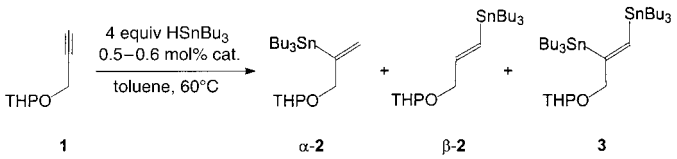
Tungsten-Catalyzed Distannation

Development of a New Catalyst for the Distannation of Alkynes**

*Sascha Braune and Uli Kazmaier**



Scheme 1. Mono- and distannation of **1**. THP = tetrahydropyranyl.

Vinylstannanes have become important building blocks in natural product chemistry as a result of the diverse range of palladium-catalyzed cross-coupling reactions they undergo with halides, acid chlorides, or triflates.[1] The broad applicability and high tolerance against functional groups has stimulated a keen interest in synthesizing these organotin derivatives. The most direct route to these compounds is by hydrostannation, namely the addition of tin hydrides to C≡C bonds. Besides this route, only a small number of approaches exist to introduce two functionalities simultaneously. One is the nickel-catalyzed carbostannation of terminal alkynes, in which a tributyltin and an allylic fragment are introduced simultaneously.[3] Other possibilities are the palladium-catalyzed addition of a silyl and a stannyl group (silastannation) to an alkyne or[4] distannation, mainly developed by Mitchell et al.[5] Best results have been obtained in the palladium-catalyzed distannation of alkynes by using hexamethyldistannane, a compound that is not unproblematic to handle in terms of its toxicity. Chemoselective transformations of both tin fragments are possible, underlining the synthetic use of these distannylated (*Z*)-olefins in organic chemistry.[6] The distannation of nonterminal acetylenic esters to (*Z*)-bis(trimethyltin)alk-2-enoates was achieved by Piers et al. in high yields.[7] Herein we report that distannylated (*Z*)-olefins can not only be obtained by palladium-catalyzed reactions but also by using isonitrile transition-metal complexes of Group 6 in combination with tributyltin hydride.

Our group has been studying the regioselective hydrostannation of alkynes with $[Mo(CO)_3(CN\mathit{t}Bu)_3]$ (**A**) for several years.[8] This catalyst is very stable and reliable, and gives high selectivity for the sterically more hindered α-stannylated product. Since this catalyst does not work as well in hydrostannations of propargylic ethers as it does in the corresponding reactions with propargylic esters or alcohols, we tried to optimize the catalyst by varying the isonitrile ligands. Starting from $[Mo(CO)_6]$ and the corresponding isonitrile[9] we prepared several catalysts by ligand exchange, for example, $[Mo(CO)_3(CNPh)_3]$ (**B**).[10] This complex shows a slower conversion rate and a poor ratio of α- to β-products as well as a surprising side product: 19% (relative to the whole conversion) of the distannylated product **3** in the "hydrostannation" of the tetrahydropyranylpropargylic ether (**1**; Scheme 1). This side product was also obtained in the hydrostannation of propargylic compouds with the other catalysts, but always in less than 5%.This result was initially surprising for us, and we assumed that based on the lower reactivity of the phenyl isocyanide complex (**B**), the decomposition of the tin hydride by elimination of H_2 and the formation of the distannane competes with the hydrostannation. This would explain the formation of the distannylated product as a metal-catalyzed addition of an in situ prepared distannane to a C≡C bond. Decompositions of this type are well known for palladium-catalyzed reactions,[11] and palladium complexes also catalyze the addition of distannanes to alkynes.[5] Only recently Lautens et al. reported an analogous side product in a palladium-catalyzed hydrostannation.[4e] To verify our mechanistic hypothesis we tried to react hexabutyldistannane with **1** in the presence of our molybdenum catalysts, but in no case were we able to isolate any stannylated product. Evidently, a "free" distannane is not the reagent responsible for the addition, but the "decomposition" must take place in the coordination sphere of the metal, probably in the presence of coordinated alkyne.

It is known that tungsten and molybdenum form stable complexes with trialkyltin compounds.[12] Bel'skii et al. were able to crystallize complexes of the type Mo-$HSnBu_3$ and characterize them by X-ray crystallography in 1986.[13] Brown et al. showed that $[HMo(CO)_3Cp]$ and $HSnBu_3$ react to form a complex of the type $[Bu_3SnMo(CO)_3Cp]$ under reductive elimination of hydrogen.[14] In 1991 Schubert et al. observed that $[MesCr(CO)_3]$ forms a stable complex with triphenyltin hydride after dissociation of one carbonyl ligand. This complex contains a three-centered hydrogen bond Cr-H-Sn.[15] They were also able to detect the appearance of complexes like $[(CO)_4(Ph_3P)W(H)SnPh_3]$ by spectroscopy, but unfortunately because of the lability of the tungsten complexes they were not able to crystallize them. However, they observed that with an excess of tin hydride, hydrogen is eliminated and the corresponding distannylated complex $[(CO)_4(Ph_3P)W(SnPh_3)_2]$ is obtained.

