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Published on Web 09/10/2002

Transition Metal-Catalyzed Hydro-, Sila-, and Stannastannation of Cyclopropenes: Stereo- and Regioselective Approach toward Multisubstituted Cyclopropyl Synthons

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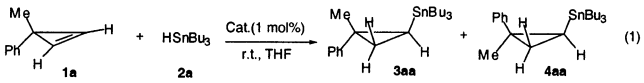
Received May 29, 2002

Cyclopropylstannanes, highly attractive versatile synthons, are extensively used nowadays as stable precursors for a number of cyclopropylmetal reagents with defined configurations.[1] Furthermore, they are employed in Pd-catalyzed oxidative homocoupling,[2] Stille cross-coupling reactions,[3] as well as in various destannylative transformations[4] and rearrangements into other useful organotin derivatives.[5] Although more than a few methods for the preparation of cyclopropylstannanes have been developed,[6] usually these methods lack generality and, in most cases, are limited to the preparation of mono- to trisubstituted cyclopropanes. A direct hydrostannation[7] of the cyclopropene double bond potentially can be seen as a very attractive, straightforward, and atom-economic alternative route to highly substituted cyclopropylstannanes. The 54 kcal/mol of strain energy in cyclopropene versus cyclopropane is a reason for the high affinity of its double bond toward various addition reactions.[8] However, transition metal-catalyzed hydrostannation of cyclopropenes has never been reported, probably because of a general belief that, except for some scattered reports,[9] palladium, as well as some other transition metal complexes, is well known to cause ring-opening,[10] oligomerization,[11] or polymerization[12] of cyclopropenes.[13] Herein we wish to report the first highly stereo- and regioselective transition metal-catalyzed hydro-, sila-, and stannastannation reactions of cyclopropenes[14] which allow for the synthesis of up to pentasubstituted cyclopropane derivatives in very good yields.

Table 1. Catalyst Optimization for Hydrostannation of **1a**



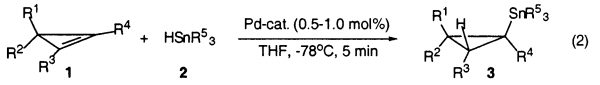
(1)

#	catalyst	time	**3**, %[a]	**4**, %[a]	**3**:**4**[a]
1	$Ru(PPh_3)_3Cl_2$	20 h	67	3	96:4
2	$Pt(PPh_3)_4$	20 h	66	4	94:6
3	$Rh(PPh_3)_3Cl$	20 h	75	4	95:5
4	$Ni(dppp)Cl_2$	20 h	32	1	97:3
5	$Ni(dppe)_2$	5 h	2		
6	$Pd(PPh_3)_2Cl_2$	5 min	36	16	69:31
7	TCPC[b]	5 min	15	14	52:48
8	$Pd(OAc)_2$/TDMPP	5 min	19	15	56:44
9	Pd_2dba_3/*o*-Tol_3P	5 min		>1	
10	[π-allyl-PdCl]$_2$/MOP	5 min	29	6	83:17
11	[π-allyl-PdCl]$_2$/MOP[b]	5 min	32	8	80:20
12	$Pd(PPh_3)_4$	5 min	79	>1	98:2
13	**$Pd(PPh_3)_4$** [c]	**5 min**	**86**[d]	**>1**	**>99:1**
14	none	5 min	20	24	46:54

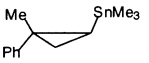
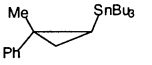
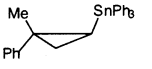
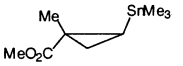
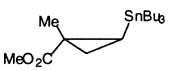
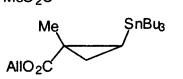
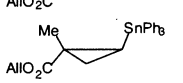
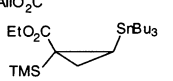
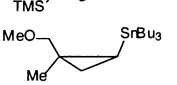
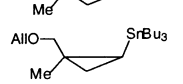
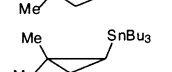
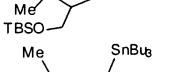
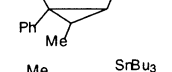
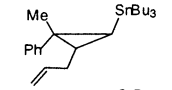
[a] GC data. [b] TCPC = [1,2,3,4-tetrakis(methoxycarbonyl)-1,3-butadiene-1,4-diyl]palladium. [c] Reaction was performed at −78 °C. [d] Isolated yield.

