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Indium(III) Chloride-Promoted Intramolecular Addition of Allylstannanes to Alkynes

Katsukiyo Miura,* Naoki Fujisawa, and Akira Hosomi*

Department of Chemistry, 21st Century COE, Graduate School of Pure and Applied Sciences, University of Tsukuba, and CREST, Japan Science and Technology Corporation (JST), Tsukuba, Ibaraki 305-8571, Japan

miura@chem.tsukuba.ac.jp; hosomi@chem.tsukuba.ac.jp

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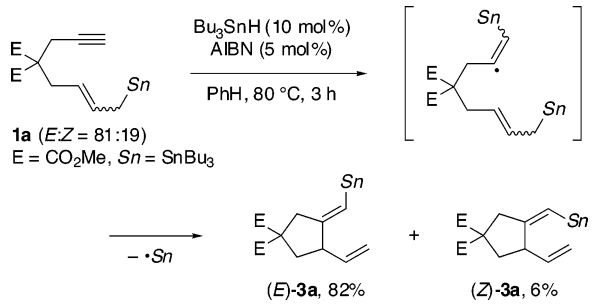
In the presence of an equimolar amount of $InCl_3$, 8-tributylstannyl-6-octen-1-ynes (allylstannanes bearing an alkynyl group) were efficiently cyclized to 2-allyl-1-methylenecyclopentanes. In contrast, catalytic use of $InCl_3$ gave 2-allyl-1-(tributylstannylmethylene)cyclopentanes mainly by intramolecular allylstannylation. These cyclizations could proceed via intramolecular addition of an allylindium intermediate.

Introduction

Allylstannanes are considerably valuable for regio- and stereoselective allylation of a wide range of carbon electrophiles.[1] In recent years, much attention has been focused on allylation and allylstannylation reactions of unactivated alkynes with allylstannanes for stereoselective synthesis of multisubstituted alkenes. Transition metal complexes,[2] π-Lewis acids,[3,4] and radical initiators[5] are known to be effective catalysts for these reactions. In the course of our study on the radical-initiated allylstannylation,[5] we have reported that allylstannanes **1** undergo intramolecular allylstannylation leading to vinylstannanes **3** in the presence of Bu_3SnH−AIBN (Scheme 1).[6] This article discloses that $InCl_3$ also promotes the cyclization of **1** to give the allylation and allylstannylation products, **2** and **3**. A similar intramolecular allylation has been achieved by using electrophilic late transition metal chlorides such as $PtCl_2$ and $AuCl_3$, which work as π-Lewis acids for electrophilic activation of alkynes.[4] However, the present cyclizations are quite different from the π-Lewis acid-catalyzed cyclization in mechanistic aspects although $InCl_3$ is frequently utilized as a mild Lewis acid.[7]

SCHEME 1



Results and Discussion

Allylstannanes **1a**−**c**,**e** were prepared efficiently from 2-vinylcyclopropane-1,1-dicarboxylates by radical-mediated ring-opening reaction with Bu_3SnH and subsequent propargylation (Scheme 2, see the Supporting Information).[6,8] Reduction of **1a** with $LiAlH_4$ followed by methylation with MeI gave **1d**. Trimethylsilylation of **1a** with Me_3SiCl and *i*-Pr_2NLi was performed for the synthesis of **1f**.

Initially, we found that, in the presence of $InCl_3$, **1a** was slowly cyclized to methylenecyclopentane **2a** in CH_2Cl_2 at room temperature. We then examined solvent effects of this cyclization with an equimolar amount of $InCl_3$ or $GaCl_3$ (Table 1). As a result, MeCN was fairly effective in the $InCl_3$-promoted cyclization (entry 2). The use of MeCN gave **2a** in a high yield along with a small amount of the allylstannylation product **3a**. $GaCl_3$, as well as $InCl_3$, works as a good promoter in CH_2Cl_2 or MeCN (entries 1 and 2). Further investigation revealed that $In(OTf)_3$ showed moderate activity in MeCN (78% yield of **2a**, rt, 2 h), and other commercially available indium salts ($In(OAc)_3$, $In(acac)_3$, and $In(OH)_3$), $AlCl_3$, and BCl_3 did not promote the cyclization at all.

