terminal region of melittin binds to the phospholipid bilayer of cell membranes in the helical mode when the axis of the helix is parallel to the surface. In view of the absence of tertiary structure, it is not surprising to observe such a clear segregation of the structural and functional role of different segments of the peptide chain. The limited possibilities of well-defined secondary structures for peptides would then suggest that amphiphilic helical segments might be found in a variety of biologically important oligopeptides such as hormones. We hope that the results reported in this paper demonstrate the power of rational design of peptides based on secondary structural considerations for the investigation of structure–functional relationships in biologically active peptides.

Acknowledgment. The work presented in this paper was supported by USPHS Program Project HL-18577. We thank Dr. D. Fukushima and Dr. S. Yokoyama for help with the preliminary experiments and for many useful discussions, Dr. R. Josephs for the electron microscopy, and Dr. R. L. Heinrikson and Ms. P. Keim for the sequence analysis of peptide **1**.

Evidence for a Second Mode of Hydroxypalladation in Aqueous Solution

N. Gragor and P. M. Henry*

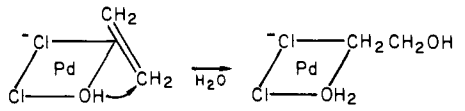
Guelph-Waterloo Centre for Graduate Work in Chemistry
University of Guelph, Guelph
Ontario, Canada, N1G 2W1

Received November 17, 1980

It is universally agreed that the oxidation of ethene to acetaldehyde by palladium(II) chloride in aqueous solution proceeds by a mechanism involving conversion of a π-bonded olefin to a palladium(II) β-hydroxylalkyl, a process called hydroxypalladation.[1] The rate expression for the oxidation (eq 1) has

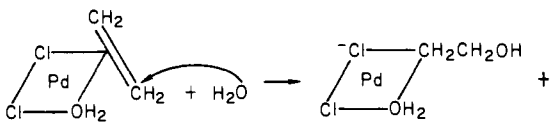
$$\frac{-d[C_2H_4]}{dt} = \frac{k[PdCl_4^{2-}][C_2H_4]}{[H^+][Cl^-]^2} \quad (1)$$

been interpreted in terms of formation of the hydroxypalladation intermediate, **1**, by either a cis attack of coordinated hydroxyl (eq 2)[2] or trans attack of external water (eq 3).[3-5] The first was



(2)

1

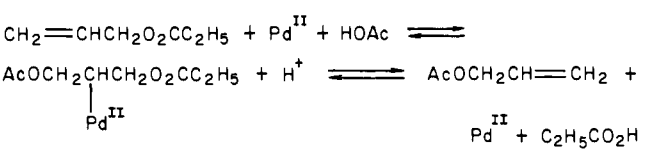


(3)

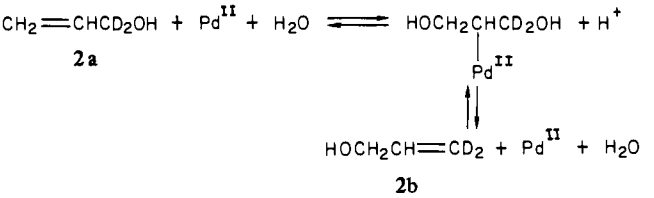
1

originally selected as most likely on the basis of isotope effects[2] but the latter has more recently been suggested because of stereochemistry studies which suggest hydroxypalladation occurs by attack of water from outside the coordination sphere of palladium(II).[3,4,6] The most convincing of these studies[4] involves the oxidation of ethene at high chloride (3.3 M) and high cupric chloride concentrations (2.7 M), conditions under which chloroethanol becomes the main product.[7] It was found that the configurations of the chloroethanol-d_2 products from oxidation of (*Z*)- and (*E*)-ethene-d_2 were consistent with trans hydroxypalladation. Assuming that $CuCl_2$ was intercepting the intermediate, **1**, a mechanism analogous to the second route (eq 3) was suggested.[4] This communication provides evidence that an intermediate other than **1** is actually being intercepted in the reaction forming chloroethanol.

