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Trans-Hydrometalation of Alkynes by a Combination of $InCl_3$ and DIBAL-H: One-Pot Access to Functionalized (*Z*)-Alkenes

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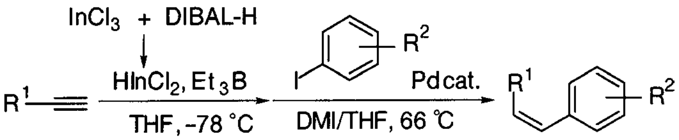
ABSTRACT



Triethylborane-induced hydrometalation of alkynes proceeds in an anti manner to afford the corresponding (*Z*)-alkenylmetal compounds stereoselectively, where dichloroindium hydride would play a key role. A variety of functional groups including hydroxy, carbonyl, and carboxy groups were tolerant under the reaction conditions. Following iodolysis and cross-coupling reaction of the (*Z*)-alkenylmetal species show the usefulness of this strategy.

Alkenylmetals are versatile reagents in organic synthesis. Hydrometalation of alkyne is a promising way to prepare an alkenylmetal. However, hydrometalation usually affords (*E*)-alkenylmetal reagents. Hydroboration of alkyne always proceeds in a syn fashion to provide (*E*)-alkenylborane. Preparation of a (*Z*)-alkenylborane reagent, starting from alkyne, usually requires multistep synthesis.[1] Moreover, protection of hydroxy and carboxy groups is necessary in conducting hydroboration. Hydrostannylation of alkyne[2] is also an efficient method to prepare a vinylic metal. However, both palladium-catalyzed[3] and radical[4] hydrostannylations afford (*E*)-alkenylstannanes as a sole or major product, although the reactions are attractive as a result of compatibility with a variety of functional groups. Transition metal-catalyzed hydrosilylation also mainly yields (*E*)-alkenylsilane.[5] Very recently, hydrometalation reactions affording (*Z*)-alkenylmetals were reported.[6] However, operationally simple and mild procedures for tailored preparation of (*Z*)-alkenylmetal species from alkyne are very limited.

Herein we report a novel access to a (*Z*)-alkenylmetal reagent by a combination of indium trichloride and diisobu-

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[1] (a) Brown, H. C.; Imai, T. *Organometallics* **1984**, *3*, 1392−1395. (b) Negishi, E.; Williams, R. M.; Lew, G.; Yoshida, T. *J. Organomet. Chem.* **1975**, *92*, C4−C6. (c) Campbell, J. B., Jr.; Molander, G. A. *J. Organomet. Chem.* **1978**, *156*, 71−79. (d) Srebnik, M.; Bhat, N. G.; Brown, H. C. *Tetrahedron Lett.* **1988**, *29*, 2635−2638. (e) Deloux, L.; Srebnik, M. *J. Org. Chem.* **1994**, *59*, 6871−6873. (f) Takahashi, K.; Takagi, J.; Ishiyama, T.; Miyaura, N. *Chem. Lett.* **2000**, 126−127.

[2] (a) Davies A. G. *Organotin Chemistry*; VCH: Weinheim, 1997, Chapters 3.4 and 6.3. (b) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524.

[3] Ichinose, Y.; Oda, H.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3468−3470.

[4] (a) Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547−2548. (b) Corey, E.; Ulrich, P.; Fitzpatrick, J. M. *J. Am. Chem. Soc.* **1976**, *98*, 222.

[5] (a) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 8, p 763. (b) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley: New York, 1989, p 1479.