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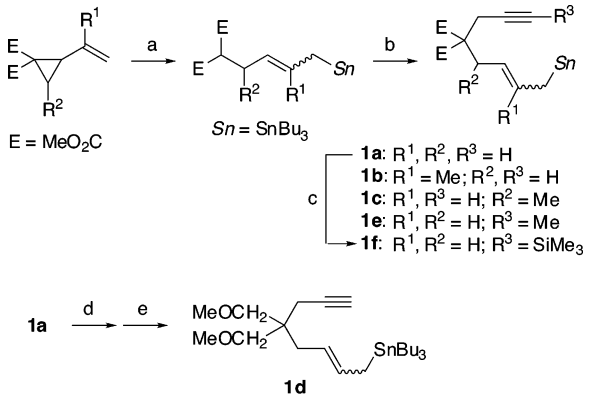
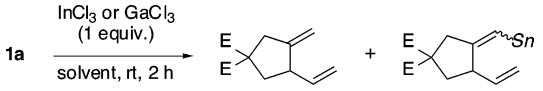
SCHEME 2[a]



[a] Reagents and conditions: (a) Bu_3SnH, cat. AlBN, benzene; (b) NaH, 3-bromo-1-propyne or 1-bromo-2-butyne, DMF; (c) *i*-Pr_2NLi, Me_3SiCl, THF; (d) $LiAlH_4$, Et_2O; (e) NaH, MeI, DMF.

TABLE 1. Solvent Effect on Cyclization of Allylstannane 1a



		yield of **2a** (**3a**)/%[a]	
entry	solvent	with $InCl_3$	with $GaCl_3$
1	CH_2Cl_2	55[b]	87
2	MeCN	96[c] (4)[c,d]	82
3	MeOH	0	0
4	acetone	75	0
5	1,4-dioxane	18	41
6	DME	13	44
7	Et_2O	70	12

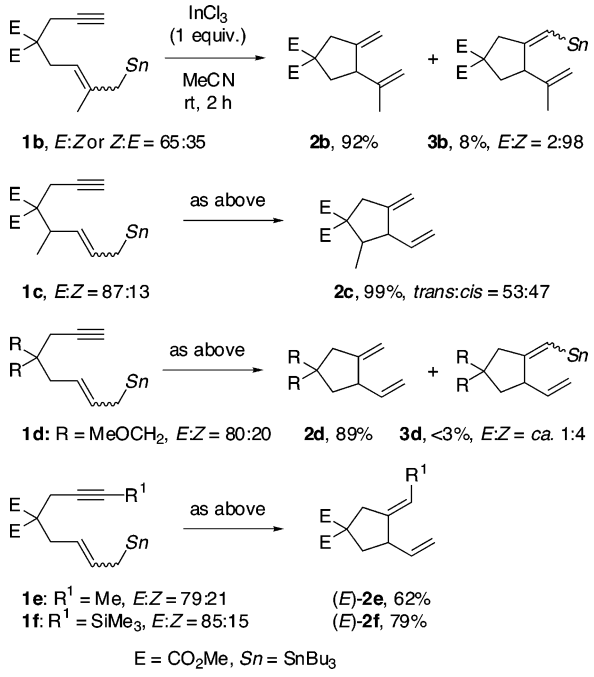
[a] Determined by ^1H NMR analysis of the crude product. [b] The reaction was carried out for 60 h. [c] Isolated yield. [d] *E*:*Z* = 15:85.

The $InCl_3$-promoted system with MeCN as solvent was successfully used for the cyclization of other allylstannanes **1b**−**f** (Scheme 3). Similar to the case with **1a**, the reaction of **1b** formed the allylstannylation product **3b** as a minor product with high *Z*-selectivity. Allylstannane **1c** was converted into **2c** in a quantitative yield, but with low diastereoselectivity. The use of **1d** demonstrated that the ether functionality was compatible with the present cyclization. Allylstannanes **1e** and **1f**, bearing an internal triple bond, were less reactive than those with a terminal triple bond. Interestingly, the intramolecular allylation of these substrates proceeded in a cis addition mode to give only *E*-isomers of the allylation products **2e** and **2f**.

