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PALLADIUM(II)-CATALYZED CYCLIZATION OF γ-BENZYL GLUTAMATE WITH FORMATION OF BENZALDEHYDE

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γ-Benzyl glutamate in water at neutral pH undergoes palladium-(II)-catalyzed cyclization with oxidation of the ester bond to give pyroglutamic acid, benzaldehyde, and palladium metal. The reaction is specific for γ-benzyl glutamate and not observed for β-benzyl aspartate and γ-methyl glutamate.

Palladium(II) catalyzes oxidation reactions in which it is reduced to palladium metal.[1] Various alcohols including benzyl alcohol are oxidized by palladium-(II) to the corresponding aldehydes or ketones in boiling water,[2] and the Wacker process[1] is a famous example of the industrial production of acetaldehyde from ethylene through π-complex formation with palladium(II).[3] In the course of the studies on palladium(II) complexes of amino acids in aqueous solution, we have recently found a novel formation of pyroglutamic acid (Pyroglu) and benzaldehyde in a solution containing palladium(II) and γ-benzyl glutamate (GluOBzl), and concluded it to be the result of a palladium(II)-catalyzed specific cyclization with oxidation of the benzyl ester group.

γ-Benzyl L-glutamate (1.2×10^{-4} mol) dissolved in aqueous NaOH was mixed with an aqueous solution of Na_2PdCl_4 (6×10^{-5} mol) at room temperature, and the pH of the resulting mixture was adjusted at ~7, when a clear yellow–yellowish brown solution (*ca.* 3×10^{-2} mol dm^{-3}) was obtained. On standing at room temperature, the solution gradually precipitated palladium metal, giving an aldehyde odor. After a few days, the pH of the reaction mixture decreased to ~3.5 with nearly complete precipitation of palladium. The reaction was faster in acid solution and much slower in alkaline solution, and under N_2 it was complete in 2 h at pH 6.8. Gas and liquid chromatographic analyses of the reaction mixture confirmed the existence of benzaldehyde, benzoic acid, and benzyl alcohol. Their recoveries (%) based on the total amount of GluOBzl used are summarized in Table 1 together with the recovery of palladium metal determined by gravimetric analysis. Benzoic acid detected is probably the oxidation product of benzaldehyde, and the other decomposition reactions might have occurred during the reaction. A small amount of glutamic acid (Glu) was detected by amino acid analysis, but no significant amount of GluOBzl was traced in the chromatogram.[4] The ^{13}C NMR spectrum of the aqueous portion of the reaction mixture was nearly identical with that of Pyroglu. In accordance with this, a neutral solution of the 1:2 Pd(II)–GluOBzl system was found to exhibit shortly after preparation a circular dichroism (CD) spectrum very similar to that of the 1:2 Pd(II)–

Table 1. Recoveries of Reaction Products[a)]

No.	Initial pH	Temp/°C	Recovery/%			
			Pd	C_6H_5CHO	C_6H_5COOH	$C_6H_5CH_2OH$
1	6.8	r.t.[b)]	96	37	4	14
2	4.5	r.t.	99	22	10	17
3	6.8	60	—[c)]	23	24	14
4[d)]	6.8	r.t.	—	40	9	8

a) Based on the total amounts of Pd(II) and GluOBzl used.
b) Room temperature (~30°C).
c) Not measured because the residue ignited on drying.
d) Under N_2.

Pyroglu system, which supports the view that the glutamate moiety is converted to Pyroglu or its analogue before oxidation.[5)] The ^1H NMR spectra showed that the signal ascribable to the benzyl methylene protons decreased with time, indicating the dehydrogenation by palladium(II) at this CH_2 group.

Platinum(II) (K_2PtCl_4) also decomposed GluOBzl to give benzaldehyde. However, neither palladium(II) nor platinum(II) afforded the aldehyde from β-benzyl aspartate (AspOBzl) or γ-methyl glutamate (GluOMe), and the reaction has been revealed to be specific for GluOBzl. On the other hand, an aqueous solution containing benzyl alcohol and $Pd(Glu)_2$ at neutral pH remained unchanged for many days with no detectable redox reaction. γ-Phenethyl glutamate (GluOPhen) in the presence of palladium(II) showed a CD spectrum similar to that of $Pd(Pyroglu)_2$ and thus appeared to be converted to a pyroglutamate derivative,[5)] although it was not oxidized by palladium(II) under the same conditions. Further studies on the mechanism of the reaction are in progress.

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References and Notes

1) J. Tsuji, "Organic Synthesis by Means of Transition Metal Complexes," Springer-Verlag, Berlin(1975), p. 112.
2) A. V. Nikiforova, I. I. Moiseev, and Ya. K. Syrkin, *Zh. Obshch. Khim.*, 33, 3239 (1963).
3) R. Jira, J. Sedlmeir, and J. Smidt, *Justus Liebigs Ann. Chem.*, 693, 99(1966).
4) On the basis of amino acid analysis, hydrolysis of GluOBzl in alkaline solution in the absence of palladium(II) was estimated to be less than 10 % under the conditions employed.
5) The CD spectra exhibited by the systems $Pd(GluOBzl)_2$, $Pd(GluOPhen)_2$, and $Pd(Pyroglu)_2$ are similar to each other with large extrema at ~390 nm ($\Delta\varepsilon\simeq 2$) and ~330 nm ($\Delta\varepsilon\simeq -2$), whereas those exhibited by $Pd(GluOMe)_2$, $Pd(AspOBzl)_2$, $Pd(Glu)_2$, and $Pd(Asp)_2$ (Asp: aspartate) have smaller extrema at ~350 nm ($\Delta\varepsilon\simeq 0.2$—1) and ~310 nm ($\Delta\varepsilon\simeq -0.8$—−1.5).

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