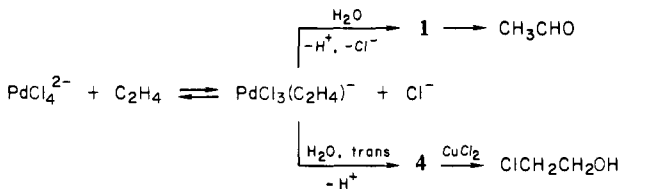
Scheme I



Scheme II



Scheme III



Allylic groups such as esters can be exchanged in a nonoxidative palladium(II)-catalyzed reaction.[8] An example is the exchange of allyl propionate with acetic acid solvent, a reaction which almost certainly occurs by the oxypalladation–deoxypalladation mechanism shown in Scheme I.[9,10]

In order to determine if other modes of hydroxypalladation might exist in aqueous solution, the isomerization of propenol-*1,1*-d_2 (**2a**) to a 50:50 mixture of **2a** and propenol-*3,3*-d_2 (**2b**) was studied by using H^1 NMR spectroscopy under conditions where the oxidation reaction, which gives acrolein as main product,[11] is slow.

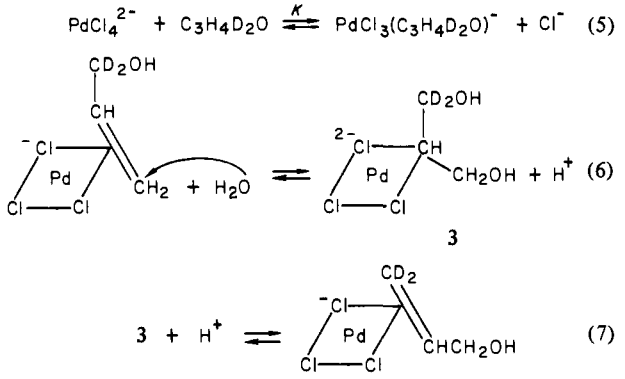
The isomerization did not take place in the absence of palladium(II) chloride but did occur readily in its presence. The rate expression for isomerization is given by eq 4 ($C_3H_4D_2O$ = propenol-*1,1*-d_2) where $k_i = 1.5 \times 10^{-3}$ s^{-1}.

$$\text{rate} = \frac{k_i[PdCl_4^{2-}][C_3H_4D_2O]}{[Cl^-]} \quad (4)$$

The most plausible route for this isomerization is given by Scheme II which is analogous to that given in Scheme I for ester exchange. Since the rate expression for isomerization (eq 4) is quite different from that for oxidation, the modes of hydroxypalladation for the two processes must also be different. The first power chloride inhibition and lack of a proton inhibition term are consistent with the reaction scheme given in eq 5-7. The trans hydroxypalladation shown in eq 6 is consistent with the first power chloride inhibition since insertion of H_2O in the coordination sphere

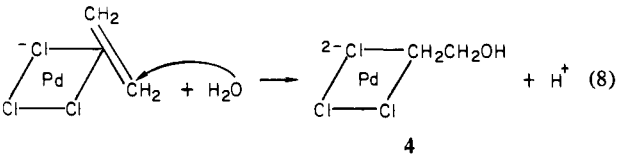
(1) For general discussion and references, see: Henry, P. M. "Palladium Catalyzed Oxidation of Hydrocarbons"; D. Reidel: Dordrecht, Holland, 1979; pp 41-84.
(2) Henry, P. M. *J. Am. Chem. Soc.* **1964**, *86*, 3246-3250; **1966**, *88*, 1595-1597.
(3) Stille, J. K.; Divakarumi, R. *J. Organomet. Chem.* **1979**, *169*, 239-248.
(4) Bäckvall, J. E.; Åkermark, B.; Ljunggren, S. O. *J. Am. Chem. Soc.* **1979**, *101*, 2411-2416.
(5) In eq 3 both cis and trans isomers of **1** are likely present. Only the cis form is shown for simplicity.
(6) Stille, J. K.; James, D. E. *J. Organomet. Chem.* **1976**, *108*, 401-408.
(7) Stangl, R.; Jira, R. *Tetrahedron Lett.* **1970**, 3589-3592.
(8) Sabel, A.; Smidt, J.; Jira, A.; Prigge, H. *Chem. Ber.* **1969**, *102*, 2939-2950.
(9) Henry, P. M. *J. Am. Chem. Soc.* **1972**, *94*, 1527-1532.
(10) Henry, P. M. *Acc. Chem. Res.* **1973**, *6*, 16-24.
(11) Smidt, J.; Hafner, W.; Jira, R.; Sieber, R.; Sedlmeier, J.; Sabel, A. *Angew. Chem.* **1959**, *71*, 176-182.

