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A HIGHLY STEREO- , REGIO- , AND CHEMOSELECTIVE SYNTHESIS OF CONJUGATED DIENES BY THE PALLADIUM-CATALYZED REACTION OF (E)-1-ALKENYLZIRCONIUM DERIVATIVES WITH ALKENYL HALIDES[1]

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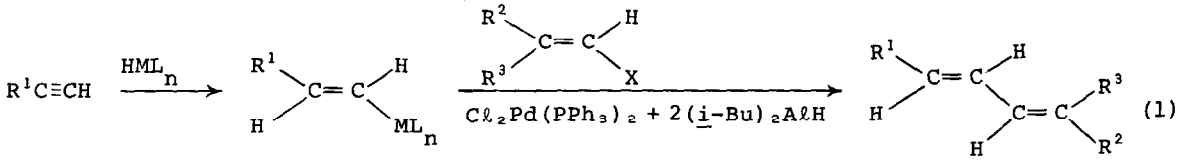
We have recently reported a highly stereo- and regioselective procedure for the synthesis of conjugated dienes by a Pd-catalyzed reaction of alkenylalanes with alkenyl halides[2] (eq 1: $ML_n = A\ell(Bu\text{-}i)_2$).

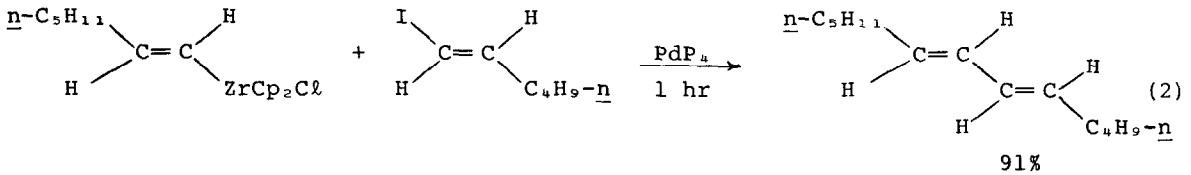


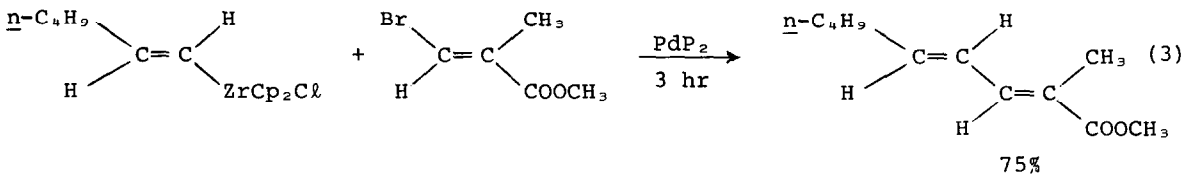
(1)

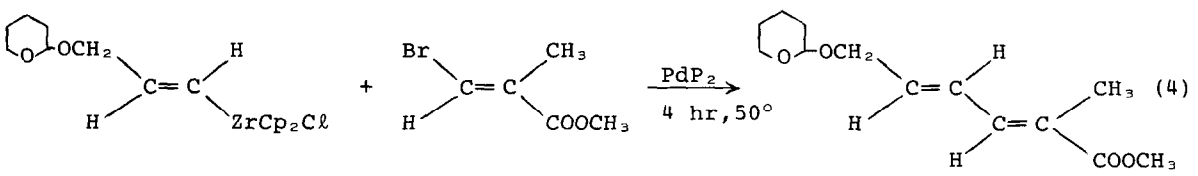
$ML_n = A\ell(Bu\text{-}i)_2$ or $C\ell ZrCp_2$

However, the fact that hydroalumination is incompatible with various common oxy-functionalities in the R^1 group[3] has limited its synthetic usefulness. We have subsequently found that hydrozirconation[4] can tolerate certain ether functionalities, such as OEt and OTHP groups,[5] and that the (E)-1-alkenylzirconium compounds thus obtained can be reacted with aryl halides in the presence of a catalytic amount of $Ni(PPh_3)_4$ to form arylated alkenes containing such functional groups.[5]

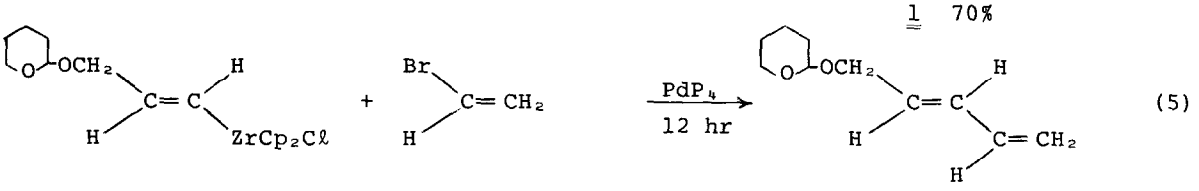
Based on these findings we decided to test the feasibility of applying these findings to the development of a selective synthesis of conjugated dienes *via* the alkenylzirconium compounds, and have indeed found out that the conjugated diene synthesis shown in eq 1 can be successfully achieved with the (E)-1-alkenylzirconium compounds in place of the corresponding organoalanes, as indicated by the results shown in eq 2-6.



