Carbamoylstannation of Terminal Alkynes with Carbamoylstannanes: Catalyst-Dependent Regiochemical Reversal

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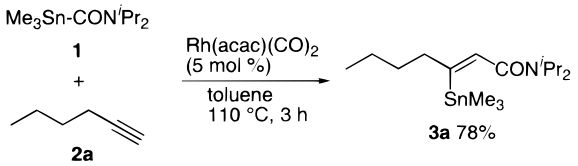
Summary: Rh(acac)(CO)$_2$ catalyzes addition of (N,N-diisopropylcarbamoyl)trimethylstannane to terminal alkynes to give (Z)-β-stannyl-α,β-unsaturated amides with terminal attachment of the amide group, while the use of Ni(cod)$_2$ results in the reversal of the regioselectivity. A mechanism initiated by the oxidative addition of the carbamoylstannane was proposed on the basis of the isolation of (trimethylstannyl)(N,N-diisopropylcarbamoyl)[1,2-bis(dimethylphosphino)ethane]palladium.

Development of transition-metal-complex-catalyzed addition reactions of E−E′ bonds (E ≠ E′, E, E′ = heteroatom, functional group) to alkynes is a research field of considerable interest.[1] These reactions provide simple and efficient routes to doubly functionalized alkenes, which are useful synthetic intermediates. However, the addition reactions of E−C bonds to alkynes are still rare.[2] Among possible reactions of this category, the addition of E−COOR compounds is particularly useful in organic synthesis. Our study aiming at the creation of a wide spectrum of E−COOR bond addition reactions has disclosed that chloroformates add to alkynes, offering a straightforward method to prepare 3-chloro-2-alkenoic acid esters in high yields.[2e] In a continued study we have found that rhodium complexes catalyze the addition of Sn−CONR$_2$ across the C≡C triple bond: i.e., carbamoylstannation of alkynes with carbamoylstannanes. The very recent paper by Hiyama and co-workers reporting similar reactions[3] prompted us to disclose our results, which include the catalyst-dependent reversal of the regioselectivity.

When a mixture of (*N*,*N*-diisopropylcarbamoyl)trimethylstannane (**1**;[4] 0.3 mmol), 1-hexyne (**2a**; 0.36 mmol), and Rh(acac)(CO)$_2$ (acac = acetylacetonato; 0.015 mmol, 5 mol % relative to **1**) in toluene (0.3 mL) was heated to 110 °C for 3 h, (*Z*)-*N*,*N*-diisopropyl-3-(trimethylstannyl)-2-heptenamide (**3a**[5]) was regio- and stereoselectively formed (99% selectivity) in 78% GC yield (based on the amount of **1** charged), together with *N*,*N*-diisopropylformamide (**4**; 3%) and 1-(trimethylstannyl)-1-hexyne (**5**; 3%) arising from simple substitution[6] (eq 1). Kugelrohr distillation (bath temperature



(1)

90 °C/1.6 Torr) followed by chromatography through a short Al_2O_3 column (∼10 cm, hexane as eluent) led to isolation of pure **3a** as a colorless oil.

The structure of **3a** is readily confirmed by NMR spectroscopy; its ^{1}H NMR spectrum displays an olefinic proton signal at 6.8 ppm as a doublet with a $^3J_{Sn-H}$ value of 132 Hz.[7] The $^3J_{Sn-H}$ value agrees with the stannyl group being trans to the olefinic proton and, hence, suggests the attachment of Sn to the internal olefinic carbon via cis addition of **1**. The cis addition is also evidenced by an NOE experiment, in which irradiation of the triplet at δ 2.5 ppm assignable to the allylic protons resulted in a 10% enhancement of the olefinic proton signal at δ 6.8 ppm. Finally, treatment of **3a** with acetic acid at room temperature for 2 h afforded *N*,*N*-diisopropyl-2-heptenamide (**6**),[8] unequivocally confirming the structure of **3a**.