[6] Rhodium-catalyzed hydroboration, (a) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990−4991. Radical hydrostannylation, (b) Nakamura, E.; Machii, D.; Inubushi, T. *J. Am. Chem. Soc.* **1989**, *111*, 6849−6850. Rhodium-catalyzed hydrosilylation, (c) Mori, A.; Takahisa, E.; Kajiro, H.; Hirabayashi, K.; Nishihara, Y.; Hiyama, T. *Chem. Lett.* **1998**, 443−444. Ruthenium-catalyzed hydrosilylation, (d) Na, Y.; Chang, S. *Org. Lett.* **2000**, *2*, 1887−1889. (e) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2001**, *123*, 12726−12727. Lewis acid-mediated synthesis of (*Z*)-alkenylsilanes and -stannanes, (f) Asao, N.; Liu, J.-X.; Sudo, T.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 4568−4571. (g) Sudo, T.; Asao, N.; Gevorgyan, V.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2494−2499. (h) Asao, N.; Yamamoto, Y. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1071−1087.

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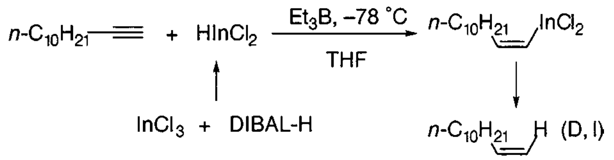
tylaluminum hydride (DIBAL-H). Treatment of $InCl_3$ (1.35 mmol) in THF with DIBAL-H (1.30 mmol) at 0 °C yielded dichloroindium hydride ($HInCl_2$).[7] 1-Dodecyne (1.0 mmol) and a catalytic amount of triethylborane (0.20 mmol) as a radical initiator[8] were added to the solution at −78 °C. The resulting solution was stirred for 2.5 h at the same temperature. Acidic workup followed by silica gel column purification provided 1-dodecene quantitatively (Scheme 1). Without triethylborane, 1-dodecene was produced in only 34% yield.[9] Furthermore, 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) inhibited the reaction (0.2 equiv, 48%; 0.4 equiv, 10%). These observations suggest that the reaction would involve a radical mechanism. The reduction of 1-dodecyne proceeded in an anti fashion to yield *(Z)*-1-dodecenylmetal. Quenching with DCl yielded *(Z)*-1-deuterio-1-dodecene exclusively (96% D, *E/Z* < 1/99). Iodolysis of the reaction mixture also afforded the corresponding *(Z)*-isomer selectively in 92% yield.[10]

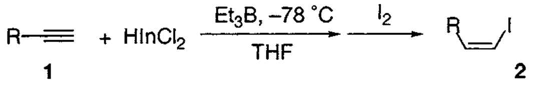
Scheme 1



We assume that the reaction would proceed via a radical addition of indium hydride reagent across a carbon−carbon triple bond.[11] The selectivity is mostly due to the low reactivity of dichloroindium radical toward *(Z)*-alkenylindium dichloride that is initially formed.[12] If the further addition occurs, diindium species is formed, which leads to isomerization of the *(Z)*-alkenylindium compound into its *(E)*-form via an addition−elimination sequence.

A variety of alkynes were subjected to the hydroindation reaction and following iodolysis (Table 1). Noteworthy is the fact that many functional groups including hydroxy, carbonyl, and carboxy groups did not interfere with the reaction (entries 3−7). The hydroindation proceeded much faster at the alkynyl moiety than at the alkenyl group to yield iodo diene selectively starting from enyne (entry 8). Addition to phenylacetylene yielded a mixture of *E/Z* isomers with slightly lower selectivity (7/93, entry 9). No desired product was obtained in the reaction of trimethylsilylacetylene.

