Tetrahedron Letters No. 4, pp 355 - 358, 1977. Pergamon Press. Printed in Great Britain.

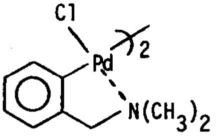
ADDITION OF ENONES TO ARYL PALLADIUM COMPLEXES

Robert A. Holton[1]
R. B. Wetherill Laboratory of Chemistry, Purdue University,
West Lafayette, Indiana 47907

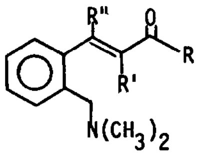
(Received in U.S.A. 30 November 1976; received in U.K. for publication 28 November 1976)

Arylation of olefins in the presence of various palladium (II) species has been a topic of recent interest.[2] Unambiguous demonstration of the presumed intermediacy of aryl palladium complexes in such processes has been neglected,[3,4] despite the ready availability of stable aryl palladium complexes containing chelating benzylic amino functionality in the ortho position.[5] We wish to report the addition of enones to ortho palladated benzylic amines, a reaction which, by virtue of its high yields, mild conditions, and complete regiospecificity, we believe to be a valuable addition to synthetic methodology.

Treatment of complex 1[5] with methyl vinyl ketone in refluxing toluene or benzene containing excess triethylamine for 1-2 hr gives rise to metallic palladium and adduct 2a ($R=CH_3$, R'=R''=H): bp 133-135 (1mm); ir($CHCl_3$) 3.36, 5.98, 7.38, and 8.00 µ; nmr ($CDCl_3$) 2.18 (s, 6), 2.31 (s, 3), 2.43 (s, 2), 6.56 (d, 1, J=17Hz), 7.24 (m, 3), 7.56 (m, 1), and 8.08δ (d, 1, J=17Hz);



1

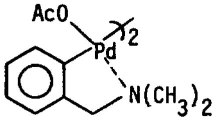


2a-f

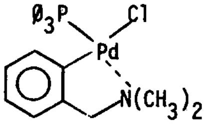
in 92% isolated yield. That tertiary amine is a necessary ingredient is demonstrated by the conversion of 1 to a mixture containing approximately equal parts of 2 and dimethylbenzylamine (after basic extraction) when the reaction is conducted in toluene or benzene containing no added tertiary amine. This observation may be rationalized on the basis that complex 1 competes favorably with amine 2 for hydrochloric acid generated as the reaction proceeds. Indeed, 1 reacts instantaneously with dry hydrochloric acid in dichloroethane to produce dimethylbenzylamine hydrochloride in quantitative yield.

Despite the sensitivity of 1 to hydrochloric acid, this complex may be recovered unchanged from treatment with acetic acid in dichloroethane for several hours at room temperature. Furthermore, the reaction of 1 with enones is accelerated in the presence of acetic acid; the addition to methyl vinyl ketone (4 equiv) proceeds to completion (>90% isolated 2a) within 5 hr at room temperature in acetic acid/dichloroethane (3/1) containing 5 equiv diisopropylethylamine (utilization of a stoichiometric amount of enone requires 15-20 hr at room temperature for the production of 2a in 90% yield). Deletion of diisopropylethylamine from this reaction mixture results in the production of 2a and dimethylbenzylamine in a 7:3 ratio. Although the use of trifluoracetic acid does not lead to rapid reduction of 1, neither does its presence appear to exert an accelerating effect on the reaction comparable to that of acetic acid. Added boron trifluoride etherate to a solution of 1 in dichloroethane containing methyl vinyl ketone is ineffectual for the production of 2a.

The acetoxy complex 3[6] does not appear to be an intermediate in this process. Treatment of 3 with methyl vinyl ketone in either refluxing toluene or acetic acid/dichloroethane at room temperature produces adduct 2a much more slowly than does the corresponding chloro complex. Addition of silver acetate to the previously described mixture of 1, methyl vinyl ketone, and diisopropylethylamine in acetic acid/dichloroethane produces no perceptible acceleration in the rate of production of 2a.



