

Indium Chemistry ~ from Dr. Baba's works ~



Akio Baba was born in Kochi, Japan, in 1949. He received his B.S. (1971) and Ph.D. degrees (1976) from Osaka University under the guidance of Professor Toshio Agawa. He worked for Mitsubishi Kasei Industries (now Mitsubishi Chemicals, Inc.) from 1976 to 1981. He became an Assistant Professor at Osaka University in 1981 and Associate Professor in 1987, working with Professor Haruo Matsuda. He became Full Professor in 1995. He is now also working as one of the project leaders at the Handai Frontier Research Center.

Baba et al. *The Chemical Record*. **2005**, 5, 323.

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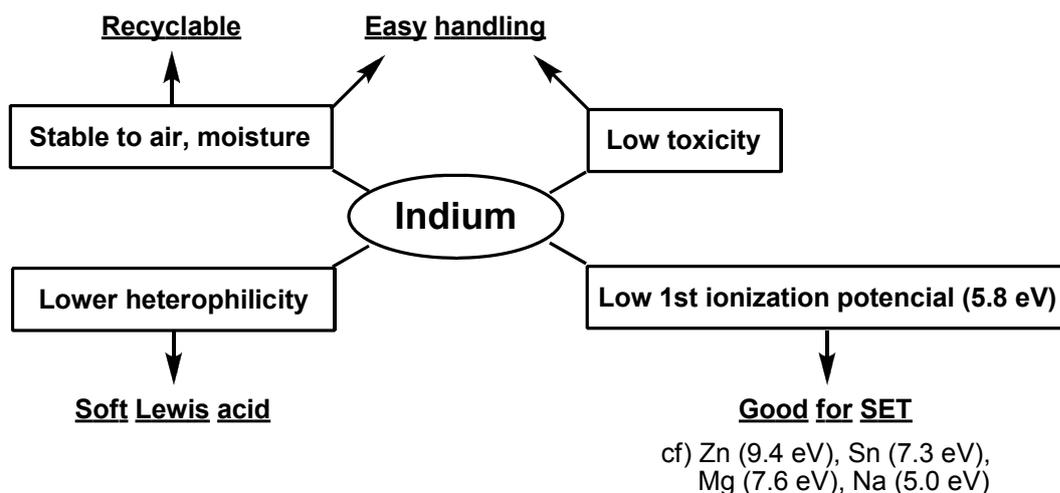
0. Introduction

0-1. What is indium?

Cintas, *SYNLETT*, **1995**, 1087.

Reddy et al. *Eur. J. Chem.* **2010**, 591.

| | | |
|----|----|----|
| 12 | 13 | 14 |
| | B | C |
| | Al | Si |
| Zn | Ga | Ge |
| Cd | In | Sn |
| Hg | Tl | Pb |



Indium has these good points. But the prices of indium species is not cheap.

cf) $\text{In}(\text{OH})_3$: 12900 Yen/10g, Wako.

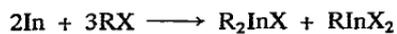
InCl_3 : 13300 Yen/10g, Ald.

InBr_3 : 17400 Yen/10g, Ald.

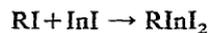
$\text{In}(\text{OTf})_3$: 14900 Yen/5g, Ald.

0-2. Primary reactions

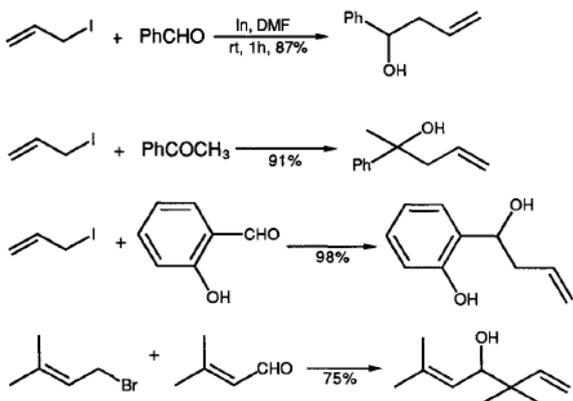
Gynane et al. *J. Org. Chem.* **1972**, *40*, C9.