Table 1. Triethylborane-Induced Hydroindation of Alkynes Followed by Iodolysis

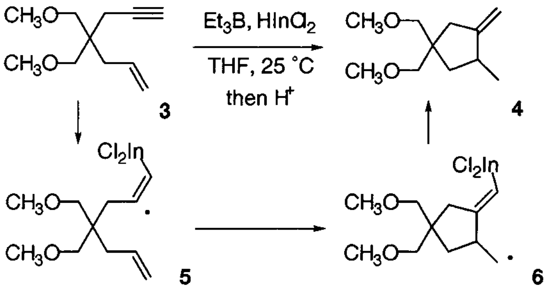


entry	1	R	2	yield/%	*E/Z*[a]
1	**1a**	$PhCH_2O(CH_2)_3$	**2a**	79	1/99
2[b]	**1a**	$PhCH_2O(CH_2)_3$	**2a**	91	2/98
3	**1b**	$C_2H_5O_2C(CH_2)_6$	**2b**	99	<1/99
4	**1c**	$HO(CH_2)_4$	**2c**	78	<1/99
5	**1d**	$HOCH_2$	**2d**	57	<1/99
6	**1e**	n-$C_4H_9CO(CH_2)_6$	**2e**	73	<1/99
7	**1f**	$HO_2C(CH_2)_6$	**2f**	98	3/97
8	**1g**	$CH_2{=}CH(CH_2)_8$	**2g**	74	1/99
9[b]	**1h**	Ph	**2h**	99	7/93

[a] Determined by ^{1}H NMR. [b] The reaction was performed at −40 °C.

Interestingly, hydroindation of enyne **3** at 25 °C afforded **4** in 30% yield (Scheme 2). The formation of **4** was highly suggestive of a radical mechanism for this hydroindation reaction. Namely, radical addition of indium-centered radical to the alkyne moiety of **3** would produce vinyl radical **5**. Following 5-exo ring closure mostly constructs methylenecyclopentane skeleton.

Scheme 2



Increasing attention has been paid to the cross-coupling reaction of organic halides with organoindiums.[13] However,

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(7) ^{1}H NMR measurements revealed the formation of $HInCl_2$. The hydride attached to aluminum of DIBAL-H appeared at δ 3.8 ppm (broad) in THF-d_8. A new broad signal (δ 6.8 ppm) was observed after treatment of $InCl_3$ with DIBAL-H. Baba reported that hydride of $HInCl_2$, prepared from $InCl_3$ and n-Bu_3SnH, appeared at δ 6.5 ppm. See, Miyai, T.; Inoue, K.; Yasuda, M.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1998**, *39*, 1929−1932. However, Baba's $HInCl_2$ did not add to alkynes. The reason for the different reactivity is not clear. Diisobutylaluminum chloride might coordinate to $HInCl_2$, thereby changing the reactivity.

(8) (a) Oshima, K.; Utimoto, K. *J. Synth. Org. Chem. Jpn.* **1989**, *47*, 40−52. (b) Yorimitsu, H.; Oshima, K. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001, Chapter 1.2. (c) Ollivier, C.; Renaud, P. *Chem. Rev.* **2001**, *101*, 3415−3434.

(9) Indium hydride spontaneously induces radical reaction. See ref 11. Moreover, some organoaluminum compounds can initiate a radical reaction. See, Chakraborty, A.; Marek, I. *Chem. Commun.* **1999**, 2375−2376.

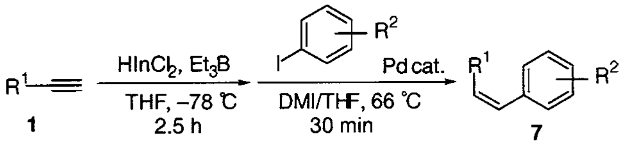
(10) The hydroindation reaction at 0 °C, −10 °C, and −40 °C yielded a mixture of stereoisomers (*E/Z* = 20/80, 6/94, and 3/97, respectively) after iodolysis.

(11) Reduction of organic halides via a radical process was recently reported. Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 906−907.

(12) (a) Ichinose, Y.; Nozaki, K.; Wakamatsu, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1987**, *28*, 3709−3712. (b) Nozaki, K.; Ichinose, Y.; Wakamatsu, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2268−2272. (c) Taniguchi, M.; Nozaki, K.; Miura, K.; Wakamatsu, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 349−354. (d) Chatgilialoglu, C.; Ballestri, M.; Ferreri, C.; Vecchi, D. *J. Org. Chem.* **1995**, *60*, 3826−3831.