Initially, we tested hydrostannation of disubstituted cyclopropene **1a**[15] in the presence of a number of transition metal catalysts (eq 1, Table 1). The ruthenium, platinum, rhodium, and nickel complexes tested initiated rather slow reactions which produced moderate to good yields of products albeit with high facial selectivity (Table 1, entries 1−4). Most of the Pd-catalysts showed high reaction rates, but yields and selectivity were disappointingly

Table 2. Pd-Catalyzed Hydrostannation of Cyclopropenes



(2)

entry	cyclopropene **1** R^1	R^2	R^3	R^4	tin hydride **2** R^5	cyclopropane **3**, yield (%)[a]
1	Me	Ph	H	H **(a)**	Me	 **3ab**, 91[b]
2	Me	Ph	H	H **(a)**	Bu	 **3aa**, 92
3	Me	Ph	H	H **(a)**	Ph	 **3ac**, 92
4	Me	CO_2Me	H	H **(b)**	Me	 **3bb**, 83
5	Me	CO_2Me	H	H **(b)**	Bu	 **3ba**, 85
6	Me	CO_2All	H	H **(c)**	Bu	 **3ca**, 87
7	Me	CO_2All	H	H **(c)**	Ph	 **3cc**, 78
8	CO_2Et	TMS	H	H **(d)**	Bu	 **3da**, 82
9	CH_2OMe	Me	H	H **(e)**	Bu	 **3ea**, 67[c]
10	CH_2OAll	Me	H	H **(f)**	Bu	 **3fa**, 80[d]
11	Me	Me	CH_2OTBS	H **(g)**	Bu	 **3ga**, 68[e]
2	Me	Ph	Me	H **(h)**	Bu	 **3ha**, 83[f]
13	Me	Ph	All	H **(i)**	Bu	 **3ia**, 63
14	Me	Me	TMS	CO_2Me **(j)**	Bu	 **3ja**, 82

[a] Isolated yield. [b] Formation of 5% of **4ab** was detected. [c] Combined yield of 4:1 mixture of **3ea**:**4ea**. [d] Combined NMR yield of 4:1 mixture of **3fa**:**4fa**. [e] NMR yield. [f] Formation of 5% of **4ha** was observed.

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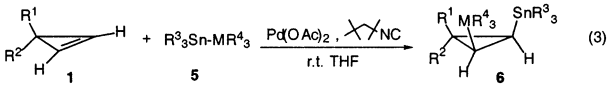
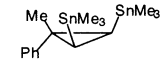
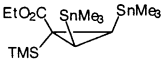
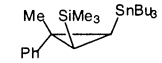
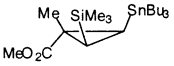
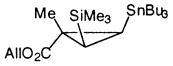
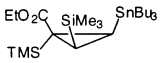
10.1021/ja027095k CCC: $22.00

Table 3. Pd-Catalyzed Distannation and Silastannation of Cyclopropenes



entry	cyclopropene **1** R^1	R^2	tin species **5**	Isolated yield of **6** (%)	
1	Me	Ph **(a)**	$Me_3SnSnMe_3$ **(a)**		**6aa**, 83
2	CO_2Et	TMS **(d)**	$Me_3SnSnMe_3$ **(a)**		**6da**, 89
3	Me	Ph **(a)**	$Bu_3SnSiMe_3$ **(b)**		**6ab**, 94
4	Me	CO_2Me **(b)**	$Bu_3SnSiMe_3$ **(b)**		**6bb**, 84
5	Me	CO_2All **(c)**	$Bu_3SnSiMe_3$ **(b)**		**6cb**, 69
6	CO_2Et	TMS **(d)**	$Bu_3SnSiMe_3$ **(b)**		**6db**, 85

