

Isamu Arai and G. Doyle Daves, Jr.

Department of Chemistry and Biochemical Sciences,
Oregon Graduate Center, Beaverton, Oregon 97005

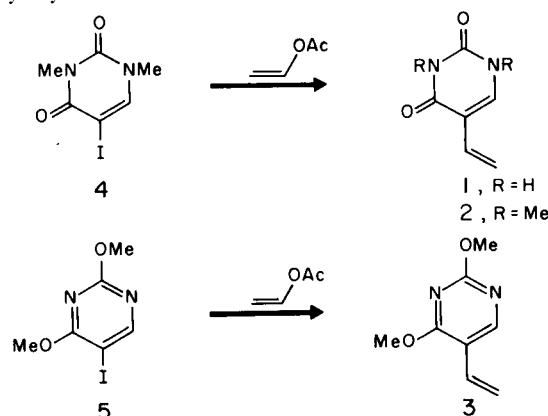
Received January 9, 1978

Reactions of 1,3-dimethyl-5-iodouracil or 2,4-dimethoxy-5-iodopyrimidine with vinyl acetate in the presence of a catalytic amount of diacetato-*bis* (triphenylphosphine) palladium (II) resulted in good yields of the corresponding 5-vinylpyrimidines. The reactions are viewed as resulting from regioselective addition of an initially formed 5-pyrimidinyl palladium species to the double bond of vinyl acetate followed by elimination of a palladium acetate with regeneration of the double bond and formation of the 5-vinylpyrimidine product.

J. Heterocyclic Chem., 15, 351 (1978)

Sir:

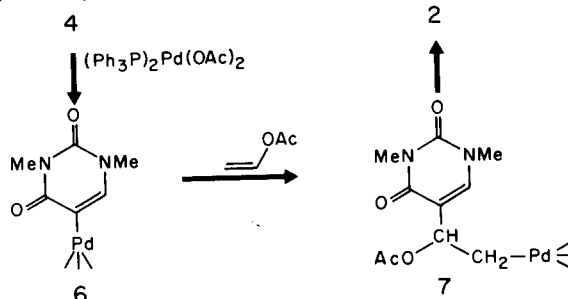
The demonstration that 5-vinyluracil (1) is incorporated into deoxynucleic acid of microorganisms, *e.g.*, *E. coli* (1,2) and *M. capri* (2), has stimulated interest in synthetic methods for preparing 5-vinylpyrimidines and a number of syntheses have been reported (3-7). We now describe a new and convenient, one-pot synthesis which involves the palladium catalyzed reaction of a 5-iodopyrimidine (*e.g.*, 4 or 5) with vinyl acetate and yields the corresponding 5-vinylpyrimidine (2 or 3) directly (8). It is important to note that the present results differ significantly from those reported by Heck (9,10) in which palladium catalyzed arylation of enol acetates yielded primarily arylated enol acetates.



In the present study, 1,3-dimethyl-5-vinyluracil (2) and 2,4-dimethoxy-5-vinylpyrimidine (3) were prepared in isolated yields of 60 and 58 per cent respectively. Thus a mixture consisting of 1.34 g. (5 mmoles) of 1,3-dimethyl-5-iodouracil (4) (11), 1.0 g. (10 mmoles) of triethylamine, 0.037 g. ($5 \cdot 10^{-2}$ mmole) of diacetato-*bis* (triphenylphosphine) palladium (II) (12) and 25 ml. of vinyl acetate was heated in a sealed tube at 100° for 5 hours. The cooled reaction mixture was partitioned between chloroform and water and the chloroform soluble portion was chromatographed on silica gel using dichloromethane to yield 0.5 g. (60%) of 1,3-dimethyl-5-vinyluracil (2), m.p. 65°, dec., (13) (recrystallized from hexane) which exhibited uv λ max 237,292 nm; ¹H nmr (deuteriochloro-

form): δ 3.40, 3.46 (NMes), 5.24, 5.91, 6.49 (ABX system, $J = 2, 11, 18$ Hz), 7.24 (C-6H) and ms: m/e 166 (M^+). In exactly the same way 2,4-dimethoxy-5-iodopyrimidine (5) (14) was converted to 2,4-dimethoxy-5-vinylpyrimidine (3), isolated as a colorless viscous oil in 58% yield. 2,4-Dimethoxy-5-vinylpyrimidine (3) was characterized by uv λ max 247,280 (sh) nm; ¹H nmr (deuteriochloroform): δ 4.00, 4.30 (OMes), 5.28, 5.77, 6.65 (ABX system, $J = 2, 12, 18$), 8.28 (C-6H) and ms: m/e 166 (M^+).