(1) For our recent review, see: Han, L.-B.; Tanaka, M. *Chem. Commun*. **1999**, 395 and references therein.

(2) Si−C: (a) Sakurai, H.; Imai, T. *Chem. Lett*. **1975**, 891. (b) Takeyama, Y.; Nozaki, K.; Matsumoto, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn*. **1991**, *64*, 1461. (c) Chatani, N.; Takeyasu, T.; Horiuchi, N.; Hatafusa, T. *J. Org. Chem*. **1988**, *53*, 3539. Sn−C: (d) Shirakawa, E.; Yoshida, H.; Kurahashi, T.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc*. **1998**, *120*, 2975. (e) Shirakawa, E.; Yoshida, H.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc*. **1999**, *121*, 4290. Cl−C: (f) Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem*. **1996**, *61*, 6941. (g) Hua, R.; Shimada, S.; Tanaka, M. *J. Am. Chem. Soc*. **1998**, *120*, 12365.

(3) Shirakawa, E.; Yamasaki, K.; Yoshida, H.; Hiyama, T. *J. Am. Chem. Soc*. **1999**, *121*, 10221.

(4) For the preparation of **1**, see: Lindsay, C. M.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 569.

(5) Attempts to isolate adduct **3a** by column chromatography on silica gel were unsuccessful because the C−Sn bond in **3a** was easily cleaved to give (*Z*)-*N*,*N*-diisopropyl-2-heptenamide. Pure adduct **3a** was isolated by Kugelrohr distillation (bath temperature 90 °C/1.6 Torr), followed by chromatography (Al_2O_3) through a short column. Data for **3a**: ^{1}H NMR (C_6D_6) δ 6.77 (s, 1H, $^3J_{Sn-H}$ = 132 Hz), 3.80 (br, 1H), 3.36 (br, 1H), 2.50 (t, 2H, *J* = 7.0 Hz, $^3J_{Sn-H}$ = 55 Hz), 1.49−1.29 (m, 10H), 0.91−0.79 (m, 9H), 0.48 (s, 9H, $^2J_{^{119}Sn-H}$ = 54 Hz, $^2J_{^{117}Sn-H}$ = 52 Hz); ^{13}C NMR (C_6D_6) δ 170.8, 166.7, 128.7, 47.1, 45.9, 39.7 ($^2J_{Sn-C}$ = 44 Hz), 32.3 ($^3J_{Sn-C}$ = 14 Hz), 22.9, 21.1, 20.6, 14.1, −5.64 ($J_{^{119}Sn-C}$ = 371 Hz, $J_{^{117}Sn-C}$ = 355 Hz); ^{119}Sn NMR (C_6D_6) δ −65.5; IR (neat) 2968, 2932, 1624, 1448, 1135, 1046, 768 cm^{-1}; GCMS *m*/*z* (% relative intensity) 360 (M^+ − Me, 100), 318 (30), 258 (27), 165 (64), 135 (46), 100 (56), 55 (70); HRMS *m*/*z* calcd for $C_{16}H_{33}NOSn$ − Me 360.1349, found 360.1423.

(6) Heating a toluene solution of **1** and 1-hexyne (1:1.5) at 110 °C for 8 h in the absence of the catalyst afforded **4** and **5**, both in 90% yield.

(7) $^3J_{^{117}Sn-H}$ and $^3J_{^{119}Sn-H}$ could not be resolved to display separate signals. For coupling constants between tin and olefinic protons in alkenylstannane compounds, see: Leusink, A. J.; Budding, H. A.; Marsman, J. W. *J. Organomet. Chem*. **1967**, *9*, 285.

(8) Data for **6**: ^{1}H NMR (C_6D_6) δ 7.08 (dt, 1H, *J* = 15/7.5 Hz), 6.14 (d, 1H, *J* = 15 Hz), 3.59 (br, 2H), 1.99−1.92 (m, 2H), 1.35−1.21 (m, 10H), 0.89−0.75 (m, 9H); GCMS *m*/*z* (% relative intensity) 211 (M^+, 2), 196 (4), 168 (9), 154 (27), 111 (62), 86 (100), 55 (92).