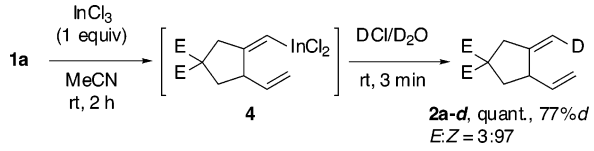
To gain mechanistic insight, DCl quenching of the reaction mixture was carried out (Scheme 4). The $InCl_3$-promoted reaction of **1a** followed by treatment with DCl/D_2O gave the deuterated product **2a**-*d*. The deuteration took place at the *exo*-methylene carbon with high *Z*-selectivity. This observation suggests the presence of (*Z*)-vinylindium **4** in the reaction mixture.

To our surprise, the reaction of **1** with a catalytic amount of $InCl_3$ gave **3** as the major product along with **2** (the upper equation in Scheme 5). The intramolecular allylstannylation favored cis addition to form thermodynamically less stable (*Z*)-**3** selectively. The $InCl_3$-catalyzed cyclization of **1** followed by destannylation with

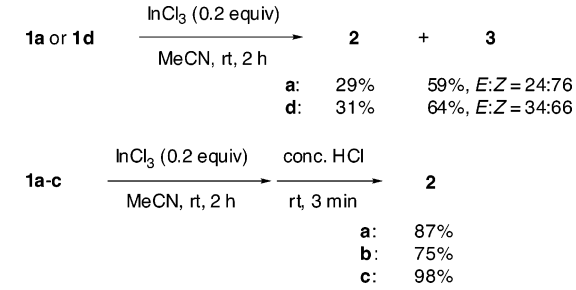
SCHEME 3



SCHEME 4



SCHEME 5

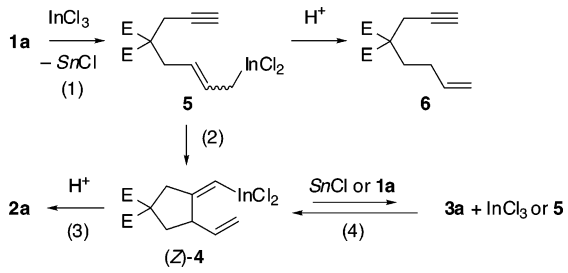


concentrated HCl gave only **2** in good yields (the lower equation in Scheme 5).

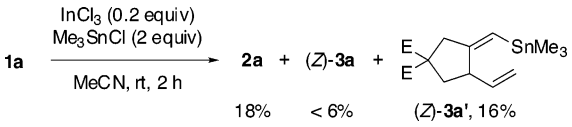
As described above, the $InCl_3$-promoted intramolecular allylation and allylstannylation of alkynes favor a cis addition mode. Judging from these stereochemical outcomes, a pathway involving electrophilic activation of the C−C triple bond by $InCl_3$ is not suitable for the present cyclizations because such a π-Lewis acid-catalyzed reaction is known to proceed in a trans addition mode.[3] RajanBabu et al. have reported the Pd-catalyzed intramolecular *cis*-allylstannylation of alkynes, which is proposed to involve allylpalladation of the triple bond with a π-allylpalladium intermediate as the key step.[2c] Similarly, the $InCl_3$-promoted cis addition of allylstannanes is attributable to a concerted allylmetalation step.

A plausible mechanism for the cyclizations of **1a** to **2a** and **3a** is as follows (Scheme 6): (1) transmetalation of **1a** with $InCl_3$ forms allylindium **5** and Bu_3SnCl,[9] (2) **5** is transformed into vinylindium (*Z*)-**4** by intramolecular allylindation, (3) hydrolysis of (*Z*)-**4** by an aqueous

SCHEME 6



SCHEME 7



workup gives **2a**, and (4) the reaction of (*Z*)-**4** with Bu_3SnCl forms **3a** and $InCl_3$. The stannylation of (*Z*)-**4** to **3a** may be caused by transmetalation with **1a** accompanied by the formation of **5**.