Mechanistically, it is most convenient to view these reactions as involving initial formation of a 5-pyrimidinyl-palladium derivative (6) (8,15) followed by regioselective *syn* addition of this organopalladium reagent (6) to vinyl acetate forming a second nonisolated intermediate (7) which upon loss of palladium acetate regenerates the catalyst and yields the 5-vinylpyrimidine product 2.



The intermediacy of 7 in which the new carbon-carbon bond occurs selectively at the olefinic oxygen-bearing carbon indicates electronic effects are more important than steric effects in the adduct forming step. This result parallels closely reactions of 5-pyrimidinyl-palladium compounds with cyclic enol ethers which we have reported recently (15) and contrasts somewhat with earlier work of Heck (16) in which arylpalladium intermediates prepared from the corresponding aryl mercuric species reacted with enol esters, including vinyl acetate, with less specificity leading to product mixtures.

It is noteworthy that the two quite different pyrimidinyl species, *i.e.*, 5 which is aromatic and 4 which is a substituted α, β -unsaturated amide, react similarly and both result in good yields of essentially a single product.

This suggests that the reaction will prove quite general.

Acknowledgment.

Appreciation is expressed to the American Cancer Society for financial support of this research.

REFERENCES AND NOTES

- (1) E. T. J. Chelton, C. H. Evans, A. S. Jones and R. T. Walker, *Biochim. Biophys. Acta*, **312**, 38 (1973).
- (2) A. S. Jones and R. T. Walker, *Nucleic Acids Res.*, Spec. Pub. No. 1, sl (1975).
- (3) J. D. Fissekis and F. Sweet, *J. Org. Chem.*, **38**, 264 (1973).
- (4) C. H. Evans, A. S. Jones and R. T. Walker, *Tetrahedron*, **29**, 1611 (1973).
- (5) J. D. Fissekis and F. Sweet, *J. Org. Chem.*, **38**, 1963 (1973).
- (6) A. S. Jones, G. P. Stephenson and R. T. Walker, *Nucleic Acids Res.*, **1**, 105 (1974).
- (7) R. A. Shama and M. Bobek, *J. Org. Chem.*, **40**, 2277 (1975).
- (8) D. E. Bergstrom and J. L. Ruth, *J. Am. Chem. Soc.*, **98**, 1587 (1976) prepared a palladium derivative from 5-chloromercuriuridine and allowed it to react with ethylene; no 5-vinyl product was formed. In contrast, the palladium catalyzed reaction of phenylmercuric chloride with ethylene produces styrene in good yield (R. F. Heck, *ibid.*, **90**, 5518, 5526 (1968)).
- (9) R. F. Heck, *Organomet. Chem. Synth.*, **1**, 445 (1972).
- (10) R. F. Heck, *J. Am. Chem. Soc.*, **90**, 5535 (1968).
- (11a) R. D. Youssefeyeh and L. Lichtenberg, *J. Chem. Soc., Perkin Trans. I*, 2649 (1974); (b) N. M. Bui, R. Gillet and P. Dumont, *Int. J. Appl. Radiat. Isot.*, **16**, 337 (1965).
- (12) T. A. Stephenson, S. M. Morehouse, A. R. Powell, J. P. Heffer and G. Wilkinson, *J. Chem. Soc.*, 3632 (1965).
- (13) Compound **2** is unstable when stored at room temperature and polymerizes within a few days.
- (14) M. Prystas and F. Sorm, *Collect. Czech. Chem. Commun.*, **29**, 121 (1964).
- (15) I. Arai and G. D. Daves, Jr., *J. Am. Chem. Soc.*, **100**, 287 (1978).
- (16) R. F. Heck, *J. Am. Chem. Soc.*, **90**, 5535 (1968).