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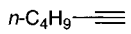
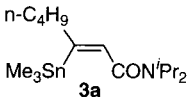
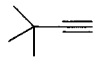
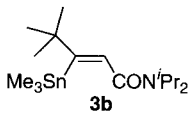
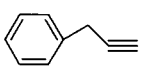
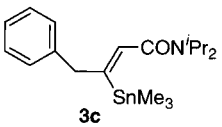
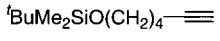
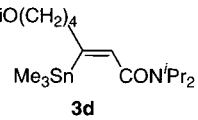
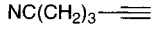
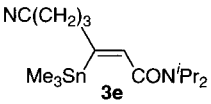
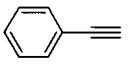
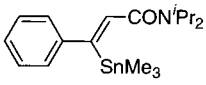
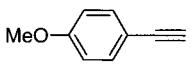
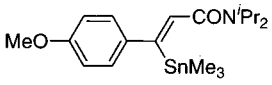
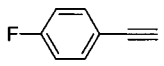
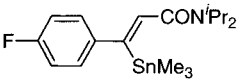
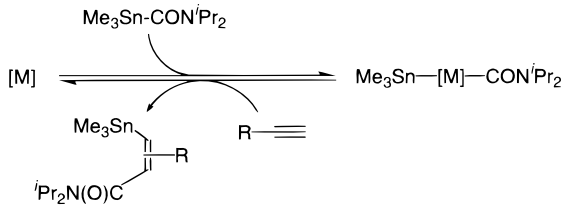
Table 1. Carbamoylstannation of Terminal Alkynes[a]

alkyne	adduct	yield (%)[b]
 **2a**	 **3a**	78 (99)
 **2b**	 **3b**	81 (100)
 **2c**	 **3c**	69 (94)
 **2d**	 **3d**	71 (100)
 **2e**	 **3e**	74 (90)
 **2f**	 **3f**	70 (100)
 **2g**	 **3g**	37[c] (100)
 **2h**	 **3h**	46[c] (100)

[a] The reactions were carried out at 110 °C for 3 h by using 0.3 mmol of carbamoylstannane **1**, 0.36 mmol of alkynes, and 0.015 mmol of $Rh(acac)(CO)_2$ in 0.3 mL of toluene. [b] GC yield based on the amount of **1** used. Values in parentheses are the regioselectivities. [c] ^1H NMR yield.

As shown in Table 1, the reactions of **1** with terminal alkynes are all regio- and stereoselective, forming (*Z*)-*β*-stannyl-α,*β*-unsaturated amides via cis addition. Negligible traces of dimers and trimers of the alkynes were generally formed. The size of the alkyne substituents did not significantly affect the reactivity or the regiochemistry. Functional groups such as siloxy and cyano groups were tolerated. Phenylacetylene also reacted normally. However, its *p*-methoxy and *p*-fluoro derivatives reacted somewhat slowly and less selectively. The occurrence of the side reaction leading to formation of equal quantities of *N*,*N*-diisopropylformamide and the stannylalkyne appeared to be dependent on the acidity of the alkynyl hydrogen; ethyl propynoate, having a highly electron-withdrawing ester group, formed, besides two isomeric trimers of the propynoate,[9] large quantities of these side products. Internal alkynes do not undergo the addition reaction under the present

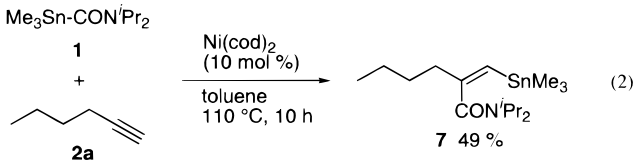
Scheme 1[a]



[a] [M] = Rh, Ni. Only actively reacting ligands are illustrated in the scheme, with disregard of other incidental ligands that may be bound to the central metal.

conditions. For instance, heating a solution of **1** with 4-octyne at 110 °C for 100 h resulted in 50% conversion of **1**, but 4-octyne mostly remained unchanged. Dimethyl acetylenedicarboxylate did not react either.

