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Palladium-Catalyzed Hydrocarbonation and Hydroamination of 3,3-Dihexylcyclopropene with Pronucleophiles

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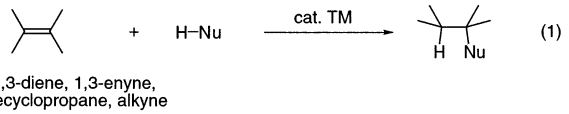
The reaction of 3,3-dihexylcyclopropene **1** with carbon and amine pronucleophiles **2** in the presence of palladium catalysts proceeded smoothly to give the corresponding hydrocarbonation products **3**, allylated nucleophiles, in good to high yields. For example, in the presence of catalytic amounts of $Pd(PPh_3)_4$ and dppf, the reaction of 3,3-dihexylcyclopropene with ethyl 2-cyanopropionate and ethyl 2-cyanophenylacetate gave ethyl 2-cyano-2-methyl-4-undecenoate and ethyl 2-cyano-2-phenyl-4-undecenoate in 82 and 86% yield, respectively.

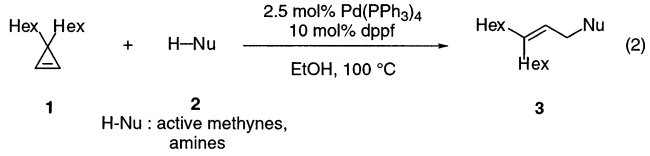
Introduction

The carbon−carbon and carbon−heteroatom bond-forming reaction is one of the most important tools for organic synthesis. Especially, catalytic addition of a carbon−hydrogen and heteroatom−hydrogen bond of pronucleophiles to a carbon−carbon multiple bond is an ideal method for this purpose, since this methodology is an atom-economic and ecological process (eq 1).[1−3] Recent



research has revealed that transition metal catalysts promote the addition of pronucleophiles (H−Nu) to rather activated carbon−carbon multiple bonds such as allenes, 1,3-dienes, 1,3-enynes, methylenecyclopropanes, and alkynes.[2]

It occurred to us that cyclopropene derivatives,[4] which also have another activated C−C multiple bond, would react with pronucleophiles in the presence of palladium catalysts. Functionalized cyclopropene derivatives, such as cyclopropenone ketals, have been widely utilized for carbometalation reactions using main group organometallics and organocuprates.[5] However, to the best of our knowledge, there have been only a few reports on the transition metal-catalyzed reaction of cyclopropene derivatives.[6] Herein, we report that the addition of carbon pronucleophiles and nitrogen pronucleophiles **2** to 3,3-dihexylcyclopropene **1** takes place in the presence of palladium catalyst, producing the corresponding allylated products **3** in good to excellent yields (eq 2).



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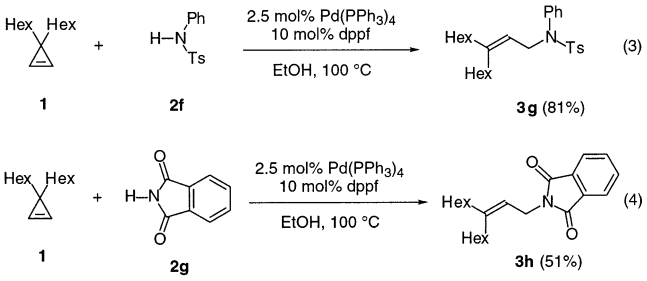
Results and Discussion

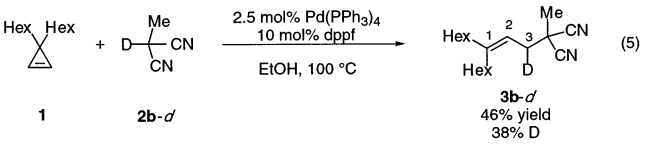
The results are summarized in Table 1. In the presence of 2.5 mol % of $Pd(PPh_3)_4$ and 10 mol % of 1,1′-bis(diphenylphosphino)ferrocene (dppf), the reaction of ethyl 2-cyanopropionate **2a** with 2 equiv of 3,3-dihexylcyclopropene **1** in ethanol proceeded smoothly and the corresponding hydrocarbonation product **3a** was obtained in 82% yield (entry 1). The reaction of **1** with **2a** with other transition metal catalysts, such as $Pd(OAc)_2$, $Pd(dba)_2$, $PdCl_2(PPh_3)_2$, and $Pt(PPh_3)_4$, gave **3a** in lower yields. The reaction of **1** with methylmalononitrile **2b** in the presence of catalytic amounts of $Pd_2(dba)_3{\cdot}CHCl_3$ and dppf at 60 °C gave **3b** in 82% yield along with a trace amount (8%) of **4** (entry 2). The reaction of ethyl phenylcyanoacetate **2c** proceeded very smoothly (entry 3). Malononitrile **2d** reacted with **1** producing the diallylated product **3d** in 69% yield (entry 4). The reaction of ethyl acetoacetate **2e** with **1** afforded a mixture of the diallylated product **3e** and the monoallylated product **3f** (entry 5).