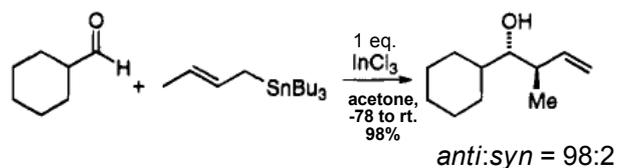
Gynane et al. *J. Org. Chem.* **1972**, *43*, 257.



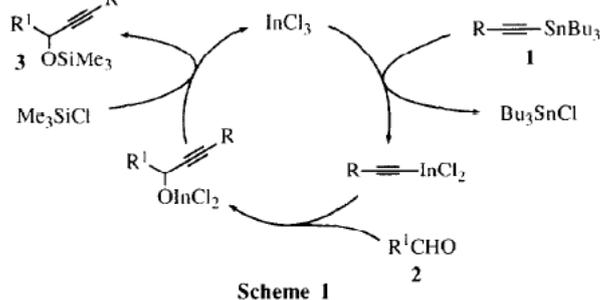
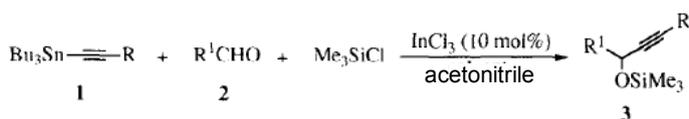
Butsugan et al., *JOC.*, **1988**, *53*, 1831.



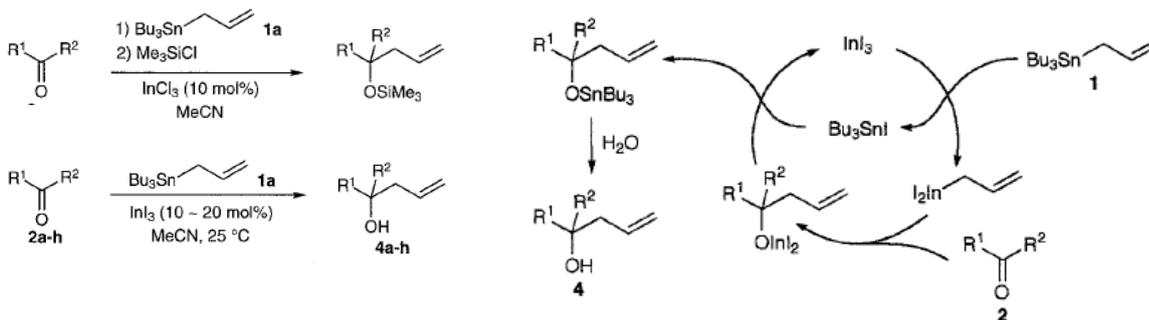
Marshall et al. *JOC.* **1995**, *60*, 1920.



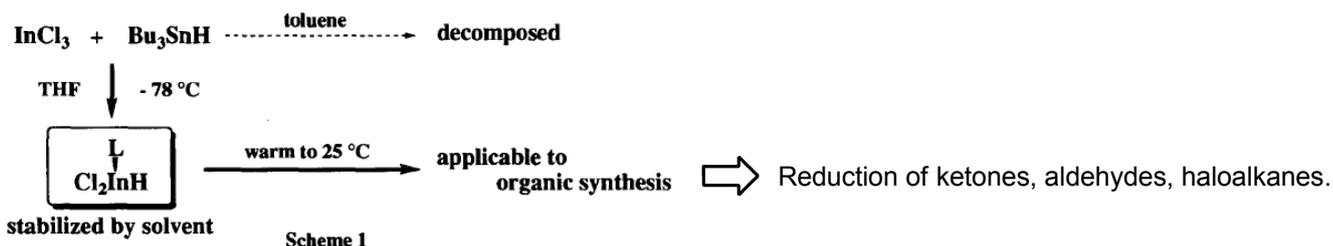
Baba et al. *TL.* **1995**, *36*, 9497.



Baba et al. *SYNLETT*, **1997**, 699.