Thus, it wasn't as surprising as initially throught that we obtained the distannylated product. The next question was, how can we alter the ratio of distannation to hydrostannation. Clearly, the electron-donating *tert*-butyl group of **A** favors the hydrostannation, whereas the rather electron-withdrawing phenyl ring in the phenyl isocyanide complex **B** favors the decomposition of the tin hydride. Therefore, we explored the effects of further electron-withdrawing groups at the phenyl ring on the product ratio (see Scheme 1) and synthesized "electron-poor" isonitriles[16] and the corresponding molybdenum and tungsten isonitrile complexes **C**–**G**.[9,17]

First we examined the molybdenum complexes **C**–**E** and confirmed that electron-withdrawing groups in the isonitrile

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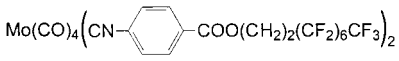
[**] This work was supported by the Deutsche Forschungsgemeinschaft (SFB 247 and Ka880/5) and by the Fonds der Chemischen Industrie.

  1433-7851/03/4203-0306 $ 20.00+.50/0



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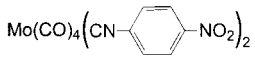

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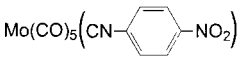

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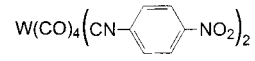

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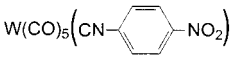


G

Table 1: Mono- and distannation of **1**.

Catalyst	Yield [%] α-**2**	β-**2**	**3**
A	94	1	3
B	42	18	14
C	14	2	29
D	21	2	40
E	2	1	44
F	5	4	77
G	1	1	93

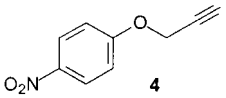
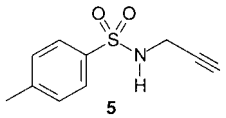
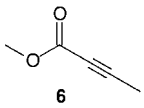
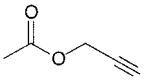
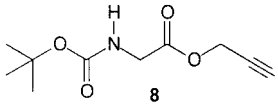
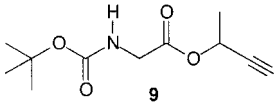
part of the complex discriminate the hydrostannation (Table 1). Surprisingly we found the best selectivity with the monoisonitrile complex **E**, which yields nearly exclusively the distannylated product. But we were not able to improve the yield above 50% even by careful optimization of the reaction parameters.

We hoped to achieve a further improvement by using the corresponding tungsten-based catalyst, since tungsten because of its larger atomic volume should be more willing to bind two sterically demanding fragments like the tributyltin groups.[15] Indeed the tungsten complexes show a higher reactivity than the corresponding molybdenum complexes, and the monoisonitrile complex **G** proved to be the best catalyst: the *cis*-distannylated products are obtained almost exclusively in near quantitative yields. Even though only 0.5–0.6 mol% of catalyst were used in all the reactions, the conversion was complete after 5 h at the most.

Furthermore we were able to show the general use of catalyst **G** in the selective distannation of functionalized terminal alkynes (Table 2). In nearly all cases the ratio of distannation/hydrostannation was better than 20/1. This was valid for ethers (**4**) as well as for amides (**5**). In the case of **6** we found only distannylated product, though the yield decreased. This example demonstrated that even substituted alkynes can be distannylated selectively. We obtained very good yields and excellent selectivities in the case of propargylic esters (**7, 8**). Steric hindrance has, however, a strong influence especially on the yields as a comparison of **8** and **9** shows. Simple alkynes are less suitable as substrates for our catalyst systems; for example, in the reaction of 1-decyne, only negligible amounts of distannylated product were obtained, and without significant selectivity.

In conclusion, we could show that the tungsten isonitrile complex **G** is a highly efficient and selective catalyst for distannations of alkynes, in which tributyltin hydride can be used as the tin source. Mechanistic studies on this exceptional reaction are in progress.

Table 2: Distannation of alkynes with the tungsten isonitrile complex **G**.