3

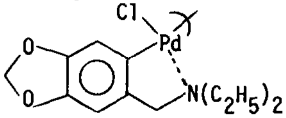
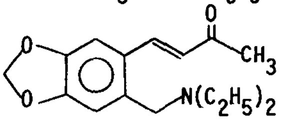


4

Coordination of the olefinic moiety in an <u>apical</u> position of the square planar palladium complex is implicated by the following experiments: Monomeric triphenylphosphine complex 4[7] undergoes addition to methyl vinyl ketone at essentially the same rate as does 1. However, significant rate retardation is observed when the addition of 4 to methyl vinyl ketone is conducted in the presence of 1 equiv of added triphenylphosphine.

As shown in the results listed in the Table, this reaction seems to be generally applicable to vinyl ketones. Although the bulk of the enone α' substituent has little effect on the rate of reaction or the yield of the β-aryl enone product, steric effects appear to play a major role in suppressing the addition when the starting enone bears substituents in either the α or β position. Thus, no detectable adduct is generated under any of the above conditio an enone containing a β substituent; 3-pentene-2-one and cyclopentenone fail to react lex 1. Enones bearing substituents in the α position react somewhat sluggishly, 3-phen ene-2-one requiring approximately 30 hr for complete addition to 1.

Table

Palladium Complex	Enone	Adduct[a] R	R'	R''	% Yield[b,c]
1	methyl vinyl ketone	2a; CH_3	H	H	92[d], 95(90)
1	ethyl vinyl ketone	2b; C_2H_5	H	H	93(88)
1	cyclohexyl vinyl ketone	2c; Cyclo-C_6H_{11}	H	H	96(91)
1	phenyl vinyl ketone	2d; C_6H_5	H	H	94(89)
1	3-pentene-2-one	2e; CH_3	H	H	0
1	3-phenyl-3-butene-2-one	2f;[e] CH_3	C_6H_5	H	80(76)
 5	methyl vinyl ketone	 6			95(93)

(a) Structures consistent with ir, nmr, and mass spectra. All new compounds give correct analytical data. Only trans adducts have been isolated, cis adducts have not been detected. (b) All yields refer to isolated, chromatographically and spectrally homogeneous material. Yields are based on palladium complex (acetic acid, dichloroethane, diisopropyethylamine, room temperature, 6-30 hr). (c) Yields in parentheses are for the overall two-step conversion of benzylic amine to enone adduct. (d) Toluene, triethylamine, reflux 45 min. (e) Stereochemistry undetermined.

This conversion is clearly applicable to tertiary benzylic amines bearing a variety of substituents on the aromatic ring. Exemplary of this point is the recovery of adduct 6 in 95% yield upon treatment of complex 5[8] with methyl vinyl ketone under the conditions described above.

Adducts similar to 2 and 6, previously available by comparatively circuitous routes, have been used as intermediates in alkaloid synthesis.[9] We are currently attempting to exploit this reaction in the synthesis of aromatic alkaloids. The intramolecular version of this reaction is under active investigation in our laboratory. The results of these studies will be reported in due course.

Acknowledgement. We wish to thank the Public Health Service for support of this research.

REFERENCES AND NOTES

1. DuPont Assistant Professor of Chemistry.
2. R. F. Heck, *J. Amer. Chem. Soc.*, **90**, 5535, 5538 (1968); Y. Fujiwara, I. Moritani, S. Danno, R. Asano, and S. Teranishi, *ibid.*, **91**, 7166, (1969).
3. J. Tsuti, *Accts. Chem. Res.*, **2**, 142 (1969), claimed that **1** adds to styrene "easily"; no conditions or yields were reported.
4. M. Julia, M. Duteil, and J. Y. Lallemand, *J. Organometal. Chem.*, **102**, 239 (1975), have reported the addition of ethyl acrylate to the palladium complex of 1-dimethylaminomethylnaphthalene.
5. A. C. Cope and E. C. Friedrich, *J. Amer. Chem. Soc.*, **90**, 909 (1968).
6. J. M. Thompson and R. F. Heck, *J. Org. Chem.*, **40**, 2667 (1975).
7. Prepared in quantitative yield from **1** and triphenylphosphine (2.2 equiv) in dichloroethane at room temperature, mp 188-190°; see S. Otsuka, A. Nakamura, T. Kano, and K. Tani, *J. Amer. Chem. Soc.*, **93**, 4301 (1971).
8. Prepared in 98% yield from dimethylpiperonyl amine, triethylamine, and lithium tetrachloropalladate in methanol at room temperature, mp 183-185°(d).
9. B. Ganem, *Tetrahedron Lett.*, 4105 (1971).