Baba et al. *TL*, **1998**, *39*, 1929.



1. Alkyl indium

1-1. Cyclopropylmethylenylation

Cyclopropylmethylenylation of α -iodoketones

Baba et al. *Organometallics*, 2009, 28, 132.

Table 2. Reaction of 1 with α -Iodocarbonyl Compounds 2^a

| entry | iodocarbonyl | yield/ % | (under N ₂) ^c |
|-------------------|---------------------------------------------------|--------------|--------------------------------------|
| 1 | PhO-CO-CH ₂ -I 2a | 3a 79 | (64) |
| 8 | EtO-CO-CH ₂ -I 2h | 3h 65 | (47) |
| 9 | 2i | 3i 80 | (98) |
| 10 | PhO-CO-CH ₂ -I 2j | 3j <5 | (<5) |
| 11 ^{b,d} | | 15 | (30) |
| 12 ^{b,d} | Et ₂ N-CO-CH ₂ -I 2k | 3k 54 | (62) |
| 13 | Ph-CO-CH ₂ -I 2l | 3l 71 | (67) |

^a All entries were carried out at room temperature in solvent (1 mL) with 1.0 mmol of 1, 1.0 mmol of 2, and 0.5 mmol of InBr₃. Tin compound 1 was added to the mixture of 2 and InBr₃ in toluene. ^b Iodocarbonyl 2 was added to the mixture of 1 and InBr₃ in toluene that had been previously stirred at room temperature for 30 min. ^c Reactions were carried out on the bench using a nitrogen-flowing flask. ^d Reactions were carried out at 100 °C.

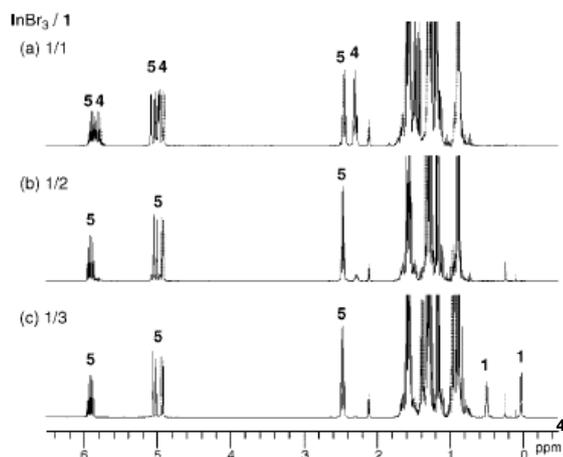
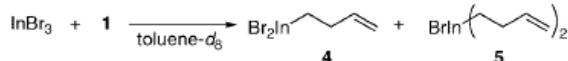


Figure 2. ¹H NMR spectra of the reaction mixtures of InBr₃ and 1 with (a) 1/1, (b) 1/2, and (c) 1/3 ratios in toluene-*d*₆.

Two alkyl indium species were observed.

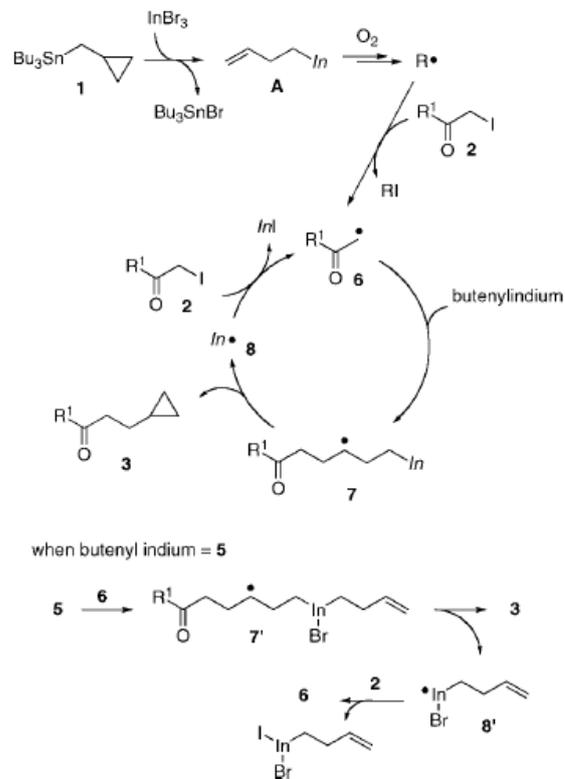
Table 1. Optimization of Reaction Conditions^d

