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LETTERS

The Catalysis of Intramolecular [4+2] Cycloaddition Reaction by Palladium Complexes

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ABSTRACT : Palladium (II) acetate and triphenylphosphine in the ratio of 1:2 catalyze intramolecular [4+2] cycloaddition reaction.

Diels Alder reaction has become one of the most commonly used method in organic synthesis because of its ability to construct six membered rings in highly stereoselective and largely predictable fashion. Although both intra and intermolecular reaction are well known, they typically involve electronically dissimilar components. Application of the method to electronically comparable components has been limited due to extreme reaction conditions required for the reaction.[2] A number of examples have appeared in literature that list the limitation due to temperature requirments,[3] for example deca-7,9-dien-1-yne require 72 hr. at 150°C to achieve cyclization.[4] It has been found that certain transition - metals complexes can accelerate both inter and intramolecular reaction.[5]

Recently, while attempting to obtain certain substrates for biocatalyzed reactions via palladium chemistry, we came across certain observations, which resulted in the development of a new catalyst for [4+2] cycloaddition reaction. Thus, a solution of 1-(2-propynoloxy)-2,4-hexadiene **1** in THF was warmed to 50°C under argon, triphenylphospine (10 mol %) and palladium (II) acetate (5 mol %) were added sequentially[6] and the mixture stirred for 10 min. The color of the reaction changed from deep red to transparent brown. Usual work up of the reaction mixture gave cycloadduct **2** in 85 % yield.[7,8] Similarly, the reaction of **3** yielded cycloadduct **4**.[7,8] The effect of ligand concentration, solvent and temperature was studied. The results are presented in Table 1. That the reaction occurred with terminal alkynes and at 0°C is significant. Typically it requires a powerful activating group at dienophile to reach such low temperatures[9]. In the absence of catalyst 1 cyclized to the extent of only 20 % after 24 hr at 120°C.[5e] The reaction failed with substrate **5**, in which triple bond is replaced with a double bond. The mechanistic details of the reaction have not been investigated so far, but the reaction may be proceeding by the mechanism proposed earlier for Rh(I) and Ni(0) catalyzed intramolecular [4+2]cycloadditions.[5d,e] It is pertinent to state that $Pd(OAc)_2$ and a phosphine can generate *in situ* zero valent palladium complexes.[10]

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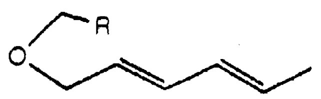
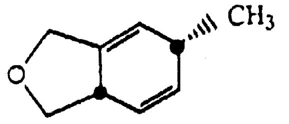
Table 1 : Palladium Catalyzed [4+2] Cycloaddition Reactions

Substrate	solvent	ligand:Pd ratio	temp (°C)	time	Product (yield%)
1	THF	2 : 1	50	10 min	**2**(87)
1	THF	2 : 1	25	2 hr	**2**(81)
1	THF	2 : 1	0	5 hr	**2**(73)
1	THF	3 : 1	50	4 hr	no reaction
1	CH_2Cl_2 or CH_3CN	2 : 1	50	4 hr	no reaction
3	THF	2 : 1	50	15 min	**4**(89)
5	THF	2 : 1	50	4 hr	no reaction
5	THF	3 : 1	50	4 hr	no reaction



1, R = C:CH
5, R = CH:CH$_2$



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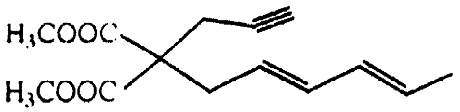

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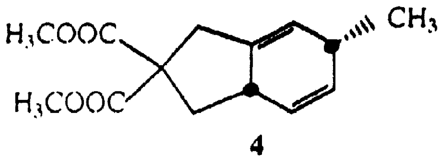

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6. In our experience, palladium acetate must be added as the last component for success of the reaction.
7. The work up procedure involved evaporation of solvent followed by flash chromatography over silica gel ; the structure of all the compounds was confirmed by IR and NMR.
8. The compounds **2** and **4** are known compounds; their relative stereochemistry as indicated was assigned based on nuclear Overhauser enhancement difference (NOED) spectroscopy and identical spectral (NMR, IR and Mass) data with the samples prepared by the method of Livinghouse.[5e]
9. For example, Gassman, P.G.; Gorman, D.B., *J.Am. Chem. Soc.*, **1990**, *112*, 8624 and references cited their-in.
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