*-5-fluoro-6-methoxyuracil.[17e]

Regarding the photoepoxidation of simple olefins, a radical mechanism has been proposed and two possible pathways have been considered,[2] i.e., whether the initial step involves the interaction of the α-diketone with a double bond or with oxygen to yield the diradical **9**.[18] In methanolic solution, **2a** sensitized photooxidation of **1a** was found to result in a >95% recovery of **1a** and the complete oxidation of **2a**. This finding, along with those above, suggests that **9** may be the initial intermediate which reacts with pyrimidines to give **7** in an aprotic solvent. In methanol **9** is trapped by the solvent, thus precluding its reaction with the pyrimidine. However, the possibility that a mechanism may involve an ionic intermediate cannot be excluded because there have been such suggestions recently concerning the dye-sensitized photooxidation of pyrimidines[3c] or indoles.[19] Consequently, more detailed mechanistic study is being undertaken.

In short, the evidence indicates that pyrimidine epoxides may be formed as initial photooxidation products. It also shows that such intermediates are exceedingly susceptible to the attack of nucleophiles, yielding compounds corresponding to **3**, and that **3b-e** are readily converted to **3a**, resulting in the cleavage of the newly formed covalent bond. Furthermore, the nucleophilic attack of pyrimidine epoxides offers an alternative mechanism for the formation of protein-nucleic acid cross-linkings, which command current interest[20,21] and should be relevant to the study of aging, carcinogenesis, and mutagenesis.

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(5) All irradiations were carried out at 0 °C with a Hanovia 450-W medium-pressure mercury lamp filtered by $CuSO_4$ solution to eliminate light with wavelengths shorter than 320 nm. During irradiation the solutions were oxygenated by bubbling O_2 which was passed through concentrated H_2SO_4.

(6) **3a** was identified by comparison with an authentic sample, prepared from **1a** according to the method of S. Iida and H. Hayatsu, *Biochem. Biophys. Acta*, **228**, 1 (1971), for Thy glycol.

(7) **4** was identified by comparison with an authentic sample: J. W. Clark-Lewis and M. J. Thompson, *J. Chem. Soc.* 2401 (1959).

(8) Characteristics of **5**: *m/e* 340 (M^+); NMR ($CDCl_3$, Me_4Si): δ 1.39 (6 H, s), 3.19 (6 H, s), 3.23 (6 H, s), and 4.59 (2 H, s); mp >230 °C.

(9) In contrast to **2a**, **2b** was consumed rapidly. Irradiation in CH_2Cl_2 gave a lower yield (40%) of **3b** while another product was formed in a greater yield. **3b** is readily converted quantitatively to **3a** in the presence of a catalytic amount of silica gel at room temperature. Characteristic of **3b**: mp 122 °C; *m/e* 230 (M^+); NMR ($CDCl_3$, Me_4Si): δ 1.48 (3 H, s), 2.07 (3 H, s), 3.12 (3 H, s), 3.24 (3 H, s), 5.88 (1 H, s), and 7.26 (1 H, bd).

(10) **3c** is a viscous liquid: *m/e* 132 (M^+); NMR ($CDCl_3$): 1.24 (3 H, t, J = 7.0 Hz), 1.50 (3 H, s), 2.67 (2 H, q, J = 7.0 Hz), 3.13 (3 H, s), 3.15 (3 H, s), 4.21 (1 H, s), and 5.96 (1 H, bd).

(11) **3d** has mp 136 °C; *m/e* 280 (M^+); NMR ($CDCl_3$): 1.48 (3 H, s), 2.85 (3 H, s), 3.04 (3 H, s), 3.70 (1 H, bd), 4.45 (1 H, s), and 7.29 (5 H, m).