The palladium-catalyzed reaction of **1** was extended to nitrogen pronucleophiles. The reaction of *N*-tosylaniline **2f** and phthalimide **2g** with **1** produced the corresponding hydroamination product **3g** and **3h** in 81 and 51% yield, respectively (eqs 3 and 4). Now, it is clear that the palladium-catalyzed reaction of **1** with the pronucleophiles **2** gives **3** in good to high yields.

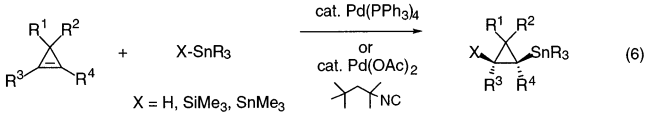


A plausible mechanism is shown in Scheme 1. Palladium(0) would oxidatively insert to a carbon−carbon bond of the cyclopropene **1** forming the palladacyclobutene intermediate **5** (route A).[6a,7] Since **5** is a sort of *σ*-allylpalladium complex, the pallada-ene type reaction with the pronucleophiles **2** would occur producing the *π*-allylpalladium intermediate **7**.[8] Reductive elimination would produce **3**. Alternatively, the reaction is able to be explained by the hydropalladation mechanism as shown in route B. Oxidative insertion of palladium(0) into a H−C or H−N bond of the pronucleophiles **2** would give the hydride palladium species **8**. Hydropalladation of a double bond of the cyclopropene **1** would give the cyclopropylpalladium intermediate **9**. Carbon−carbon bond cleavage would give the *π*-allyl palladium complex **7**.

The reaction of deuterated methylmalononitrile **2b**-*d* with **1** was carried out under the same conditions as above (eq 5). The allylated product **3b**-*d* was obtained in 46% yield (eq 5); the yield was lower than that of the reaction of nondeuterated **2b** (Table 1, entry 2).[9] The deuterium was labeled at the C-3 position (38% D) and the deuteration at any other positions was not observed. The results of this deuterium-labeling experiment are in good agreement with the proposed mechanism (Scheme 1), but the differentiation between routes A and B is not possible at present.



Quite recently, Gevorgyan and co-workers reported that the transition metal-catalyzed hydro-, sila-, and stannastannation of cyclopropenes produced the corresponding cyclopropylstannanes in good to high yields (eq 6).[10] There is a marked contrast between the present reaction (eq 2) and the Gevorgyan's findings (eq 6); in the latter case the ring opening did not take place and the addition of the X−Sn bond to the double bond of cyclopropenes occurred. As mentioned in the review article,[11] perhaps the difference between our and Gevorgyan's findings is due to the difference of the reactivity of the pronucleophiles **2** and $X{-}SnR_3$. It is reasonable to think that oxidative insertion of Pd(0) into $X{-}SnR_3$ is easier than that into H−Nu. Therefore, the addition of X−Pd−Sn to the double bond takes place in eq 6, while the insertion of Pd(0) into H−Nu is relatively slow to force the reaction to take route A in Scheme 1.[12]



Conclusion

We are in a position to transform the cyclopropene **1** into the allylated nucleophiles **3** upon treatment with pronucleophiles **2**. The reactivity difference between H−Nu and $X{-}SnBu_3$ is interesting, and the research to clarify the difference is under investigation.

Experimental Section

General Procedure of the Addition of the Pronucleophiles 2 to 3,3-Dihexylcyclopropene 1. To a mixture of $Pd(PPh_3)_4$ (8.6 mg, 0.0075 mmol), 1,1′-bis(diphenylphosphino)ferrocene (dppf) (16.6 mg, 0.03 mmol), and pronucleophiles 2 (0.3 mmol) was added ethanol (2 mL) under Ar atmosphere in a Wheaton microreactor. The mixture was stirred at 60 °C for 10 min and then 3,3-dihexylcyclopropene (125.0 mg, 0.6 mmol) was added via syringe. After heating at 100 °C for 5−20 h, the reaction mixture was filtered through a short florisil column with ethyl acetate as an eluent. Purification by silica column chromatography (hexane/ethyl acetate 19/1 as an eluent), and in certain cases, further purification by middle-pressure liquid chromatography (silica gel) with hexane/ethyl acetate 40/1 as an eluent, afforded the allylated products **3** in analytically pure form.

