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# $Mo(CO)_3(CN\text{-}t\text{-}Bu)_3(MoBI_3)$, a New Efficient Catalyst for Regioselective Hydrostannations

**Uli Kazmaier,* Dagmar Schauss, and Matthias Pohlman**

*Organisch-Chemisches Institut der Universität, Im Neuenheimer Feld 270,
69120 Heidelberg, Germany*

*ck1@popix.urz.uni-heidelberg.de*

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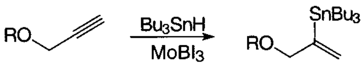
## ABSTRACT

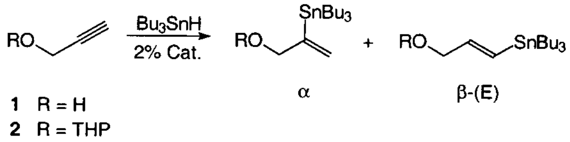


**$Mo(CO)_3(NC\text{-}t\text{-}Bu)_3$ was found to be a suitable catalyst for the regioselective hydrostannation of several types of alkynes, giving preferentially rise to the α-stannylated products. These products are not available under radical reaction conditions or by using other metal catalysts. This protocol can also be applied to sensitive substrates, which cannot be hydrometalated with the commonly used palladium catalysts.**

Transition metal catalyzed reactions are becoming more and more interesting and important to synthetic organic chemists, due in part to the fact that many of these reactions proceed under very mild conditions.[1] In general, they also tolerate a wide variety of functional groups and are therefore particularly suitable for the synthesis of complex molecules. From the various transition metals used, palladium holds a certain supremacy and is commonly used for cyclizations, allylic alkylations, cross couplings, and many other important reactions.[2] For quite some time other metal complexes have also been used for this purposes. For instance, tungsten[3] and molybdenum[4] complexes can also be applied in allylic alkylations. Isocyanide complexes such as $Mo(CO)_2(CNR)_4(MoBI_4)$ have been shown to give good results.[5]

A further important type of reactions catalyzed by transition metal complexes are hydrometalations, and herein hydrostannations are of particular interest.[6] For example, the hydrostannation of alkynes is frequently used for the synthesis of vinylstannanes, which can be further modified via Stille couplings.[7] In addition to a radical pathway, a palladium-catalyzed version of the hydrostannation has also been developed during the past few years.[1] The major drawback of both methods is the difficulty of controlling the regioselectivity of the tin hydride addition toward unsymmetrical alkynes, although the transition metal catalyzed version has the advantage of a clean cis addition, based on the mechanism of the reaction.[2] Therefore, only two products are formed during this process, while radical tin hydride additions generate *E*/*Z* mixtures of the corresponding stannylated alkenes. In addition to palladium catalysts, rhodium complexes also can be used,[8] and Guibe et al. described an application of a molybdenum catalyst.[9] $MoBr(allyl)(CO)_2(CH_3CN)_2$ was found to be suitable for the hydrostannation of propargylic alcohol derivatives, but without significant regioselectivity (Scheme 1, Table 1). But for an application of these reactions to the synthesis of

**Scheme 1**



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(1) Hegedus, L. S. *Organische Synthese mit Übergangsmetallen*; VCH: Weinheim, 1995.

(2) A comprehensive survey on palladium-catalyzed reactions can be found in Malleron, J. L.; Fiaud, J. C.; Legros, J. Y. *Handbook of Palladium-Catalyzed Organic Reactions*; Academic: San Diego, 1997.

(3) Trost, B. M.; Hung, M. H. *J. Am. Chem. Soc.* **1983**, *105*, 7757. Lehmann, J.; Lloyd-Jones, G. C. *Tetrahedron* **1995**, *51*, 8863.

(4) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1983**, *105*, 3343. Faller, J. W.; Mazzieri, M. R.; Nguyen, J. T.; Parr, J.; Tokunaga, M. *Pure Appl. Chem.* **1994**, *66*, 1463.

(5) Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590.

(6) Davies, A. G. In *Comprehensive Organometallic Chemistry II*; Pergamon: New York, 1995; Vol. 2, p 217 ff.

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**Table 1.** Catalytic Hydrostannation of Alkynes **1** and **2**

| entry | substrate | catalyst | yield, % | selectivity |
|---|---|---|---|---|
| 1 | **1** | PdCl$_2$(PPh$_3$)$_2$ | 41 | 55:45 |
| 2 | **1** | MoBr(allyl)(CO)$_2$(MeCN)$_2$ | nr[a] | 67:33 |
| 3 | **2** | PdCl$_2$(PPh$_3$)$_2$ | 68 | 67:33 |
| 4 | **2** | MoBr(allyl)(CO)$_2$(MeCN)$_2$ | nr | 64:36 |
| 5 | **1** | Mo(CO)$_3$(CN-$t$-Bu)$_3$ | 81 | 91:9 |
| 6 | **2** | Mo(CO)$_3$(CN-$t$-Bu)$_3$ | 98 | 98:2 |

[a] Not reported.

complex molecules via subsequent cross coupling reactions, the control of the regioselectivity is an extraordinary important issue. Therefore the search for new, more selective catalysts is an important task.