0002-7863/81/1503-681$01.00/0 © 1981 American Chemical Society



of Pd(II) for a cis attack would have required a square chloride inhibition.

Since allyl alcohol undergoes this trans attack of water to give **3**, it is almost certain that ethene also undergoes a similar hydroxypalladation to give **4** (eq 8) with a rate expression analogous to eq 4. Of course, in the case of ethene there would be no way



of detecting this type of hydroxypalladation unless the adduct, **4**, was intercepted by some reagent such as $CuCl_2$. The adduct **4** must therefore by considered as a possibility for the intermediate which is actually intercepted in the stereochemical studies using ethene-d_2. One experimental observation, in fact, strongly favors **4** as this intermediate. In the original studies[7] on chloroethanol formation it was found that high chloride concentration (ca. 5 M) *as well as* high cupric chloride concentration (ca. 4 M) was required for chloroethanol formation. If only cupric chloride is present the product was almost exclusively acetaldehyde. These results are *not* consistent with $CuCl_2$ intercepting the same intermediate, **1**, which decomposes to give acetaldehyde, but are consistent with repression of the acetaldehyde formation, which has a square chloride inhibition (eq 1), so that chloroethanol becomes the predominate reaction. This situation would only arise if chloroethanol formation does not have as strong a chloride inhibition as acetaldehyde formation. Chloroethanol formation, if it does proceed via **4**, would have only a first-order chloride inhibition and thus be strongly favored over acetaldehyde formation at high $[Cl^-]$. A reaction sequence consistent with these considerations is shown in Scheme III.[12] The trans stereochemistry observed for chloroethanol formation[4] is expected on the basis of this scheme. Thus the present results provide a plausible alternate reason for the stereochemistry observed in chloroethanol-d_2 formation. In any case the detection of the second mode of hydroxypalladation does demonstrate the hazards of interpreting stereochemical results in terms of kinetic results especially if the stereochemistry is not studied under the same conditions as the kinetics. Of course the choice between the two routes given by eq 2 and 3 cannot be made on the basis of the present results, but the question as to which is operative remains open.

Acknowledgment. This investigation was supported by the Natural Sciences and Engineering Research Council of Canada. We thank Dr. W. K. Wan for the sample of propenol-*1,1*-d_2 and Dr. A. Woon-Fat for the ^1H NMR measurements.

(12) The reason **1** decomposes to acetaldehyde while **4** does not could be that the cis H_2O ligand in **1** is more labile than the cis Cl^- ligand in **4**. The decomposition of **1** by hydride elimination has recently been discussed,[1,4] and the need for a vacant coordination site for hydride elimination has been indicated by kinetic studies.[13,14]

(13) Whitesides, G. M.; Gaasch, J. F.; Stedronsky, E. R. *J. Am. Chem. Soc.* **1972**, *94*, 5258-5270.

(14) Winstein, S. W.; McCaskie, J.; Lee, H. B.; Henry, P. M. *J. Am. Chem. Soc.* **1976**, *98*, 6913-6918.