Such a transmetalation process as step 1 has been reported by Marshall and Baba.[9] We attempted to trap the allylindium intermediate **5** by hydrolysis; however, even when the $InCl_3$-promoted reaction of **1a** was carried out at −40 °C for 30 min (54% conversion, 38% yield of **2a**), only a small amount of the destannylated product **6** (6% yield) was formed due to rapid cyclization to (*Z*)-**4**. In connection with step 2, there are several reports on intermolecular allylindation of unactivated alkynes.[10] Quite recently, Salter et al. have introduced an intramolecular version of the allylindation.[11] Allylindation of alkynes is generally believed to proceed in a cis addition mode. Judging from the result shown in Scheme 4, the formation of (*E*)-**3a** is not due to the isomerization of (*Z*)-**4**. The trans adduct may be formed directly from (*Z*)-**4** in the stannylation step (step 4) or by the isomerization of (*Z*)-**3a**. However, the latter path is less likely because the treatment of (*Z*)-**3a** with a catalytic amount of $InCl_3$ (0.2 equiv) resulted in no isomerization.

To ascertain the validity of step 4, we carried out the $InCl_3$-catalyzed cyclization of **1a** in the presence of Me_3SnCl (Scheme 7). The reaction gave vinylstannane (*Z*)-**3a′**, bearing a trimethylstannyl group, along with **2a** and (*Z*)-**3a** although the total yield was not good. This observation supports the participation of Bu_3SnCl in the stannylation of (*Z*)-**4**. The exclusive formation of **2a** with stoichiometric use of $InCl_3$ indicates that the stannylation is reversible and an increased amount of $InCl_3$ suppresses the formation of **3a**. Indeed, treatment of **3a** with $InCl_3$ (1 equiv) followed by hydrolysis gave **2a** efficiently. In the case of catalytic use of $InCl_3$, rapid consumption of

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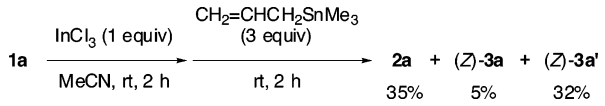
(11) Salter et al. have disclosed that allylindiums generated from In(0) and allyl bromides in aqueous solvent react with unactivated alkynes intramolecularly. The cyclization yields are up to 74%. Salter, M. M.; Sardo-Inffiri, S. *Synlett* **2002**, 2068.

SCHEME 8



$InCl_3$ by step 1 would induce the formation of **3a** in the reversible stannylation step.

We also examined the possibility of the other path of step 4 (stannylation of (*Z*)-**4** with **1a**) by the reaction of (*Z*)-**4** with allyltrimethylstannane. The $InCl_3$-promoted reaction of **1a** was first run to prepare (*Z*)-**4**. Treatment of the reaction mixture with allyltrimethylstannane provided **2a**, **3a**, and **3a′** (Scheme 8). The formation of **3a′** suggests that the stannylation of (*Z*)-**4** is due to direct transmetalation with **1a**. At present it is not clear which path (stannylation with Bu_3SnCl or **1a**) is operative in step 4.

Conclusion

We have demonstrated that an equimolar amount of $InCl_3$ efficiently promotes intramolecular allylation of alkynes with allylstannanes. Catalytic use of $InCl_3$ also realizes intramolecular addition of allylstannanes, in which allylstannylation products are formed as the major products. The catalytic cyclization followed by destannylation with HCl affords only allylation products in good to high yields. Similar to the palladium-catalyzed intramolecular allylstannylation,[2c] these cyclizations leading to allylation and allylstannylation products proceed in a cis addition mode. The reaction mechanism probably involves allylindation with an allylindium intermediate arising from the allylstannane moiety rather than its nucleophilic addition to an alkyne−$InCl_3$ complex. Although a similar cyclization involving intramolecular allylindation has been reported by Salter et al.,[11] the present reaction provides valuable information about the stereochemical aspect of intramolecular allylindation (cis or trans addition) and catalytic use of indium salts. We are now investigating the indium salt-catalyzed reaction of allylsilanes bearing an alkynyl group. The results will be reported in due course.

Experimental Section

$InCl_3$-Promoted Cyclization of Allylstannanes 1 (Typical Procedure). Under N_2 allylstannane **1a** (154 mg, 0.300 mmol) was added to a solution of $InCl_3$ (66.4 mg, 0.300 mmol) in CH_3CN (1.5 mL, freshly distilled from CaH_2) at room temperature. The mixture was stirred for 2 h and quenched with saturated aqueous $NaHCO_3$. The extract with *t*-BuOMe was dried over Na_2SO_4 and evaporated. The residue was diluted with *t*-BuOMe (5 mL), and DBU (0.3 mL) was added to the solution. After being stirred for 5 min, the resultant mixture was passed through a short silica gel column and evaporated. Purification of the crude product by silica gel column chromatography (hexane−AcOEt 30:1) gave methylenecyclopentane **2a** (64.6 mg, 0.288 mmol, 96%) along with (stannylmethylene)cyclopentane **3a** (6.2 mg, 0.012 mmol, 4%, *E*:*Z* = 15:85). Identification of **2a** was based on its spectral data previously reported.[4]