In connection with our investigations on chelate enolate Claisen rearrangements,[10] we were interested in the synthesis of α-stannylated allylic alcohols or their derivatives. For this reason we examined first the hydrostannation of propargylic alcohol **1** and the THP-protected derivative **2** as well (Scheme 1). In the presence of transition metal catalysts the cis hydrostannation products (α,$\beta$-($E$)) are formed exclusively as a regioisomeric mixture (Table 1, entries 1−4).[9] This is true for the generally applied palladium catalysts and the already mentioned molybdenum complex as well.[11] The molybdenum complex shows a comparable, or even slightly higher, selectivity in favor of the desired α-product.[12] This is especially true if sterically more hindered alkynes are used.[9]

The catalytically active species are probably Pd(0) and Mo(0) complexes, formed in situ via reduction with tin hydride. This encouraged us to investigate the application of Mo(0) complexes such as Mo(CO)$_6$ as catalysts for hydrostannations. Our first investigation clearly showed that in principle carbon monoxide complexes of molybdenum are suitable for this reaction, although the reaction was slow and the yields obtained with our test substrates were only modest. The regioselectivities observed were comparable to the results of Guibe (Table 1, entries 2 and 4).

This is the point at which a question arises: how can the reactivity and selectivity toward the desired α-product be increased? To find solutions to this question we replaced several CO ligands on the molybdenum. Isocyanides, which are isoelectronic with carbon monoxide, appeared to be promising ligand candidates, for several reasons: 1. These ligands are retained in solution if dissociated from the metal, a fact which should have a positive influence on the lifetime of the catalyst. 2. Isocyanides should bond less tightly to the molybdenum in comparison to carbon monoxide,[5] which should facilitate their dissociation, resulting in an increased reactivity. 3. The steric demand of the catalyst can be tuned by variation of the number and the size of the isocyanide ligands, which should have an effect on the regioselectivity of the hydrostannation. Keeping this in mind, and on the assumption that two to three free coordination sites on the molybdenum are required for the reaction, we chose Mo(CO)$_3$(CN-$t$-Bu)$_3$(MoBI$_3$) as a catalyst. This complex can easily be obtained by ligand exchange from Mo(CO)$_6$,[13] and therefore it is rather inexpensive. MoBI$_3$ is also stable toward air and can easily be purified by flash chromatography. These features coupled with its catalytic properties make MoBI$_3$ the catalyst of choice for regioselective hydrostannations. The results obtained with our test substrates exceeded all our expectations (Table 1, entries 5 and 6).

For the reasons discussed, this complex is much more reactive in comparison to Mo(CO)$_6$, giving higher turnovers and yields. Because of its stability, the catalyst can be recovered (by flash chromatography) and reused without any loss of reactivity. This is especially interesting for large scale preparations, although the amount of catalyst required is not very high (0.1−2%). Probably because of the sterically demanding $t$-Bu groups, MoBI$_3$ shows excellent regioselectivities. For example, with **2** a nearly perfect yield and selectivity were obtained. Although the hydrostannation of these terminal alkynes already proceeds at room temperature, sterically more hindered alkynes might require higher reaction temperatures. In these cases, or at low catalyst concentrations, the temperature can be increased without problems to 50−70 °C for good turnovers. Under these circumstances hydroquinone should be added to avoid competitive radical hydrostannations. Further applications are shown in Table 2.[14]

Generally high α-selectivities were obtained with terminal alkynes (**1**−**7**), even with secondary propargylic alcohols bearing sterically high demanding protecting groups such as **3**. Several functional groups are tolerated in the substrates. Halogenated benzyl ethers (**4**) for example were hydrostannated without reduction of the aromatic halide,[15] giving rise to interesting substrates for intramolecular Stille couplings.

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[7] Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: New York, 1985. Stille, J. K. *Angew. Chem.* **1986**, *98*, 504; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1986. Davies, A. G. *Organotin Chemistry*; VCH: Weinheim, 1997.

[8] Kikukawa, K.; Umekawa, H.; Wada, F.; Matsuda, T. *Chem. Lett.* **1988**, 881.

[9] Zhang, H. X.; Guibe, F.; Balavoine, G. *J. Org. Chem*. **1990**, *55*, 1867.

[10] Review: Kazmaier, U. *Liebigs Ann./Recl.* **1997**, 285.

[11] Unfortunately no yields were given by the authors for the molybdenum-catalyzed reaction (see ref 9).