For the reaction of **2a** with **1**, a number of other catalysts were examined. Although $Cp^*Rh(CO)_2$ gave ca. 25% of adduct **3a**, $RhCl(PPh_3)_3$, $RhCl(CO)(PPh_3)_2$, RhCl(CO)(dppf) (dppf = 1,1′-bis(diphenylphosphino)-ferrocene), and $RhH(CO)(PPh_3)_2$ did not exhibit catalytic activity at all. Other metal complexes such as $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, NiCl(dppp) (dppp = 1,3-bis(diphenylphosphino)propane), and $RuCl_2(PPh_3)_3$ did not give the adduct either. However, $Ni(cod)_2$ did display catalytic activity, as Hiyama and co-workers also recently reported for the reaction of internal alkynes.[3] Very interestingly, the use of this catalyst displayed reversal in the regioselectivity in the reaction of terminal alkynes to introduce tin to the terminal carbon of the triple bond. For example, heating a mixture of **1** (0.3 mmol), 1-hexyne (4 equiv), and $Ni(cod)_2$ (0.03 mmol, 10 mol % relative to **1**) to 110 °C for 10 h afforded adduct **7** in 49% GC yield (92% regioselectivity), as shown in eq 2, with 25%



(2)

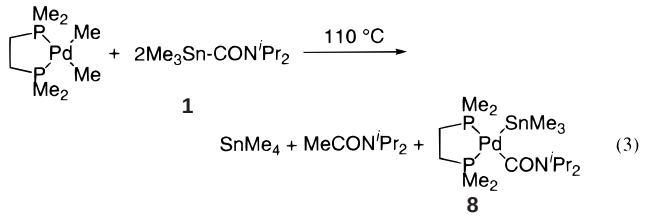
recovery of **1**. The NOE experiment, which showed a 9% enhancement between the allylic and the olefinic hydrogens, agrees with the *Z* configuration. The small J_{Sn-H} value of 69 Hz observed for the olefinic hydrogen centered at δ 5.90 ppm confirms the geminal attachment of tin relative to the hydrogen.[10]

The mechanism, inclusive of the origin of the catalyst-dependent reversal of the regioselectivity, remains to be clarified. However, the following observation appears to suggest the oxidative addition of the $Sn-CONPr^i_2$ bond being the initiation step of the catalysis, as shown in Scheme 1. Attempted reactions of **1** with $RhCl(N_2)$-

(9) HRMS data for one of the trimers: *m*/*z* (relative intensity) 294 (M^+, 10), 266 (16), 249 (100), 238 (15), 221 (55), 210 (20), 193 (40). HRMS data for the other trimer: *m*/*z* 294 (M^+, 5), 265 (1), 249 (30), 237 (1), 221 (100), 193 (50).

(10) Data for **7**: ^1H NMR (C_6D_6) δ 5.90 (s, 1H, $^2J_{Sn-H}$ = 69 Hz), 3.78 (br, 1H), 2.94 (br, 1H), 2.23 (t, 2H, *J* = 7 Hz), 1.56−1.27 (m, 10H), 0.89−0.84 (m, 9H), 0.31 (s, 9H, $^2J_{Sn-H}$ = 54 Hz); ^{13}C NMR (C_6D_6) δ 171.8, 157.8, 129.3 (J^{119}_{Sn-C} = 453 Hz, J^{117}_{Sn-C} = 433 Hz), 49.6, 45.4, 38.5 ($^3J_{Sn-C}$ = 59 Hz), 30.7, 22.5, 20.8, 14.1, −8.12 (J^{119}_{Sn-C} = 354 Hz, J^{117}_{Sn-C} = 338 Hz); ^{119}Sn NMR (C_6D_6) δ −52.15 ppm; IR (neat) 2966, 2934, 1630, 1437, 1371, 1340, 1214, 1135, 828 cm^{-1}; GCMS *m*/*z* (% relative intensity) 360 (M^+ − Me, 94), 318 (44), 258 (37), 165 (100), 135 (55), 111 (16), 55 (53); HRMS *m*/*z* calcd for $C_{16}H_{33}NOSn$-Me 360.1349, found 360.1367.