Dimethyl 3-Ethenyl-4-((*Z*)-tributylstannylmethylene)-cyclopentane-1,1-dicarboxylate ((*Z*)-3a). Bp 160 °C (0.40 Torr, bath temperature). IR (neat) 1738 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.72−0.97 (m, 15H), 1.19−1.57 (m, 12H), 2.10 (dd, *J* = 13.2, 7.7 Hz, 1H), 2.66 (ddd, *J* = 13.2, 7.9, 1.3 Hz, 1H),

2.95 (d, J = 16.8 Hz, 1H), 3.11−3.21 (m, 2H), 3.71 (s, 3H), 3.73 (s, 3H), 4.99−5.11 (m, 2H), 5.68 (ddd, J = 17.1, 10.0, 7.4 Hz, 1H), 5.81 (q, J = 1.7 Hz, $^2J_{Sn-H}$(coupling between ^{119}Sn and ^{1}H) = 56.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.8 ($CH_2 \times 3$), 13.7 ($CH_3 \times 3$), 27.3 ($CH_2 \times 3$), 29.1 ($CH_2 \times 3$), 41.1 (CH_2), 44.7 (CH_2), 48.2 (CH), 52.7 (CH_3), 52.7 (CH_3), 58.7 (C), 115.7 (CH_2), 122.3 (CH), 140.4 (CH), 158.8 (C), 172.1 (C × 2). Anal. Calcd for $C_{24}H_{42}O_4Sn$: C, 56.16; H, 8.25. Found: C, 56.21; H, 8.37.

Dimethyl 3-Ethenyl-4-((*E*)-tributylstannylmethylene)-cyclopentane-1,1-dicarboxylate ((*E*)-3a). The analytical sample was prepared by homolytic intramolecular allylstannylation of **1a**.[6] Bp 160 °C (0.40 Torr, bath temperature). IR (neat) 1738 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.78−1.03 (m, 15H), 1.23−1.58 (m, 12H), 2.02 (dd, J = 12.9, 11.0 Hz, 1H), 2.61 (ddd, J = 12.9, 7.7, 1.5 Hz, 1H), 2.90 (dt, J = 16.8, 2.3 Hz, 1H), 3.00 (d, J = 16.8 Hz, 1H), 3.11−3.23 (m, 1H), 3.73 (s, 3H), 3.74 (s, 3H), 5.04 (ddd, J = 16.6, 2.0, 0.8 Hz, 1H), 5.07 (ddd, J = 10.4, 2.0, 0.4 Hz, 1H), 5.61 (ddd, J = 16.6, 10.4, 8.2 Hz, 1H), 5.66 (q, J = 2.3 Hz, $^2J_{Sn-H}$ = 65.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 9.7 ($CH_2 \times 3$), 13.6 ($CH_3 \times 3$), 27.2 ($CH_2 \times 3$), 29.1 ($CH_2 \times 3$), 40.3 (CH_2), 42.3 (CH_2), 50.2 (CH), 52.7 ($CH_3 \times 2$), 58.6 (C), 115.9 (CH_2), 120.6 (CH), 139.7 (CH), 158.9 (C), 172.0 (C), 172.1 (C), MS m/z (rel intensity) 457 (M^+ − Bu, 27), 455 (M^+ − 2 − Bu, 21), 453 (M^+ − 4 − Bu, 12), 73 (100). Anal. Calcd for $C_{24}H_{42}O_4Sn$: C, 56.16; H, 8.25. Found: C, 55.97; H, 8.23. The stereochemical assignment is based on NOE experiments in C_6D_6. Irradiation of the proton α to the stannyl group made a 7% enhancement of the internal vinyl proton.

Acknowledgment. This work was partly supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Government of Japan.

Supporting Information Available: Experimental procedures for the synthesis of **1** and spectral characterization data for **1**−**3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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