Ring Opening in the Hydrostannation of Methylenecyclopropanes: Effect of the Catalyst and Substrate

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The generation of organometallic species by hydrometalation of carbon−carbon multiple bonds is a fundamental reaction in synthetic organic chemistry.[1] Of particular interest in this field is the hydrostannation reaction, due to the numerous possibilities of further manipulation of the newly formed carbon−tin bond.[2]

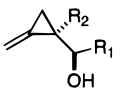
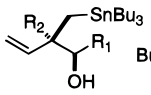
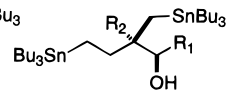
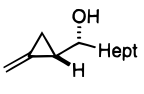
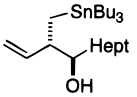
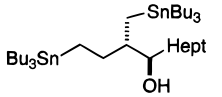
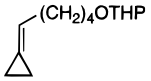
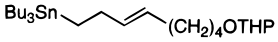
In general, the hydrostannation of carbon−carbon multiple bonds has been achieved under radical conditions[3] or by using transition metal catalysis.[4] However, the methods described were found to be unsuitable for a wide range of simple *unactivated alkenes*. Indeed, the reversibility of the addition of the tributyltin radical onto a carbon−carbon double bond in the absence of a stabilizing group generally restricts this reaction to activated alkenes.[3b] On the other hand, little information concerning the metal-catalyzed processes was available and essentially dealt with conjugated reductions of alkenes.[4a]

We recently reported the hydrostannation of oxabicyclic compounds using soluble palladium catalysts[5] and found that, in the case of unactivated alkenes, the only reaction observed was the disproportionation of tributyltin hydride to hexabutylditin and molecular hydrogen.[3b,4] Fortunately, a heterogenous catalyst, such as $Pd(OH)_2/C$, successfully catalyzed the hydrostannation of a wide variety of alkenes, providing a general route to synthetically useful alkylstannanes.[6]

In the course of our studies, we were interested to assess the reactivity of other types of alkenes in hydrostannation reactions, and we now report our results with methylenecyclopropanes.

The three reactive sites in a methylenecyclopropane are the vicinal and distal cyclopropane bonds and the olefin. The majority of the palladium-catalyzed reactions (including [3 + 2] cycloadditions with alkenes and alkynes,[7] (trimethylsilyl)-cyanation of 2-aryl or 1-substituted methylenecyclopropanes,[8] and chloro-[9] and carbopalladation[10])[10] occur at the distal cyclopropane bond or the exocyclic olefin. Therefore, it was of interest to see at which site the palladium-catalyzed hydrostannation of methylenecyclopropanes would occur.

Table 1. Palladium-Catalyzed Hydrostannations of Methylenecyclopropanes

substrate	product (yield)[a]	
	$Pd(PPh_3)_4$[b]	$Pd(OH)_2/C$[b]
		
1a R_1 = Ph R_2 = H **1b** R_1 = cHex R_2 = H **1c** R_1 = Hept R_2 = H **1d** R_1 = cHex R_2 = Me **1e** R_1 = cHex R_2 = OMe	**2a** 68% **2b** 65% **2c** 67% **2d** 90% **2e** not isolated[c]	**3a** 64% **3b** 62% **3c** 59% **3d** 85% **3e** 61%
		
1c'	**2c'** 58%	**3c'** 60%
		
4	**5**	
	87%	76%

[a] Isolated yields of analytically pure products. [b] Bu_3SnH (1.5 or 3 equiv) was added over 1 or 1.5 h to a 0.1 M solution of the substrate in THF containing $Pd(PPh_3)_4$ (3 to 5 mol %) or $Pd(OH)_2/C$ (5 mol %). [c] See text.

We report herein the different pathways in the hydrostannation of methylenecyclopropane derivatives in the presence of homogeneous and heterogeneous catalysts.