$(PPr^i_3)_2$, $RhCl(PMe_3)_3$, $Rh(acac)(CO)_2$, $RhCl(CO)(PPhMe_2)_2$, $Rh(acac)(CO)(PPh_3)$, $Rh(acac)(CO)(PMe_3)$, and $Cp^*Rh(CO)_2$ resulted in either no reaction or rapid decomposition of the possible adducts, which did not allow isolation or spectroscopic study. $Ni(PEt_3)_4$ or the nickel species generated by the treatment of $Ni(cod)_2$ with dmpe (dmpe = 1,2-bis(dimethylphosphino)ethane) did not give an oxidative addition product either. However, when $PdMe_2$(dmpe) (0.1 mmol) was treated with **1** (0.3 mmol) in C_6D_6 (0.5 mL) at 110 °C for 2 h, the colorless mixture turned to pale yellow. GCMS analysis of the solution showed that $SnMe_4$ (0.09 mmol) and $CH_3CONPr^i_2$ (0.1 mmol) were formed with recovery of **1** (0.1 mmol), as shown in eq 3. NMR spectroscopy also revealed the formation of these and a new palladium complex (**8**). Addition of hexane (2 mL) to the mixture precipitated a white solid of analytically pure **8** (0.087 mmol), which displayed satisfactory analytical data and ^1H, ^{31}P, and ^{119}Sn NMR spectra.[11] Unfortunately, complex **8** did not form **3a** upon treatment with 1-hexyne, presumably because of the strong donation and chelation.



(3)

In summary, carbamoylstannane **1** adds to terminal alkynes stereo- and regioselectively in the presence of transition-metal-complex catalysts. The rhodium catalyst introduces the stannyl and amide moieties to the internal and terminal carbons of the triple bond, respectively. The regiochemistry was reversed by the use of the nickel catalyst. Further study to clarify the mechanism and broaden the scope the new addition reaction is currently in progress.

Acknowledgment. We thank the Japan Science and Technology Corporation (JST) for financial support through the CREST (Core Research for Evolutional Science and Technology) program and for a postdoctoral fellowship to R.H.

Supporting Information Available: Text describing experimental details and spectroscopic and/or analytical data of compounds **3a**−**g** and **6**−**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Data for **8**: ^1H NMR (C_6D_6) δ 4.89 (m, 1H), 3.23 (m, 1H), 1.85 (d, 3H, J = 6.7 Hz), 1.66 (d, 3H, J = 6.7 Hz), 1.21 (d, 6H, J = 6.5 Hz), 0.97−0.83 (m, 16H), 0.59 (s, 9H, $^2J_{Sn-H}$ = 35 Hz); ^{31}P NMR (C_6D_6) δ 17.9 (d, J_{P-P} = 21 Hz, $^2J_{P-Sn(cis)}$ = 269 Hz), 14.3 (d, J_{P-P} = 21 Hz, $^2J_{P-^{119}Sn(trans)}$ = 1707 Hz, $^2J_{P-^{117}Sn(trans)}$ = 1631 Hz); ^{119}Sn NMR (C_6D_6) δ 45.4 (dd, $^2J_{Sn-P(trans)}$ = 1707 Hz, $^2J_{Sn-P(cis)}$ = 269 Hz); IR (KBr) 2964, 2904, 1526, 1251, 944, 745, 609 cm^{-1}. Anal. Calcd for $C_{16}H_{39}NOP_2SnPd$: C, 35.03; H, 7.12; N, 2.55. Found: C, 35.45; H, 7.20; N, 2.36.