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PALLADIUM-CATALYZED REGIOSELECTIVE REACTIONS OF α-ACETOXY-β,γ-UNSATURATED NITRILES AND γ-ACETOXY-α,β-UNSATURATED ESTER WITH NUCLEOPHILES

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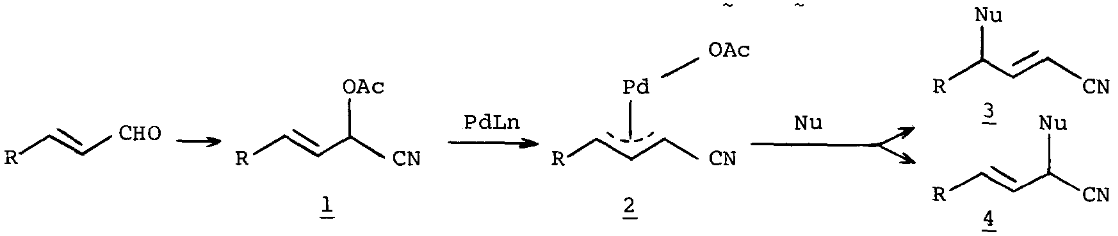
Summary: α-Acetoxy-β,γ-unsaturated nitriles react at room temperature with malonates and acetoacetates in the presence of palladium-phosphine complexes as a catalyst to give γ-substituted α,β-unsaturated nitriles selectively. Also γ-acetoxy-α,β-unsaturated ester was attacked at γ-position by malonate.

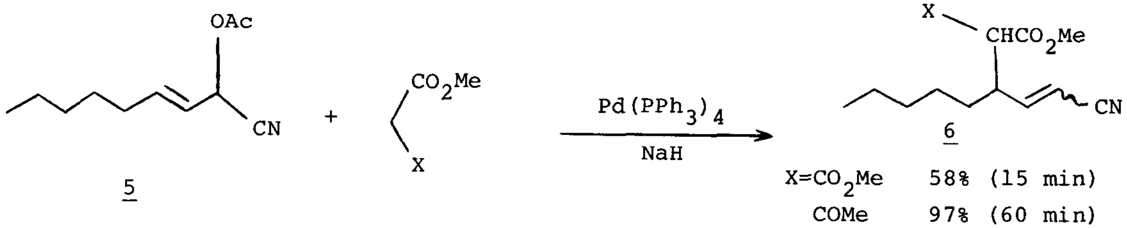
It is well-known that allylic acetates react with nucleophiles using palladium-phosphine complex as a catalyst.1) The reaction is believed to proceed via the formation of π-allylpalladium complexes, which are attacked by nucleophiles. Although this is useful for carbon-carbon bond formation, sometimes the reaction is not regioselective when unsymmetrical allylic compounds are used. We have been studying the effect of substituents on the regiochemistry of the reaction. We report here the reaction of allylic acetates substituted by nitrile and ester groups with nucleophiles in the presence of a palladium catalyst.

The substrates of the present study are α-acetoxy-β,γ-unsaturated nitriles 1, which can be prepared easily by the acetylation of cyanohydrins of α,β-unsaturated aldehydes.2) These compounds are expected to react with palladium to form π-allylpalladium complexes 2 substituted by a nitrile group, and there are following two possible routes of nucleophilic attack to afford 3 or 4.

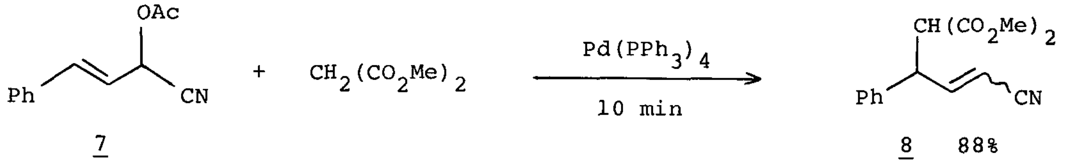


Actually we found that these compounds reacted smoothly with malonates and acetoacetates regioselectively to give only the product 3 in the presence of the palladium catalyst under mild conditions. But the double bonds generated were a mixture of E and Z isomers.

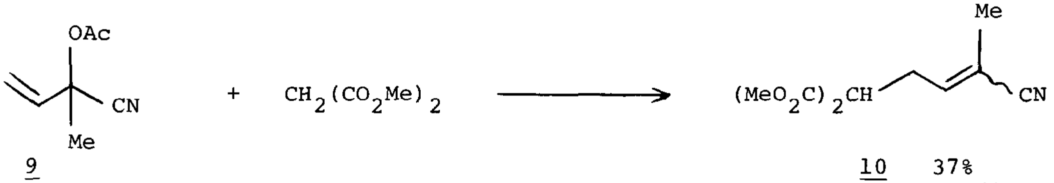
We carried out the reaction of 2-acetoxy-3-nonenenitrile (5) in THF with anion of dimethyl malonate or methyl acetoacetate at room temperature in the presence of 5 mol% of $Pd(PPh_3)_4$ as the catalyst. The reaction proceeded rapidly and the nucleophiles were introduced selectively at the γ-position to give 4-substituted 2-nonenenitrile 6 in good yield.



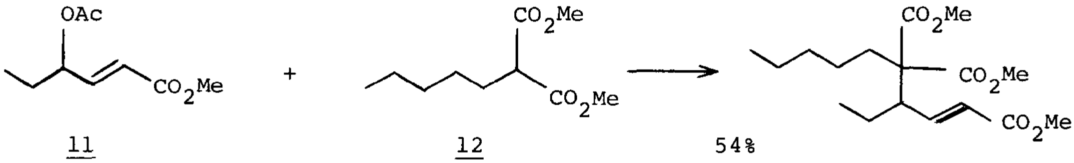
Also the reaction of 2-acetoxy-4-phenyl-3-butenenitrile (7), prepared from cinnamaldehyde, with malonate proceeded at room temperature in 10 min to give the 4-substituted nitrile 8 in 88% yield. Methyl acetoacetate reacted similarly.



Additional substituents in the π-allyl system decrease the yields. The cyanohydrin 9 reacted with dimethyl malonate regioselectively to give 10, but the yield was low (37%). A reaction of the cyanohydrin derived from citral gave a poor yield and the main path was the elimination.



An ester group showed the same effect. Methyl 4-acetoxy-2-hexenoate (11)[3] was attacked by dimethyl pentylmalonate (12) selectively at γ-position at room temperature. In this case, only the E isomer was obtained.



Clearly the electron attracting group showed decisive effect on the regioselectivity in the reaction of π-allylpalladium system, and the nucleophilic attack takes place at the electron deficient side of the π-allyl system.

References: 1) Reviews: a) J.Tsuji, Organic Synthesis with Palladium Compounds, Springer Verlag, 1980. b) B.M.Trost, Tetrahedron Report, No.32, 2615 (1977). 2) The palladium-catalyzed elimination reaction of acetic acid from α-acetoxy-β,γ-unsaturated nitrile to form diene nitrile has been reported. T.Mandai, J.Gotoh, J.Otera, and M.Kawada, Chem.Lett., 1980, 313. 3) J.Tsuji, K.Sakai, H.Nagashima, and I.Shimizu, Tetrahedron Lett., 22, 131 (1981).

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