| entry | additive | solvent | yield, % |
|-------|-----------------------------------|---------|-----------------|
| 1 | InBr ₃ | toluene | 73 |
| 10 | GaCl ₃ | toluene | 71 |
| 11 | AlCl ₃ | toluene | <5 ^e |
| 12 | BF ₃ ·OEt ₂ | toluene | 9 |
| 14 | TiCl ₄ | toluene | 13 |
| 18 | InBr ₃ ^d | toluene | <5 |

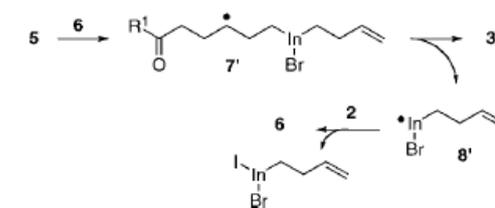
^d Addition of galvinoxyl (0.1 mmol).

Galvinoxyl (radical scavenger) inhibited the reaction.
-> This reaction is radicalic.

Scheme 2. Plausible Reaction Mechanism



when butenyl indium = 5



Which indium is the active species?

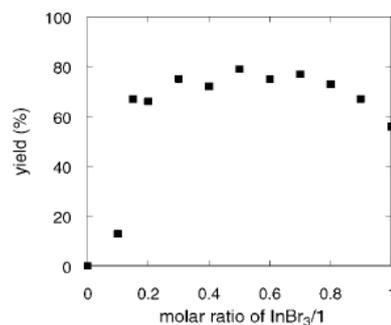


Figure 1. Relationship between amount of InBr₃ and the yield of 3a in the reaction of 1 (1 mmol) with 2a (1 mmol) at rt for 4.5 h.

1 eq. InBr₃ was not effective.

-> The active species is dibutenylindium 5.

Scheme 3. Isolation of Butenylindium Species

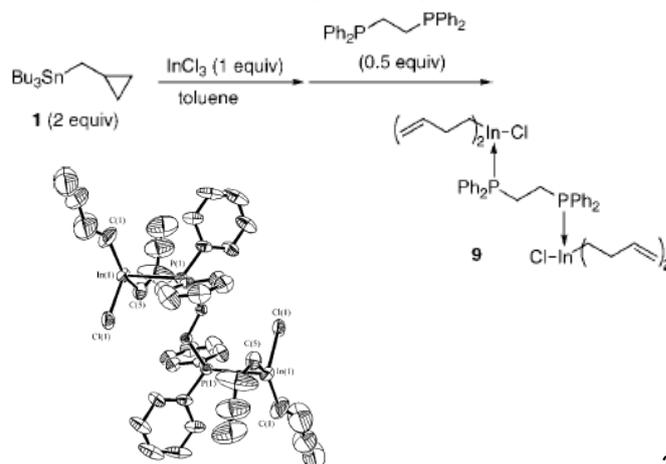
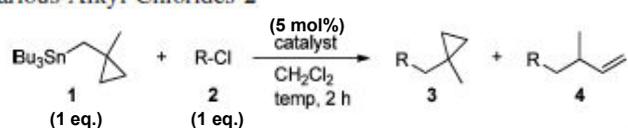
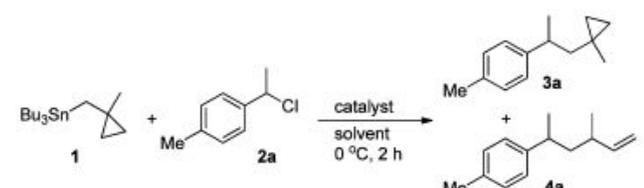


