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Heck reaction with an alkenylidenecyclopropane: the formation of arylallylidenecyclopropanes

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Abstract—The palladium–tetraphosphine catalyzed arylation of an alkylidenecyclopropane gives a simple and direct access to 1-aryl-2-methyl-1-(2,2,3,3-tetramethylcyclopropylidene)propenes. This reaction tolerates several functional groups on the aryl bromides. Even heteroaryl bromides have been used successfully. This reaction probably proceeds via a classical oxidative addition of the aryl bromide to palladium, insertion of the C=CMe_2 bond in the Ar–Pd bond followed by β-elimination to give the dienes.

The palladium-catalyzed Heck vinylation reaction is an important part of the synthesis chemist's toolbox.[1] Recently, palladium-catalyzed synthesis of 1,3-dienes from intramolecular[2] or intermolecular[3] Heck reactions of allenes and aryl halides has been described. Often, the 1,3-dienes have been trapped in situ by a Diels–Alder reaction.[4] An interesting type of allenic compounds would be the alkylidenecyclopropanes, which are very constraint hydrocarbon derivatives. These alkylidenecyclopropanes are readily available by the addition of Hatzler's carbene (alkenylidene carbene)[5] to alkenes.[6] These highly unsaturated small-ring compounds undergo thermal interconversions,[7] and present an unusual behavior in the course of electrophilic additions (acidic medium,[8] acetoxymercuration,[9] ozonolysis,[10] radical additions,[11] cycloadditions,[12] homoallenyl participation,[13]). The reaction of Fischer chromiumcarbene complexes with alkylidenecyclopropanes afforded allylidenecyclopropanes in good yields.[14] To the best of our knowledge, alkylidenecyclopropanes have rarely been used in palladium-catalyzed reactions.[15] We found only one recent report by Shi and Lu. They described that the Pd-catalyzed reactions of vinylidenecyclopropanes with acetic acid proceeded smoothly to give the corresponding cyclopropane ring-opened products acetylated dienes in moderate to good yields in the presence of DPEphos ligand.[15b]

Some years ago, we have prepared the tetraphosphine ligand, *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane or Tedicyp in which four diphenylphosphino groups are stereospecifically bound to the same face of the cyclopentane ring.[16] We have already reported the results concerning some cross-coupling reactions[17] and particularly Heck vinylation.[18]

Here, we wish to report on the palladium-catalyzed arylation of 1-(2-methylpropenylidene)-2,2,3,3-tetramethylcyclopropane **1** coming from the reaction of 3-chloro-3-methyl-1-butyne and 2,3-dimethyl-2-butene in the presence of base.[6] We observed that, with our catalyst $[Pd(C_3H_5)Cl]_2$/2 Tedicyp using *N*,*N*-dimethylacetamide as solvent and potassium carbonate as base, aryl bromides react cleanly with **1** to give 1-aryl-2-methyl-1-(2,2,3,3-tetramethylcyclopropylidene) propenes **2** without formation of by-products (Scheme 1). The efficiency of the complex authorizes a low catalyst loading reaction (ratio substrate–catalyst: 250).[19–21] These very constraint compounds[22] were obtained both from electron-poor aryl bromides such as 4-bromobenzaldehyde, 4-bromoacetophenone, 4-bromobenzophenone, methyl 4-bromo- benzoate, 4-nitrobromobenzene,

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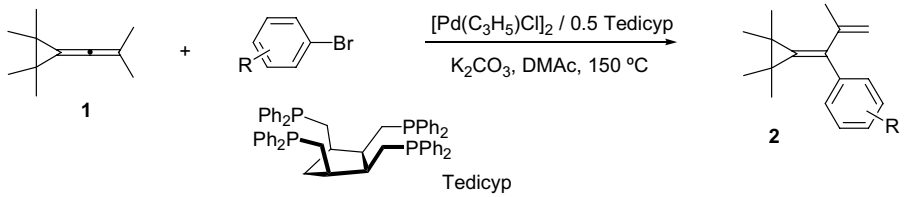


R = H, 4-MeCO, 4-PhCO, 4-HCO, 4-CO_2Me, 4-CN, 2-CN, 4-NO_2, 3-NO_2, 3-Me, 4-*tert*-Bu

Scheme 1. Heck reaction of **1** with iodobenzene and some substituted bromobenzenes.

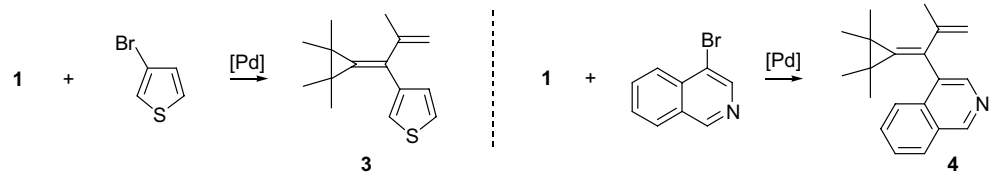
3-nitrobromobenzene, or 4-bromobenzonitrile and from electron-rich aryl bromides such as 3-bromotoluene or 4-*tert*-butylbromobenzene. These observations indicate that the rate-limiting step of the reaction is not the oxidative addition of aryl bromide to the palladium complex, but probably the insertion of the C=C double bond bearing two methyl substituents of **1** in the Ar–Pd bond. It should be noted that the reaction occurred even with the *ortho*-substituted aryl bromide: 2-bromobenzonitrile.

Moreover, the electron-poor or electron-rich heteroaryl bromides, 3-bromothiophene, and 4-bromoisoquinoline also led to the corresponding arylallylidenecyclopropanes **3** and **4** in good yields (Scheme 2).