Isotopic Labeling at Natural Abundance: Multiphoton Dissociation of Perfluoropropene†

P. A. Hackett,* C. Willis, and W. S. Nip

Laser Chemistry Group, Division of Chemistry
National Research Council of Canada
Ottawa, Canada K1A 0R6

Received September 17, 1979
Revised Manuscript Received October 8, 1980

Experiments using molecules with isotopically labeled sites provide useful insight into reaction mechanisms by helping in the identification of transition states, locating centers of radical attack, and indicating routes of isomerizations.[1] The general use of this technique has been restricted in practical terms because the synthesis of substrates with specifically labeled sites is expensive and/or tedious. Infrared laser photolysis offers the potential that this technique can be applied much more generally since it allows isotope-labeled experiments with substrates at natural abundance. Multiphoton infrared excitation is isotopically selective, and by choosing which vibrational mode is activated, one may make the isotopic labeling specific to one site in the molecule. For example, irradiation to the red edge of the ν_{15} band of hexafluoroacetone activates only $CF_3{}^{13}COCF_3$ molecules.[2] This is because the ν_{15} vibration corresponds to an asymetric C–C–C stretch[3] which will have a small isotope shift for $^{13}CF_3COCF_3$ molecules. We report here the first example of the use of this technique to obtain significant information about the topology of a chemical reaction.

We illustrate the technique with results from the isotopically selective infrared multiphoton photolysis of carbon-13 substituted perfluoropropene, obtained by using natural abundance substrates. First reports of the gas-phase pyrolysis of the compound suggested that the primary dissociation step was a bond scission to yield C_2F_4 and CF_2.[4] Subsequently it was proposed that perfluorocyclopropane must be a precursor to dissocation,[5] and indeed this compound was observed in the single-pulse shock-tube pyrolysis of perfluoropropene.[6] We have investigated the infrared multiphoton dissociation of perfluoropropene, following irradiation with the P(28) line of the $^{12}CO_2$ laser at 1039 cm^{-1}. This line is close to the maximum of the strong infrared absorption band at 1037 cm^{-1}. Preliminary results establish the following simple kinetic mechanism:[7]

$$CF_3CFCF_2 \xrightarrow{nh\nu} C_2F_4 + CF_2 \quad (1)$$

$$CF_2 + CF_2 \rightarrow C_2F_4 \quad (2)$$

We have investigated the intermediacy of the cyclopropane intermediate in reaction 1 by performing irradiations on the red edge of the 1037-cm^{-1} band using the P(16) and P(26) lines of the $^{13}CO_2$ laser[8] at 1004 and 995 cm^{-1}, respectively.

Irradiations were performed with a parallel beam at 2 J cm^{-2} incident fluence and were carried to 10% conversion in the minor isotopic component. Following irradiation the product C_2F_4 was distilled from the substrate at −160 °C and analyzed by mass spectrometry. The $C_2F_3{}^+$ ion peaks at *m/e* 81, 82, and 83 were

† Contribution No. 19037.

(1) J. Sirchis, "Methods of preparing and storing labelled compounds", Euratom, Brussels, Belgium 1968.

(2) (a) P. A. Hackett, M. Gauthier, C. Willis, and R. Pilon, *J. Chem. Phys.*, **71**, 546 (1979); (b) P. A. Hackett, C. Willis, and M. Gauthier, *ibid.* **71**, 2682 (1979).

(3) M. Pertillä, *Acta Chem. Scand.*, **28**, 933 (1974).

(4) B. Atkinson and V. Atkinson, *J. Chem. Soc.*, 2086 (1957).

(5) S. W. Benson and H. E. O'Neal, *Natl. Stand. Ref. Data Ser.* (*U.S., Natl. Bur. Stand.*), **NSRDS-NBS21** (1970).

(6) S. H. Bauer, K. Hou, and E. E. Resler, *Phys. Fluids Suppl.*, **1**, II245 (1969).

(7) W. S. Nip, M. Drouin, P. A. Hackett, and C. Willis, *J. Phys. Chem.*, **84**, 932 (1980).

(8) C. Willis, P. A. Hackett, and J. Parsons, *Rev. Sci. Instrum.*, **50**, 1141 (1979).

0002-7863/81/1503-682$01.00/0 © 1981 American Chemical Society