Table 2. GaCl₃ or InBr₃-Catalyzed Cyclopropylmethylation of Various Alkyl Chlorides 2^a


| entry | 2 | temp (°C) | product | catalyst | yield (%) ^b | |
|-----------------|---|-----------|---------|-------------------|------------------------|-------|
| | | | | | 3 | 4 |
| 1 | | 0 | | GaCl ₃ | 72 | 16 |
| 2 | | 0 | | InBr ₃ | 79 | 20 |
| 5 | | rt | | GaCl ₃ | 59 | 21 |
| 6 | | rt | | InBr ₃ | trace | trace |
| 13 | | rt | | GaCl ₃ | 45 | 12 |
| 14 | | rt | | InBr ₃ | 15 | 5 |
| 15 ^c | | 80 | | GaCl ₃ | 36 | 46 |
| 16 ^c | | 80 | | InBr ₃ | 70 | 14 |

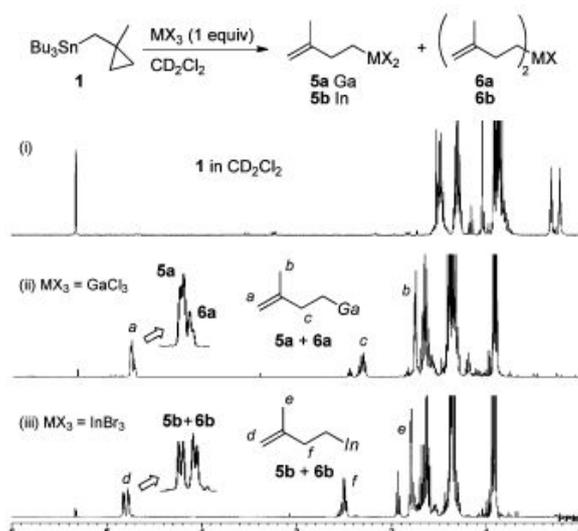
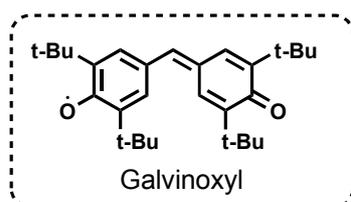
^a All entries were carried out with 1.0 mmol of **1**, 1.0 mmol of **2a**, and 0.05 mmol of catalyst. ^b Determined by ¹H NMR. ^c 1.5 mmol of **1** and 0.75 mmol of catalyst were used. ^d 0.5 mmol of catalyst was used.

Table 1. Reaction of 1-Chloro-1-(4-methylphenyl)ethane (**2a**) with Cyclopropylmethylstannane **1**^a


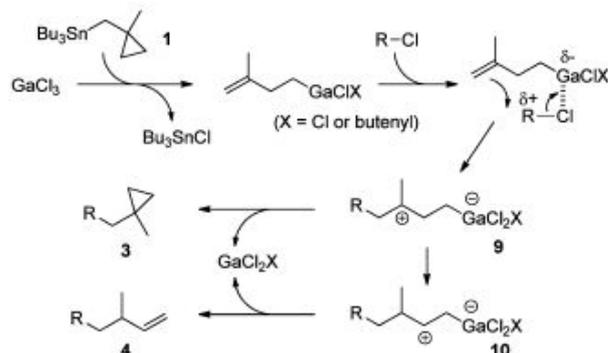
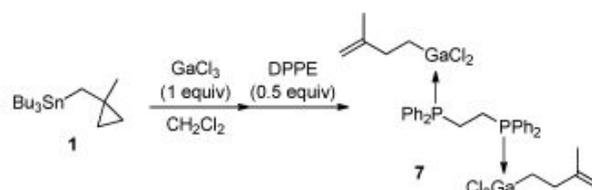
| entry | catalyst | solvent | yield (%) ^b | |
|-----------------|-------------------|---------------------------------|------------------------|----|
| | | | 3a | 4a |
| 2 | InBr ₃ | CH ₂ Cl ₂ | 81 | 19 |
| 8 | GaCl ₃ | CH ₂ Cl ₂ | 57 | 14 |
| 10 ^c | InBr ₃ | CH ₂ Cl ₂ | 55 | 15 |
| 11 ^d | InBr ₃ | CH ₂ Cl ₂ | 73 | 20 |
| 12 ^c | GaCl ₃ | CH ₂ Cl ₂ | 45 | 13 |
| 13 ^d | GaCl ₃ | CH ₂ Cl ₂ | 71 | 21 |