(12) One isomer of **3e** has mp 204 °C; *m/e* 264 (M^+); NMR (CD_3COCD_3–$CDCl_3$, Me_4Si): δ 1.56 (3 H, s), 2.96 (3 H, s), 3.17 (3 H, s), 4.22 (1 H, s), 6.80 (5 H, m), and 8.18 (1 H, bd). The other is a viscous oil with *m/e* 264 (M^+); NMR ($CDCl_3$): δ 1.68 (3 H, s), 3.03 (3 H, s), 3.27 (3 H, s), 4.68 (1 H, s), 5.00 (1 H, bd), and 6.86 (5 H, m).

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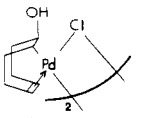
Stereochemistry of the Hydroxypalladation of Ethylene. Evidence for Trans Addition in the Wacker Process

Sir:

The hydroxypalladation step in the conversion of ethylene to acetaldehyde has been proposed,[1] on the basis of kinetic studies, to proceed with cis stereochemistry. Thus, the trans addition of methanol and palladium to chelating diolefins[2,3] was considered to be anomalous[4-8] since the chelating diolefin could not undergo a 90° rotation readily from a position perpendicular to the square plane of the complex into a position in which one of the olefin pair is coplanar with the square plane of the complex and thus adjacent to the alkoxyl function, a position necessary for cis attack. However, the trans stereochemistry of methoxypalladation of monoolefins, *cis*- and *trans*-2-butene, has been demonstrated by intercepting the β-methoxyalkylpalladium complex with carbon monoxide.[9] The presence of carbon monoxide in this reaction apparently does not alter the stereochemical course, since a β-methoxyalkylpalladium complex, isolated at low temperature, has been shown[10] to have the trans geometry.

The stereochemistry of the methoxypalladation of diolefins can no longer be considered anomalous; the presence of carbon monoxide in these reactions does not alter the stereochemical course of the reaction. The stereochemistry observed in methanol, however, does not necessarily include the reaction in aqueous media, particularly under the conditions of the Wacker process. We had demonstrated[11] that the hydroxypalladation of 1,5-cyclooctadiene in water–acetone produced the trans σ-bonded hydroxy-enyl complex **1**. In order to con-



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firm this stereochemistry, we undertook a hydroxypalladation of a monoolefin with the anticipation that the Wacker intermediate could be trapped with carbon monoxide.

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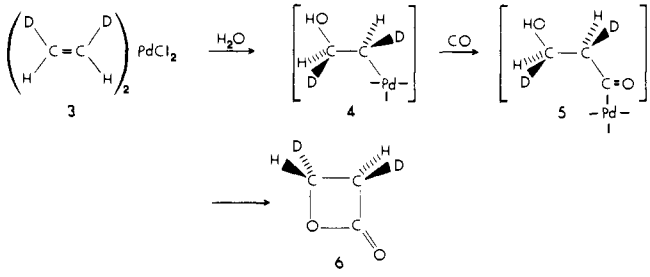
The reaction of bis(ethylene)palladium(II) chloride[12] in water-acetonitrile at −20 to −25 °C in the presence of carbon monoxide (3 atm) gave β-propiolactone **2** in a 72% yield[13] (eq 1). The direct catalytic conversion of ethylene to β-propiolactone could also be effected from a 2:1 ethylene-carbon monoxide charge (total 3 atm) using catalytic amounts of palladium, provided equivalent amounts of copper(II) chloride and sodium acetate (buffer) were present (eq 2). Although

$$(C_2H_4)_2PdCl_2 + H_2O + CO \longrightarrow \underset{\text{2}}{\text{O(CH}_2\text{)}_2\text{C(=O)}} + 2HCl + Pd + C_2H_4 \quad (1)$$

$$2CuCl_2 + CH_2{=}CH_2 + H_2O + CO \xrightarrow{PdCl_2} \mathbf{2} + Cu_2Cl_2 + 2HCl \quad (2)$$

carbon monoxide is rapidly oxidized to carbon dioxide under these conditions, the low reaction temperature apparently slows down this oxidation relative to the hydroxypalladation, and a 37% conversion of ethylene to β-propiolactone is realized. Since copper(I) can be reoxidized to copper(II) by air, this represents a unique catalytic synthesis of β-lactones from olefin, carbon monoxide, and water.