Substrate	distannation	Yield [%] α-stannation	β-stannation
 **4**	62	3	0
 **5**	76	3	1
 **6**	42	0	0
 **7**	87	1	1
 **8**	73	1	0
 **9**	32	2	1

Experimental Section

Synthesis of the catalyst **G**: *p*-Nitrophenyl isocyanide (790 mg, 5.33 mmol) dissolved in absolute toluene (10 mL) was added slowly to a suspension of $CoCl_2 \cdot 2H_2O$ (400 mg, 2.41 mmol) and $[W(CO)_6]$ (605 mg, 1.72 mmol) in absolute toluene (10 mL) at 100 °C. The mixture was refluxed for 7 h before the resulting black suspension was evaporated in vacuo. The residue obtained was purified by flash chromatography over silica using CH_2Cl_2/hexane (1/1) as eluent. Yield: 189 mg (0.40 mmol, 23%) of a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.55$ (d, $^3J = 9.1$ Hz; (CH)C–NC), 8.32 ppm (d, $^3J = 9.1$ Hz; (CH)C–NO_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 125.9$ (d; (*C*H)C–NO_2), 128.0 (d; (*C*H)C–NC), 141.8 (s; *C*–NC), 147.7 (s; C–NO_2), 194.1 (s; *cis*-CO), 195.7 ppm (s; *trans*-CO), (isonitrile-C not detected); IR (KBr): $\tilde{\nu} = 2135$ (s), 2049 (s), 1972, 1925 (vs), 1524 (m), 1344 cm^{-1} (s); FAB$^+$-HRMS [*m*/*z*, (%)]: $C_{12}H_4N_2O_7{}^{186}W$: calcd: 473.9562, found: 473.9548 (50.3); $C_{12}H_4N_2O_7{}^{184}W$: calcd: 471.9528, found: 471.9497 (56.1); $C_{12}H_4N_2O_7{}^{183}W$: calcd: 473.9521, found: 470.9500 (35.7); $C_{12}H_4N_2O_7{}^{182}W$: calcd: 469.9501, found: 469.9464 (48.0); elemental analysis (%): calcd: C 30.15, H 2.11, N 5.86; found: C 30.17, H 1.42, N 5.64.

General procedure for the distannation: The alkyne (1 mmol), catalyst **G** (3 mg, 0.6 mol%) and a point of a spatula of hydroquinone were dissolved in absolute toluene (2 mL) and heated for 15 min at 60 °C. After addition of tributyltin hydride (1 mL, 3.8 mmol), heating was continued for 12 h at 60 °C. After removal of the solvent the crude product was chromatographed over silica gel. First hexabutyldistannane and tributyltin hydride were eluted with pure hexane, then the product was isolated by using hexane/ethyl acetate/1% triethylamine (98–90% hexane).

Received: August 15, 2002 [Z19974]

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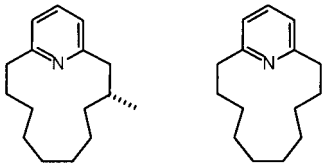
[16] M. A. Mironov, V. S. Mokrushin, *Russ. J. Org. Chem.* **1999**, *35*, 719–723.
[17] In contrast to the electron-rich isonitriles which provide mainly the tris(isonitrile) complexes under the conditions described in reference [9], with electron-poor isonitriles under the same conditions the mono- and disubstituted complexes are obtained, which can be separated by flash chromatography.

Efficient Synthetic Strategy

A Catalytic Approach to (*R*)-(+)-Muscopyridine with Integrated "Self-Clearance"**

Alois Fürstner and Andreas Leitner*

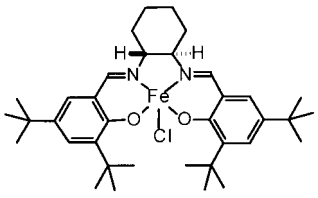
The chemist's ability to make molecules of utmost complexity[1] must not hide the fact that the practicability of many such syntheses is still low. The arithmetic demon inherent to any linear sequence constitutes one of the major hurdles in this regard. To overcome this obstacle new methodology and improved retrosynthetic logic are called for which allow more than one bond-making event to be integrated into a single synthetic operation.[2] The approaches to the odoriferous alkaloid (*R*)-(+)-muscopyridine (**1**), derived from the animal kingdom, and its naturally occurring nor-analogue **2** outlined below tackle this theme and illustrate how priority can be given to the "economy of steps"[3] by a highly orchestrated catalysis-based process. Following its isolation by Ruzicka and Prelog,[4] the unusual *meta*-pyridinophane derivative **1** has



1 **2**

been repeatedly targeted.[5–7] Despite its rather simple structure, however, none of the reported syntheses is fully satisfactory, being either unduly lengthy and/or poor yielding.[8]

Our approach to the alkaloid **1** takes advantage of the favorable application profile of an iron-catalyzed alkyl–aryl cross-coupling reaction recently developed in our laboratory as a powerful alternative to established organopalladium chemistry; in the present case the iron–salen complex **3** was applied.[9,10] The method not only allows one to replace expensive precious metal complexes by cheap iron salts, but it is also distinguished by unprecedentedly high reaction rates even at or below room temperature. While aryl chlorides as



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[**] This work was supported by the Deutsche Forschungsgemeinschaft (Leibniz program) and the Fonds der Chemischen Industrie.

  1433-7851/03/4203-0308 $ 20.00+.50/0