^a All entries were carried out at 0 °C for 2 h using 1.0 mmol of **1**, 1.0 mmol of **2a**, and 0.05 mmol of catalyst. ^b Determined by ¹H NMR. ^c TEMPO (0.05 mmol) was added. ^d Galvinoxyl (0.05 mmol) was added.

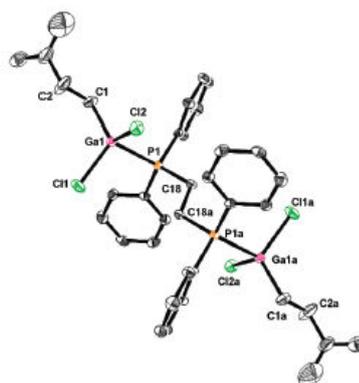
Galvinoxyl did not inhibit the reaction.
->This reaction is not radical; ionic.
Author said this is the 1st report about ionic reaction of organic halides with organoindium.

**Figure 1.** ¹H NMR spectra of (i) **1**, (ii) the mixture of GaCl₃ and **1**, and (iii) the mixture of InBr₃ and **1** in CD₂Cl₂.

Also two species were observed.

Scheme 3. Plausible Reaction Mechanism**Scheme 2. Complexation and Isolation of the Butenylgallium Species**

This structure is different from the structure in page 3.

**Figure 2.** X-ray structure of **7** (all hydrogens are omitted for clarity).

1-2. Diene utilized alkylation

Alkylation of ketones / imene

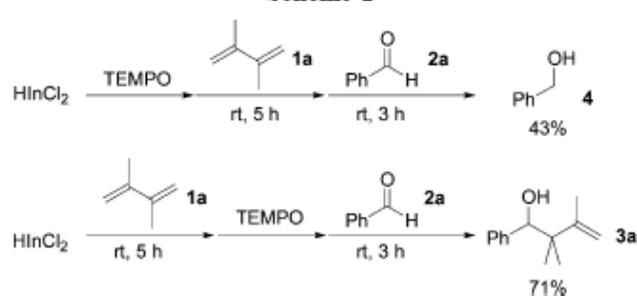
Baba et al. *Org. Lett.* **2006**, *8*, 4553.

Table 3. Reaction with 1,3-Butadiene and Isoprene^a

| entry | diene | electrophile | product (<i>syn</i> : <i>anti</i>) | yield (%) |
|-------|-------|--------------|--------------------------------------|-----------|
| 1 | | PhCHO | | 85 |
| 4 | | Ph-CH2-CHO | | 69 |
| 5 | | Ph-CH=NPh | | 52 |
| 7 | | Ph-CHO | | 70 |
| 8 | | Ph-CH=NPh | | 90 |
| 9 | | Ph-CH2-CHO | | 88 |
| 10 | | Ph-CHO | | 28 |
| 11 | | Ph-CH=NPh | | 42 |

^a Diene (4 mmol), HInCl₂ (2 mmol), electrophile (1 mmol), THF solvent (2 mL). ^b A excess amount of 1,3-butadiene was used. ^c Byproduct 3s was

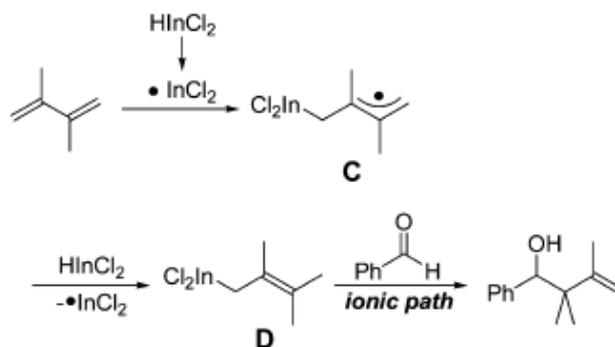
Scheme 1^a



^a HInCl₂/TEMPO/diene/aldehyde = 2/0.1/4/1 (equiv), THF solvent.