When (methylenecyclopropyl)carbinols **1**[11] were treated with a slight excess (1.5 equiv) of tributyltin hydride in THF in the presence of a catalytic amount of tetrakis(triphenylphosphine)-palladium (3−5 mol %), the corresponding ring opened homoallylstannanes **2** were obtained in good yields and as single diastereoisomers (Table 1). We could not isolate the products resulting from simple hydrostannation of the double bond even by lowering the temperature of the reaction mixture to −20 °C, indicating that methylenecyclopropanes were significantly more reactive than "simple" olefins.[6] Nevertheless, as a precaution, tributyltin hydride was usually added slowly over 1 h or more, in order to prevent its rapid decomposition by the palladium catalyst.

Reaction of **1** performed under heterogeneous conditions, with $Pd(OH)_2/C$ as a catalyst, gave a mixture of homoallylstannanes **2** and diorganostannanes **3** resulting from further hydrostannation of **2**. Increasing the amount of tin hydride to 3 equiv enables the selective formation of **3a**−**e** in good yields. We independently showed that **2a**−**e** can be hydrostannated under heterogeneous conditions which confirms that they are intermediates in the formation of the distannanes **3a**−**e**.

For **1e**, the corresponding homoallylstannane **2e** could not be isolated as a pure compound because, on silica gel, it suffers stannodemethoxylation[12] to give the corresponding dienyl alcohol.[13]

(1) Labinger, J. A.; Smith, K.; Pelter, A.; Eisch, J. J.; Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 5, p 667−792.

(2) (a) Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987. (b) Lipshutz, B. H.; Hegedus, L. In *Organometallics in Synthesis. A Manual*; Schlosser, M., Ed.; J. Wiley & Sons: New York, 1994, p 284−459.

(3) (a) Davis, D. D.; Chambers, R. L.; Johnson, H. T. *J. Organomet. Chem.* **1970**, *25*, C13. (b) Neumann, W. P. *The Organic Chemistry of Tin*; J. Wiley: New York, 1970. (c) Kuivila, H. G.; Sommer, R. *J. Am. Chem. Soc.* **1967**, *89*, 5616.

(4) (a) Four, P.; Guibé, F. *Tetrahedron Lett.* **1982**, *23*, 1825. (b) Mitchell, T. N. *J. Organomet. Chem.* **1986**, *304*, 1. (c) Ichinose, Y.; Oda, H.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3468. (d) Kikukawa, K.; Umekawa, H.; Wada, F.; Matsuda, T. *Chem. Lett.* **1988**, 881. (e) Guibé, F. *Main Group Met. Chem.* **1989**, *12*, 437. (f) Zhang, H. X.; Guibé, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1133. (g) Casson, S.; Kocienski, P. *Synthesis* **1993**, 1133. (h) Greeves, N.; Torode, J. S. *Synlett* **1994**, 537.

(5) Lautens, M.; Klute, W. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 442.

(6) Lautens, M.; Kumanovic, S.; Meyer, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1329.

(7) (a) Binger, P.; Büch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77 and references cited therein. For a review of transition metal mediated cycloadditions, see: (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49.

(8) Chatani, N.; Takeyasu, T.; Hanafusa, T. *Tetrahedron Lett.* **1988**, *32*, 3979.

(9) (a) Noyori, R.; Takaya, H. *J. Chem. Soc. D* **1969**, 525. (b) Hughes, R. P.; Hunton, D. E.; Schumann, K. *J. Organomet. Chem.* **1979**, *169*, C37. (c) Dallas, B. K.; Hughes, R. P. *J. Organomet. Chem.* **1980**, *184*, C67. (d) Albright, T. A.; Clemens, P. R.; Hughes, R. P.; Hunton, D. E.; Margerum, L. D. *J. Am. Chem. Soc.* **1982**, *104*, 5369. (e) Dallas, B. K.; Hughes, R. P.; Schumann, K. *J. Am. Chem. Soc.* **1982**, *104*, 5380. (f) Green, M.; Hughes, R. P. *J. Chem. Soc., Dalton Trans.* **1976**, 1880. (g) Goddard, R.; Green, M.; Hughes, R. P.; Woodward, P. *J. Chem. Soc., Dalton Trans.* **1976**, 1890.