The stereochemistry of the hydroxypalladation step was determined by using the bis(ethylene)palladium(II) chloride complex **3** obtained from *cis*-1,2-dideuterioethylene.[14] Thus, the reaction in water-acetonitrile in the presence of carbon monoxide afforded *trans*-2,3-dideuterio-β-propiolactone (**6**): ^1H NMR ($CDCl_3$ δ 4.3 (d, J = 4 Hz), 3.8 (d, J = 4 Hz).[15] The insertion of carbon monoxide into a carbon-palladium σ bond (**4** → **5**) is known[16] to proceed with retention of configuration at carbon; therefore, the hydroxypalladation step (**3** → **4**) must proceed with trans stereochemistry.



These results for the stereochemistry of hydroxypalladation are consistent with those reported[17] for the reaction of *trans*-1,2-dideuterioethylene under the conditions of the Wacker process. The formation of *threo*-1,2-dideuterio-2-chloroethanol also requires trans hydroxypalladation. Thus, the attack of water on the ethylene-palladium complex is from outside the coordination sphere, and the addition of OH and palladium is trans.

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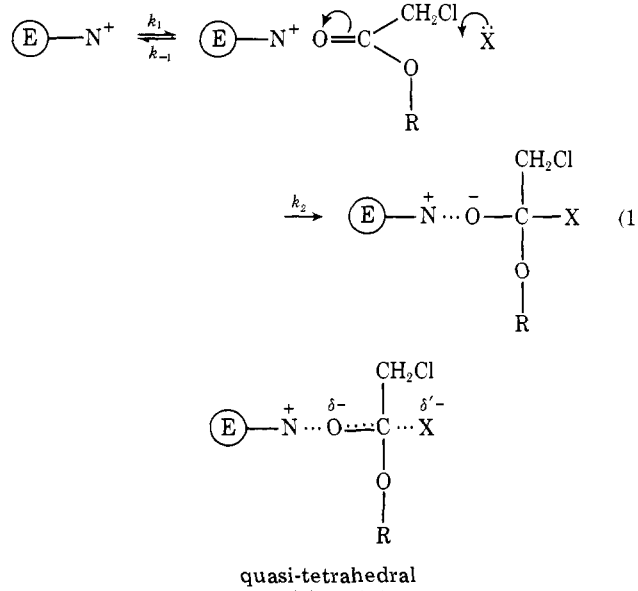
Specific Catalysis of Ester Hydrolysis by A New Water-Soluble Heterocyclophane

Sir:

Substrate specificity in enzymic reactions is understood to indicate that a specific substrate has a "best fit" to a unique array of binding site residues and that the spatial arrangement of atoms relevant to the catalysis is particularly favorable for the stabilization of the transition state.[1] Among the variety of ways in which such stabilization can arise, electrostatic stabilization is very important since most enzymic reactions involve various charged transition states. In an active site, cationic residues of protonated basic amino acids such as Lys or Arg can stabilize an anion generating in the transition state of an enzyme-catalyzed reaction.[2] For example, in ribonuclease action it is hypothesized that electrostatic stabilization of a dianionic pentacoordinate intermediate is provided by a cationic residue (probably protonated lysine).

In a previous communication we reported that certain water-soluble macrocyclic heterocyclophanes are excellent inclusion hosts toward organic substrates.[3a,b] In this communication we wish to report evidence supporting the formation of markedly stabilized transition state complexes of aromatic ester substrates with a new member of the group of water-soluble heterocyclophanes, II, leading to remarkably effective catalysis. The observed substrate specificity is shown herein



quasi-tetrahedral transition state

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