When TEMPO was added before diene, only reduction of aldehyde was observed. In contrast, when TEMPO was added after diene, alkylation proceeded.

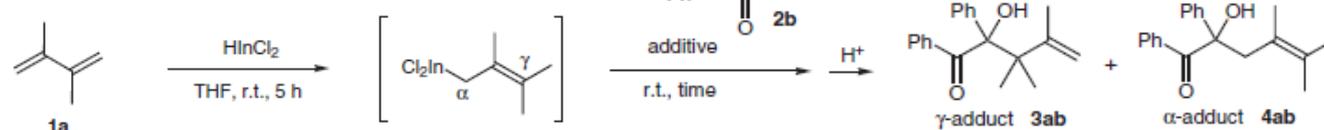
-> Generation of alkylindium is radicalic path, and alkylation step is ionic path.



Plausible mechanism

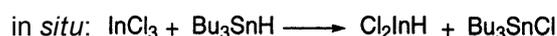
Baba et al. *SYNLETT*, **2008**, 1407.

Table 1 Allylation of Benzil by 2,3-Dimethyl-1,3-butadiene and Effect of Additives^a



| Entry | Time | Additive | Yield (%) | |
|-------|-------|---------------------------|------------------|------------------|
| | | | 3ab (γ) | 4ab (α) |
| 1 | 14 h | - | 0 | 89 |
| 2 | 3 min | - | 26 | 14 |
| 3 | 1 min | - | 14 | 0 |
| 4 | 17 h | MeOH (2 mmol) | 29 | 49 |
| 5 | 17 h | H ₂ O (2 mmol) | 85 | 8 |

^a HInCl₂ was generated by InCl₃/Bu₃SnH system. Allylic indium was generated from the reaction of diene 1a (4 mmol) with HInCl₂ (2 mmol) in THF (2 mL) at r.t. for 5 h. Benzil (2b, 1 mmol) was used.

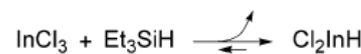


Baba et al. *TL*, **1998**, *39*, 1929.

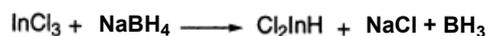
Baba et al. *TL*, **2001**, *42*, 4661.

Baba et al. *Org. Lett.* **2006**, *8*, 4553.

Other method preparing HInCl₂: Et₃SiCl



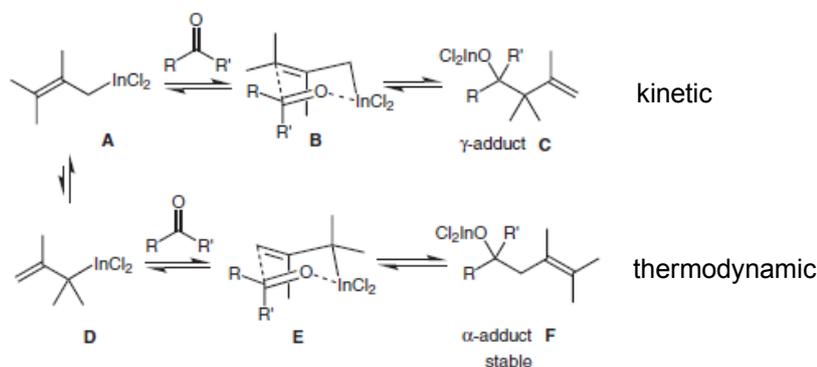
Baba et al. *Org. Lett.* **2004**, *6*, 4981.



Baba et al. *JACS*. **2002**, *124*, 906.



Oshima et al. *Org. Lett.* **2002**, *4*, 2993.



Author proposed cyclic TS.
But according to the results of Table 3
in page 3, I think cyclic TS and acyclic
TS are competitive.