(13) (a) Pérez, I.; Pérez Sestelo, J.; Sarandeses, L. A. *Org. Lett.* **1999**, *1*, 1267−1269. (b) Gelman, D.; Schumann, H.; Blum, J. *Tetrahedron Lett.* **2000**, *41*, 7555−7558. (c) Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 4095−4101. (d) Hirashita, T.; Yamamura, H.; Kawai, M.; Araki, S. *Chem. Commun.* **2001**, 387−388. (e) Pérez, I.; Pérez Sestelo, J.; Sarandeses,

Table 2. One-Pot Hydroindation/Coupling Reaction for Synthesis of *(Z)*-Alkenes



entry	1	R^1	R^2	7	yield/%	E/Z[a]
1	**1i**	n-C_6H_{13}	H	**7a**	94	5/95
2	**1i**	n-C_6H_{13}	2-NO_2	**7b**	98	5/95
3	**1i**	n-C_6H_{13}	4-NO_2	**7c**	99	5/95
4	**1i**	n-C_6H_{13}	2-CO_2-n-C_4H_9	**7d**	91	5/95
5	**1i**	n-C_6H_{13}	3-OCH_3	**7e**	89	5/95[b]
6	**1i**	n-C_6H_{13}	2-iodopyridine	**7f**	75	3/97[b]
7	**1i**	n-C_6H_{13}	3-OH	**7g**	46	1/99
8	**1b**	$C_2H_5O_2C(CH_2)_6$	H	**7h**	92	3/97
9	**1b**	$C_2H_5O_2C(CH_2)_6$	4-NO_2	**7i**	99	5/95
10	**1j**	$TBSO(CH_2)_3$[c]	H	**7j**	70	2/98
11	**1j**	$TBSO(CH_2)_3$[c]	4-NO_2	**7k**	90	5/95
12	**1c**	$HO(CH_2)_4$	4-NO_2	**7l**	99	2/98
13	**1c**	$HO(CH_2)_4$	3-OCH_3	**7m**	99	3/97[b]

[a] Determined by ^{1}H NMR. [b] Hydroindation was performed at −40 °C. [c] TBS = t-$BuMe_2Si$

most organoindium reagents used were prepared from indium trichloride and the corresponding organolithium or -magnesium reagents. With this protocol to prepare alkenylindium compounds in hand, we investigated cross-coupling reaction of aryl halides with alkenylindiums in one pot. After optimization of the reaction conditions, a DMI (1,3-dimethylimidazolidin-2-one)/THF mixed solvent system proved to be effective to obtain coupling products. DMI (3 mL) was added to a THF solution of the *(Z)*-1-octenylindium reagent prepared as aforementioned. Iodobenzene (1.0 mmol) and palladium−trifurylphosphine complex (0.5 mol %)[14] were then added. Heating the mixture at 66 °C for 30 min afforded β-hexylstyrene (**7a**, E/Z = 5/95) in 94% yield (Table 2). Various combinations of alkynes and aryl iodides were examined as summarized in Table 2. High stereoselectivity was accomplished in each case. Several functional groups were compatible in this one-pot reaction. In particular, coupling of 5-hexyn-1-ol with 3-iodoanisole represents the usefulness of the present strategy (entry 13).

In summary, triethylborane-induced hydroindation of alkyne proceeds in an anti manner to afford the corresponding *(Z)*-alkenylindium species. This method allows us to employ unprotected alkyne as a *(Z)*-alkenylmetal precursor and to synthesize functionalized *(Z)*-alkenyl iodide and *(Z)*-alkene in one pot.

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Supporting Information Available: Detailed experimental procedures and characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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L. A. *J. Am. Chem. Soc.* **2001**, *123*, 4155−4160. (f) Lee, P. H.; Sung, S.; Lee, K. *Org. Lett.* **2001**, *3*, 3201−3204. (g) Takami, K.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Org. Lett.* **2001**, *3*, 1997−1999.

(14) The palladium catalyst was prepared from $Pd_2(dba)_3 \cdot CHCl_3$ (0.0025 mmol) and $P(2\text{-furyl})_3$ (0.015 mmol) in THF (1.0 mL) in another flask.