(10) (a) Larock, R. C.; Varaprath, S. *J. Org. Chem.* **1984**, *49*, 3432. (b) Donaldson, W. A.; Brodt, C. A. *J. Organomet. Chem.* **1987**, *330*, C33−C36. (c) Fournet, G.; Balme, G.; Goré, J. *Tetrahedron* **1988**, *44*, 5809. (d) Fournet, G.; Balme, G.; Barieux, J. J.; Goré, J. *Tetrahedron* **1988**, *44*, 5821. (e) Bräse, S.; De Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2545.

(11) (a) Lautens, M.; Delanghe, P. H. *J. Am. Chem. Soc.* **1994**, *116*, 8526. (b) Lautens, M.; Ren, Y. *J. Org. Chem.* **1996**, *61*, 2210.

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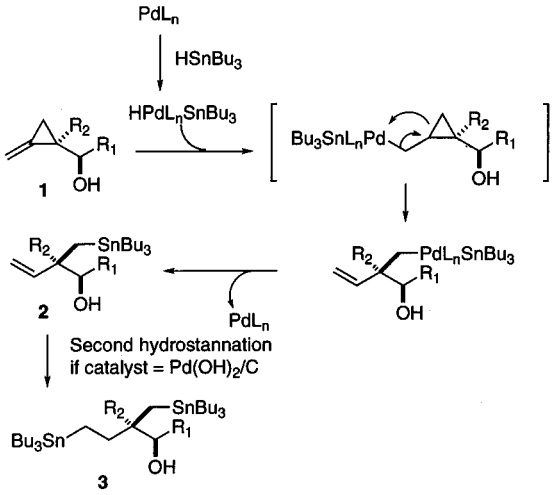
Scheme 1

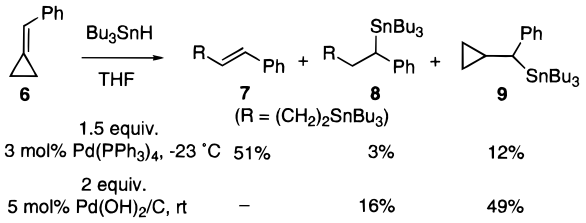


The mono- and the diorganostannanes **2** and **3** are all obtained as single diastereosiomers. Diastereoisomers **1c** and **1c′** gave the diastereoisomeric homoallylstannanes **2c** and **2c′**. Moreover, we have checked that the relative stereochemistry of the homoallylstannane **2a** corresponds to that of the parent compound **1a**, establishing that there is no loss of the stereochemical information initially present in the (methylenecyclopropyl)-carbinol **1** throughout the course of the reaction. Indeed, transmetalation of the organostannane **2a** to the organolithium,[14,15] followed by protonolysis afforded the corresponding known *syn* homoallylic alcohol.[16]

To explain the formation of compounds **2** and **3**, we propose the mechanism shown in Scheme 1.

Oxidative addition of a zero-valent palladium into the tin−hydrogen bond of tributyltin hydride first generates a stannylpalladium hydride species which hydropalladates the methylenecyclopropane derivative, thus affording a (cyclopropylmethyl)palladium stannane. The latter undergoes a highly regioselective ring opening reaction, generating a primary homoallylpalladium stannane rather than a secondary or a tertiary one, which subsequently undergoes reductive elimination to yield the homoallylstannane **2**. The fact that there is no loss of the stereochemical information present in the parent compound **1** indicates that the reductive elimination of the homoallylstannylpalladium intermediate is faster than the corresponding β-elimination observed in related carbopalladation reactions.[10] Under homogeneous conditions, the reaction stops at this stage and the palladium complex subsequently catalyzes the disproportionation of tributyltin hydride, which is announced by a sudden darkening of the reaction mixture as previously noticed.[4f,h] Under heterogeneous conditions, further hydrostannation of the less reactive double bond of **2** can readily occur as previously mentioned to give the diorganostannane **3**.[6]