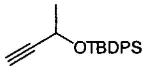
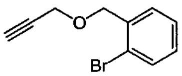
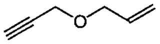
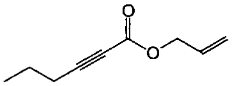
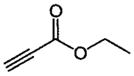
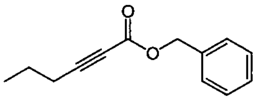
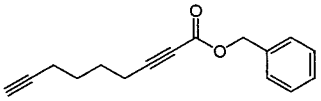
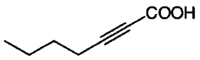
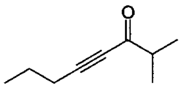
[12] The $\beta$-products can also be obtained in a highly regioselective fashion via stannylcupration: Reginato, G.; Mordini, A.; Messina, F.; Degl'Innocenti, A.; Poli, G. *Tetrahedron* **1996**, *52*, 10985. Betzer, J.-F.; Delaloge, F.; Muller, B.; Pancrazi, A.; Prunet, J. *J. Org. Chem.* **1997**, *62*, 7768.

[13] Reviews: Albers, M. O.; Coville, N. J.; Ashworth, T. V.; Singleton, E.; Swanepoel, H. E. *J. Organomet. Chem.* **1980**, *199*, 55. Albers, M. O.; Coville, N. J. *Coord. Chem. Rev.* **1984**, *53*, 227.

[14] **General Procedure for the Hydrostannation of Alkynes:** 1 mmol of the alkyne, 10 mg of hydroquinone, and 8.6 mg (20 mmol) of Mo(CO)$_3$(CN-$t$-Bu)$_3$(MoBI$_3$) were dissolved in a Schlenk tube under argon in 1 mL of THF. Then 0.8 mL (3 mmol) of Bu$_3$SnH was added slowly and the mixture was warmed to 55 °C until all starting material was consumed (generally after 3−7 h, determined by TLC). After cooling to room temperature, the reaction mixture was subjected to flash chromatography. Excess Bu$_3$SnH was removed using hexane as eluent. The stannylated products were obtained using hexanes/ethyl acetate containing 1% triethylamine as eluent.

[15] Reductive cleavage of aromatic halides with tin hydrides under radical conditions: Lorenz, D. H.; Shapiro, P.; Stern, A.; Becker, E. I. *J. Org. Chem.* **1963**, *28*, 2332. Maitra, U.; Sarma, K. D. *Tetrahedron Lett.* **1994**, *35*, 7861.

**Table 2.** MoBI$_3$-Catalyzed Hydrostannation of Substituted Alkynes

| Nr | substrate | yield (%) | selectivity α : β[a] |
|---|---|---|---|
| **3** |  | 88 | 90 : 10 |
| **4** |  | 44 | >95 : <5 |
| **5** |  | 38 | >95 : <5 |
| **6** |  | 80 | 91 : 9 |
| **7** |  | 98 | 92 : 8[b] |
| **8** |  | 68 | 90 : 10 |
| **9** |  | 74 | 82 : 18 |
| **10** |  | 88[c] | 63 : 37 |
| **11** |  | -- | 95 : 5[b] |

[a] Determined by NMR. [b] Determined by HPLC. [c] Isolated yield after esterification with $CH_2N_2$ and flash chromatography.

Double bonds (**5**, **6**) were not attacked under the reactions conditions used.[16] Allylic ester **6** is a quite interesting example, because this ester cannot be hydrostannated in the presence of palladium catalysts, probable because of decomposition via $\pi$-allyl-palladium intermediates. Results obtained with other esters, for example propiolic esters (**7**), are comparable to the results obtained with palladium catalysts.[9]

Alkynes bearing electron-withdrawing groups are obviously more reactive in comparison to unfunctionalized alkynes. Hydrostannation of diynoic ester **9** occurs preferentially at the "activated" double bond.[17] To our surprise, alkynoic acids such as **10** also could be hydrometalated in excellent yields and without protodestannylation. In general, the hydrostannation products obtained from (protected) propargylic alcohols and acetylenic esters are rather stable and can be purified via flash chromatography. This is in sharp contrast to the products obtained from the corresponding ketones. **11** shows a high reactivity and clean reaction under the reaction conditions used, but the hydrostannylated product decomposed (protodestannylation) completely during the workup.[18] Therefore, the regioselectivity of this reaction was determined after metal–halogen exchange with iodine on the corresponding vinyl iodide obtained.

In conclusion, we have developed a new, efficient, and highly regioselective catalyst for the hydrostannation of alkynes, giving good results with various types of substrates. Further investigations concerning the reaction mechanism and applications of this catalyst are currently under investigation.

**Acknowledgment.** We thank the Deutsche Forschungsgemeinschaft (SFB 247) and the Fonds der Chemischen Industrie for generous financial support.

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

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(16) For the hydrostannation of alkenes, see: (a) Lautens, M.; Meyer, C.; Lorenz, A. *J. Am. Chem. Soc.* **1996**, *118*, 10676. Lautens, M.; Kumanovic, S.; Meyer, C. *Angew. Chem.* **1996**, *108*, 1428; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1329.

(17) Although an excess of tin hydride was used (3 equiv), only 21% of the distannylated product was obtained, even though the terminal triple bond was the least hindered one.

(18) This may also be the reason for the lower yields obtained with several other substrates (**4**, **5**).