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(9) The reason for the difference is not clear at present.
(10) Rubina, M.; Rubin, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2002**, *124*, 11566.
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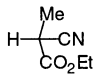
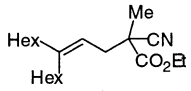
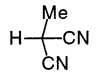
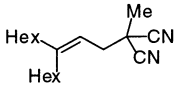
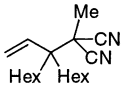
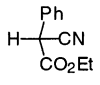
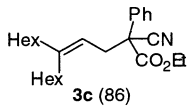
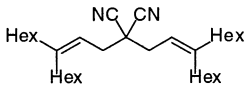
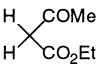
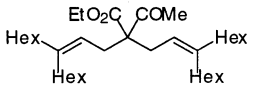
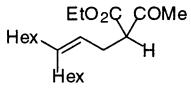
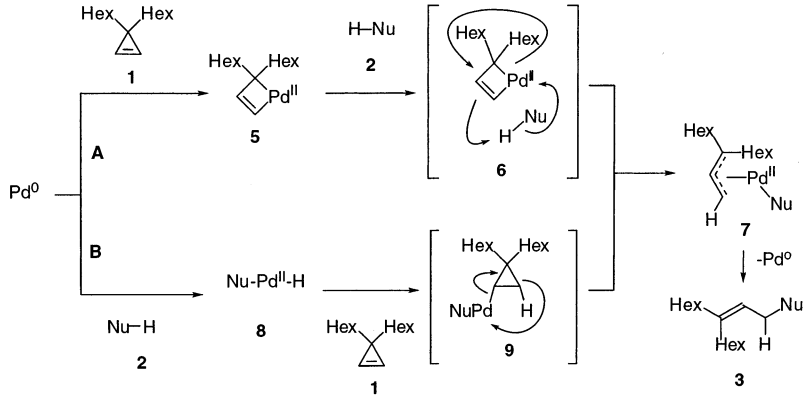
(12) This suggests that route A is more probable in comparison with route B.

TABLE 1. Palladium-Catalyzed Addition of Pronucleophiles 2 to 3,3-Dihexylcyclopropene 1[a]

entry	pronucleophiles	3 (yield / %)[b]	
1	 **2a**	 **3a** (82)	
2[c]	 **2b**	 **3b** (82)	 **4** (8)
3	 **2c**	 **3c** (86)	
4	 **2d**	 **3d** (69)	
5	 **2e**	 **3e** (41)	 **3f** (36)

[a] The reaction of 3,3-dihexylcyclopropene a (0.6 mmol) with the carbon pronucleophiles **2** (0.3 mmol) was carried out in the presence of 2.5 mol % of $Pd(PPh_3)_4$ and 10 mol % of dppf in ethanol at 100 °C. [b] Isolated yield. [c] $Pd_2(dba)_3{\cdot}CHCl_3$ was used as a palladium catalyst.

SCHEME 1



Ethyl 2-Cyano-5-hexyl-2-methyl-4-undecenoate (3a). IR (neat) 2957−2858, 1745, 1662, 1460, 1379, 1284 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, J = 6.4 Hz, 6H), 1.32−1.25 (m, 19H), 1.54 (s, 3H), 2.00−1.96 (m, 4H), 2.49 (dd, J = 7.1, 14.5 Hz, 1H), 2.62 (dd, J = 7.1, 14.5 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 5.12 (t, J = 7.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.00, 14.07, 22.57, 22.61, 28.08, 28.33, 29.00, 29.43, 30.22, 31.72, 36.18, 36.93, 43.92, 62.61, 116.03, 120.07, 146.13, 169.30. Anal. Calcd for $C_{21}H_{37}NO_2$ (335.52): C, 75.17; H, 11.12; N, 4.17. Found: C, 75.18; H, 11.25; N, 4.25. HRMS (EI) Calcd for $C_{21}H_{37}NO_2$: m/z 335.2824. Found: m/z 335.2827.

***N*-(3-Hexyl-2-nonenyl)-*N*-tosylaniline (3g).** IR (neat) 3063−2856, 1597, 1493, 1456, 1352, cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.85−0.76 (m, 6H), 1.19−1.00 (m, 16H), 1.79−1.73 (m, 4H), 2.36 (s, 3H), 4.11−4.01 (m, 2H), 4.98 (t, J = 7.0 Hz, 1H), 6.96−6.94 (m, 2H), 7.21−7.16 (m, 5H), 7.44 (d, J = 8.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.08, 21.51, 22.55, 27.66, 28.18, 28.71, 29.26, 29.94, 31.68, 36.44, 48.31, 118.62, 127.61, 127.70, 128.70, 128.99, 129.32, 135.92, 139.29, 143.14, 144.95. Anal. Calcd for $C_{28}H_{41}NO_2S$ (455.70): C, 73.80; H, 9.07; N, 3.07; S, 7.04. Found: C, 73.49; H, 9.01; N, 3.13; S, 7.01. HRMS (EI) Calcd for $C_{28}H_{41}NO_2S$: m/z 455.2858. Found: m/z 455.2856.

Supporting Information Available: Characterization data of all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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