Scheme 2



We then turned out our attention to the case of methylenecyclopropanes bearing substituents on the double bond. Methylenecyclopropane **4**[10d] gave exclusively the (*E*)-homoallylstannane **5** in very good yield, irrespective of the choice of the catalyst (Table 1). The high reactivity of **4** is noteworthy, given the reluctance of unactivated trisubstituted or α,β-disubstituted alkenes such as **5** to undergo hydrostannation, even using a heterogeneous catalyst.[6]

Reactions with benzylidenecyclopropane **6**[17] deserve further comment (Scheme 2). When the latter compound was treated with a slight exceess (1.5 equiv) of tributyltin hydride at room temperature, a 60/40 mixture of the (*E*)-homoallylstannane **7** and the diorganostannane **8** was obtained, since under these conditions, the activated double bond of the intermediate **7** is hydrostannated with the homogeneous catalyst. However, lowering the temperature of the reaction mixture to −23 °C enables the selective formation of **7**, which was isolated in 50% yield.[18] The very mild conditions required for this reaction as well as the formation of a single isomer (*E*) are noteworthy compared to the rhodium-catalyzed hydrosilylation of **6**.[19] The most surprising result is that the heterogeneous palladium-catalyzed hydrostannation gave the benzylstannane **9** as the major product and the bisorganostannane **8**, isolated in 49 and 16% yields, respectively.[18] Clearly, in this case, the reductive elimination of the intermediate benzyl tributyltin palladium postulated species is somewhat faster than the ring opening reaction.

In conclusion, we have described the first examples of palladium-catalyzed hydrostannation of methylenecyclopropane derivatives. This reaction provides a regioselective and stereospecific entry to a variety of homoallylstannanes that can be useful for organic synthesis.

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Supporting Information Available: General experimental procedures, specific details for representative reactions, and isolation and spectroscopic information for the compounds prepared (9 pages). See any current masthead page for ordering and Internet access instructions.

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(12) Koerber, K.; Goré, J.; Vatele, J.-M. *Tetrahedron Lett.* **1991**, *32*, 1187.

(13) Filtration through a short plug of neutral alumina enabled us to characterize **2e**. In contrast, the corresponding diorganostannane **3e** could be purified by rapid chromatography on silica gel, which suggests the greater instability of **2e** is attributed to the presence of the double bond enabling the formation of a conjugated diene.

(14) (a) Meyer, N.; Seebach, D. *Chem. Ber.* **1980**, *113*, 1290. (b) Newman-Evans, R. H.; Carpenter, B. K. *Tetrahedron Lett.* **1985**, *26*, 1141. (c) Brieden, W.; Ostwald, R.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 582.

(15) See Supporting Information. Quenching the organolithium with AcOD gave the corresponding monodeuterated homoallylic alcohol with ≥95% deuterium incorporation.

(16) (a) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7109. For a review on allylic organometallics, see: (b) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(17) (a) Utimoto, K.; Tamura, M.; Sisido, K. *Tetrahedron* **1973**, *29*, 1169. (b) Stafford, J. A.; McMurry, J. E. *Tetrahedron Lett.* **1988**, *29*, 2531.

(18) Separation of each of these nonpolar compounds and hexabutylditin by chromatography on silica gel is not readily accomplished, therefore the yields reported have not been optimized.

(19) (a) Bessertnykh, A. G.; Grishin, Y. K.; Donskaya, N. A.; Beletskaya, I. P. *Metalloorg. Khim.* **1993**, *6*, 30. (b) Blinov, K. A.; Tveritinova, E. V.; Donskaya, N. A. *Vestn. Mosk. Univ., Ser. 2: Khim.* **1994**, *35*, 481.