low (entries 6−11). In contrast, $Pd(PPh_3)_4$ gave both a very good yield and a very high facial selectivity (entry 12). Optimization of the reaction conditions showed that this *reaction can be carried out at as low as −78 °C!* Still, the reaction was complete in less than 5 min, and virtually a single facial isomer **3aa** was isolated in 86% yield (entry 13). A control experiment with no catalyst demonstrated that there is a background reaction which proceeds, probably, via a free radical mechanism producing nonselectively a 1:1 mixture of **3aa** and **4aa** in moderate yield accompanied with a notable amount of oligomeric products (entry 14). The best conditions (Table 1, entry 13) were applied to the hydrostannation reaction of differently substituted cyclopropenes (eq 2, Table 2).[15] The hydrostannation of most of the 3,3-disubstituted cyclopropenes was governed by steric effects regardless of the tin hydride source; addition across the cyclopropene double bond proceeded from the least hindered face (Table 2, entries 1−8).[16,17] Surprisingly, cyclopropenes **1e**,**f** revealed a notable directing effect. Apparently, a coordination of oxygen to palladium affected the facial selectivity of hydrostannation favoring the addition from the more sterically hindered face (entries 9,10).[18] Trisubstituted cyclopropene **1g** reacted smoothly to provide cyclopropylstannane **3ga** as a single stereo- and regioisomer (entry 11). Hydrostannation of **1h**,**i**, however, required the use of a $[(\pi\text{-allyl})PdCl]_2$/MOP[19] catalyst system to get cyclopropylstannanes **3ha** and **3ia** with high facial selectivity and good yields (entries 12,13). Finally, tetrasubstituted cyclopropene **1j** underwent smooth hydrostannation to produce the corresponding *pentasubstituted cyclopropylstannane **3ja** in 82% isolated yield as a single reaction product* (entry 14).[20]

To further test the scope of this methodology, we examined the Pd-catalyzed silastannation and distannation reactions (eq 3, Table 3).[15] Among the systems tested, $Pd(OAc)_2$ in combination with Walborsky's ligand[6l] gave the best results. The reactions proceeded with high facial selectivity which was entirely controlled by steric factors. All tetrasubstituted cyclopropanes **6aa**−**db** were obtained as sole reaction products in good to very high yields (Table 3).

In conclusion, the first transition metal-catalyzed hydro-, sila-, and stannastannation of cyclopropenes have been demonstrated. This method allows for the efficient and straightforward synthesis of stereodefined multisubstituted building blocks not easily available by other methods.

Acknowledgment. The support of the National Science Foundation (CHE-0096889) is gratefully acknowledged.

Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) For ring-opening in the Pd-catalyzed hydrostannation of methylenecyclopropanes, see: Lautens, M.; Meyer, C.; Lorenz, A. *J. Am. Chem. Soc.* **1996**, *118*, 10676.

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(15) For experimental procedures, see Supporting Information.

(16) Syn-stereoselectivity of addition was unambiguously proved by hydrostannation of **1a** with Bu_3SnD. See Supporting Information for details.

(17) Good scalability was demonstrated by preparation of 11 mmol of **3aa** (80% yield). See Supporting Information for details.

(18) For examples on directing effect in hydrostannation, see: (a) Betzer, J.-F.; Delaloge, F.; Muller, B.; Pancrazi, A.; Prunet, J. *J. Org. Chem.* **1997**, *62*, 7768. (b) Rice, M. B.; Whitehead, S. L.; Horvath, C. M.; Muchnij, J. A.; Maleczka, R. E., Jr. *Synthesis* **2001**, 1495.

(19) MOP = (*RS*)-2-(diphenylphosphino)-2′-methoxy-1,1′-binaphthyl.

(20) Initial experiments using chiral (*R*)-(+)-MOP ligand with cyclopropene **1b** revealed poor asymmetric induction (12% ee). Further investigation of the chiral version of this reaction is currently under way in our laboratories.

JA027095K