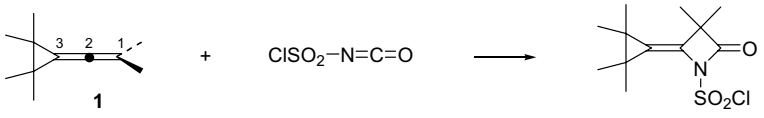
The very high regioselectivity of the insertion step is probably determined by electronic factors: calculations at the B3LYP/6-311G (d,p) level have shown that the HOMO (−5.85 eV) and the LUMO of **1** are mainly located on C(1)–C(2) double bond (Scheme 3) [HOMO, $2p_z$ atomic coefficient at C(1), 0.17; at C(2), 0.13; at C(3), −0.09] [the HOMO–1 (−6.71 eV) is located on C(2)–C(3)] and the difference of Mulliken atomic charges between C(1) and C(2) is considerable (q[C(1)] = 0.45; q[C(2)] = 0.24; q[C(3)] = −0.04). The palladium atom attacks the most charged carbon atom. The previously 2 + 2 addition of chlorosulfonyl isocyanate leading to a β-lactam derivative confirms the polarization of the HOMO (Scheme 3).[8a,23]

These results contrast with the polar addition reactions of electrophilic reagents on **1**. In general, an opening of the cyclopropane occurred with formation of an acetylenic bond (Scheme 4).[24]

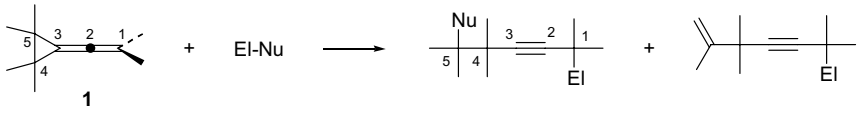
Scheme 5 summarizes the mechanism of the Heck reaction involving **1** and aryl bromides. After a classical oxi-



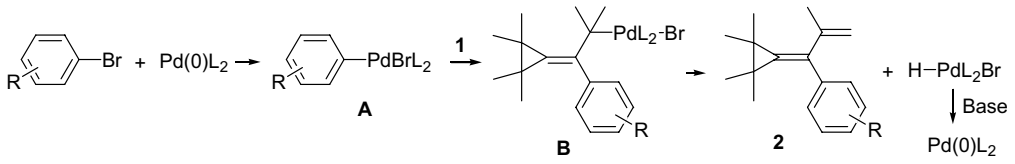
Scheme 2. Heck reaction of **1** with 3-bromothiophene and 4-bromoisoquinoline.



Scheme 3. [2+2]-Cycloaddition of chlorosulfonyl isocyanate to **1**.



Scheme 4. Electrophilic additions to alkenylidenecyclopropanes.



Scheme 5. Intermediates for the Heck reaction of aryl halides and **1**.

dative addition of the aryl bromide to palladium to give **A**, and coordination of allene **1** to **A**; an insertion of **1** in the Ar–Pd bond led to Pd intermediate **B** which liberates **2** and HPdBr after classical β-elimination. A reductive elimination assisted by potassium carbonate regenerates Pd(0).

In conclusion, we report here the construction of highly complex structures starting from very simple molecules and in only four steps (from propargyl alcohols, alkenes, and aryl halides). This reaction tolerates several functional groups on the aryl bromides, and even heteroaryl bromides have been used successfully. Moreover, this reaction can be performed using low catalyst loadings.

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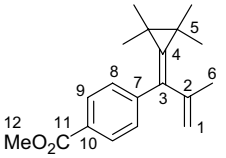
19. As a typical experiment, 4-bromoacetophenone (199 mg, 1.0 mmol), **1** (300 mg, 2.0 mmol) and K_2CO_3 (276 mg, 2.0 mmol) in DMAc (10 mL) in the presence of catalyst (Ref. 16) (0.004 mmol) were heated under argon for 20 h at 150 °C. Usual work-up gives rise to 161 mg of **2** (R = 4-acetyl) (60% yield).
20. Compound **2** (R = 4-acetyl), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, $J = 8.3$ Hz, 2H), 7.17 (d, $J = 8.3$ Hz, 2H), 5.00 (br s, 1H), 4.63 (br s, 1H), 2.60 (s, 3H), 1.99 (s, 3H), 1.24 (s, 6H), 1.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0 (s), 147.5 (s), 146.5 (s), 143.5 (s), 135.1 (s), 131.2 (s), 128.9 (d)(2C), 127.9 (d)(2C), 114.5 (t), 26.6 (q), 22.1 (s), 21.9 (q), 21.7 (q)(2C), 20.9 (q)(2C), 20.3 (s). High resolution ESI-MS calcd for $[C_{19}H_{24}O+H]^+$: 269.1899. Found: 269.1896.
21. For **2** (R = CO_2Me), interpretation of the 2D NMR, HMBC spectra enabled the attribution of each carbon atom chemical shift:



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, $J = 8.3$ Hz, 2H), 7.27 (d, $J = 8.3$ Hz, 2H), 4.99 (br s, 1H), 4.63 (br s, 1H), 3.90 (s, 3H), 1.99 (s, 3H), 1.23 (s, 6H), 0.99 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2 (C^{11}), 147.3 (C^4), 146.3 (C^7), 143.5 (C^2), 131.2 (C^3), 129.1 (C^9), 128.8 (C^8), 127.9 (C^{10}), 114.5 (C^1), 51.9 (C^{12}), 22.1 (C^5), 21.9 (C^6), 21.7 (Me_2–C^5), 20.8 (Me_2–C^5), 20.2 (C^5).
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