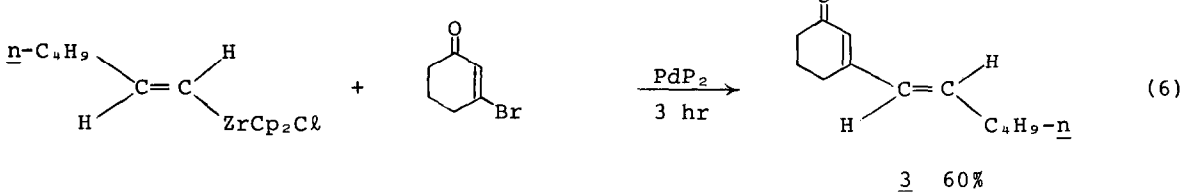




1 70%



2 77%



3 60%

PdP_4^7 = $Pd(PPh_3)_4$ PdP_2^2 = $Cl_2Pd(PPh_3)_2$ + 2 i-Bu_2AlH

In each case, the required (E)-1-alkenylzirconium intermediate was prepared from the corresponding acetylene and H(Cl)$ZrCp_2$ in benzene by the reported procedure.[4] After evaporation of benzene, THF (2-3 ml/mmol alkenyl halide), a Pd catalyst (5 mole %) in THF, and an alkenyl halide (acetylene/alkenyl halide = 1.5, except in eq 5 where the ratio was 1/5) were added sequentially at room temperature. The reaction mixture was treated with water, evaporated and extracted with pentane and/or ether. After removal of water and the solvent, the product was isolated by either distillation or column chromatography. The products were identified by ^1H and ^{13}C NMR and IR, which support the indicated stereochemistry. The ^{13}C NMR spectra indicate that the isomeric purity of the pro-

ducts are ≥97%.

The following observations and interpretations are worth noting. (1) The results shown in eq 2 and 3 indicate that the alkenylzirconium compounds are at least as satisfactory as the corresponding alkenylalanes[2] in terms of the product yield and stereoselectivity. Although no rigorous kinetic comparison has been made, the alkenylzirconium derivatives appear either as reactive as or somewhat more reactive than the corresponding alkenylalanes used. In the corresponding alkenylalane reactions examined earlier, $Pd(PPh_3)_4$ proved unsatisfactory and the use of the Pd catalyst generated *in situ* from $C\ell_2Pd(PPh_3)_2$ and two equiv of $HA\ell(Bu\text{-}i)_2$ was necessary.[2] While the same was still true in eq 3, 4, and 6, even $Pd(PPh_3)_4$ was satisfactory in the other cases. (2) No difficulty was encountered in incorporating the (*E*)-3-tetrahydropyranyloxy-1-propenyl group into conjugated dienes *via* hydrozirconation of the corresponding acetylene[7] (eq 4 and 5). (3) It might be pointed out that the product **1**:bp 113-116°C (0.25 mm); ^{1}H NMR ($CC\ell_4$, TMS) δ 1.3-1.8 (m, 6H), 1.93 (s, 3H), 3.3-4.0 (m with a sharp singlet at 3.70, 5H), 4.15 (dd, J = 6 and 6 Hz, 2H), 4.60 (s, 1H), and 5.8-7.3 (m, 3H) ppm; IR (neat) 1710(s), 1640(w), 1610(w), 1280(s), 1220(s), 1105(s), 1020(s), 965(m), 745(m) cm^{-1}, not only has the correct stereochemistry, but is suitably functionalized as a potentially attractive synthon for the construction of the "south-western" zone of maytansines.[8] (4) As shown in eq 5, vinyl bromide itself reacts quite well in the synthesis of **2**:bp 65-66°C (1-2 mm); ^{1}H NMR ($CDC\ell_3$, TMS) δ 1.3-2.0 (m, 6H), 3.3-4.5 (m, 4H), 4.60 (broad s, 1H), 4.8-5.5 (m, 2H) and 5.5-6.7 (m, 3H) ppm; IR (neat) 1600(w), 1130(s), 1110(s), 1070(s), 1030(s), 1020(s), 1000(s), 950(m), 900(s), 870 (m) cm^{-1}. (5) The reaction shown in eq 6, coupled with recent developments of highly satisfactory procedures for the synthesis of β-halocyclenones,[9] promises to provide a new facile entry into β-organosubstituted cyclenones represented by **3**: ^{1}H NMR ($CDC\ell_3$, TMS) δ 0.7-1.1 (t, J = 6 Hz, 3H), 1.1-2.6 (m, 12H), 5.70 (s, 1H) and 6.0-6.2 (m, 2H) ppm; IR (neat) 1660(s), 1630(s), 1580(w), 960(s) cm^{-1}. (6) We have previously found that, although certain nickel complexes, such as $Ni(PPh_3)_4$, are effective catalysts, they tend to induce competitive isomerization of the diene products.[2] Moreover, the maximum yield of **1** observed by using $Ni(PPh_3)_4$ as a catalyst has been only 51%. It thus appears that, at least in the synthesis of conjugated dienes, palladium catalysts offer distinct advantages over nickel catalysts. (7) Unfortunately, diorganosubstituted alkenylzirconium compounds are quite reluctant to react with alkenyl halides under comparable conditions. This point is being investigated further.

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