Scheme 4 A plausible mechanism of α -allylation

The additive effect is not clear. Does quenching indium alkoxyide of **C** prevent the retroreaction? When author tried the reaction of acetophenone with **1a** in the presence of Ph_3P or HMPA, only a small amount of α -adduct was obtained at r.t.. See Entry 5 of Table 2. In absence of Lewis base, only γ -adduct was observed at r.t..

Table 2 Regioselective Allylation Using 2,3-Dimethyl-1,3-butadiene^a

| Entry | Carbonyl compound | Conditions | Yield (%) | | | |
|----------------|-------------------|-----------------------------|-----------|-----|-----|----|
| | | | 3 | | 4 | |
| 1 | | r.t., 3 h | 3ac | >99 | 4ac | 0 |
| 2 | | r.t., 19 h then reflux, 3 h | 3ac | 0 | 4ac | 90 |
| 3 ^b | | r.t., 14 h | 3ad | 90 | 4ad | 0 |
| 4 | | r.t., 12 h | 3ad | 7 | 4ad | 71 |
| 5 ^c | | r.t., 16 h | 3ae | 50 | 4ae | 0 |
| 6 | | r.t., 3 h then reflux, 20 h | 3ae | 11 | 4ae | 66 |
| 11 | | r.t., 3 h | 3ah | 68 | 4ah | 0 |
| 12 | | r.t., 3 h then reflux, 3 h | 3ah | 0 | 4ah | 12 |
| 13 | | r.t., 16 h | 3ai | 28 | 4ai | 0 |
| 14 | | r.t., 3 h then reflux, 13 h | 3ai | 0 | 4ai | 46 |
| 21 | | r.t., 3 h | 3al | 88 | 4al | 0 |
| 22 | | r.t., 3 h then reflux, 48 h | 3al | 66 | 4al | 0 |

^a HInCl_2 was generated by $\text{InCl}_3\text{-Bu}_3\text{SnH}$ system. Allylic indium was generated from the reaction of diene **1a** (4 mmol) with HInCl_2 (2 mmol) in THF (2 mL) at r.t. for 5 h. Carbonyl compound (1 mmol) was used.

^b H_2O (2 mmol) was added before addition of ketone **2d**.

^c HInCl_2 (3 mmol) and THF (3 mL) were used.

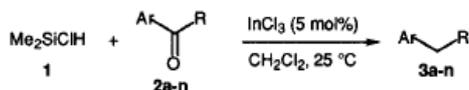
^d HInCl_2 (3 mmol) and THF (3 mL) were used. H_2O (3 mmol) was added before addition of ketone **2g**.

2. Indium as a Lewis acid

2-1. Deoxygenative functionalization

Reduction of aryl ketones

Baba et al. *SYNLETT*, **1999**, 182.

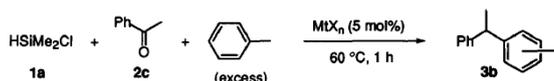


R = alkyl, haloalkyl, phenyl
Ar = phenyl, *p*-MeO phenyl, *p*-Cl phenyl, naphthanyl

Deoxygenative arylation of ketones

Baba et al. *Tetrahedron*, **1999**, 55, 1017.

Table 1. Effect of Catalyst for Reductive Friedel-Crafts Alkylation^a



| Entry | MX _n | Yield /% (o:m:p) ^b | Entry | MX _n | Yield /% ^b |
|-------|--------------------------------|-------------------------------|-----------------|-----------------------------------|-----------------------|
| 1 | InCl ₃ | 99 (15:4:81) | 6 | ZnCl ₂ | 0 |
| 2 | In ₂ O ₃ | 95 (13:4:83) | 7 | TiCl ₄ | 0 ^c |
| 3 | In(OTf) ₃ | 98 (13:7:80) | 8 | SnCl ₄ | 0 |
| 4 | InBr ₃ | 84 (18:6:76) | 9 ^d | BF ₃ ·OEt ₂ | 0 |
| 5 | InI ₃ | 93 (15:2:83) | 10 ^d | AlCl ₃ | 4 ^e |
| | | | 11 ^d | CF ₃ SO ₃ H | 0 ^f |

^a Reaction conditions: MX_n, 0.1 mmol; chlorodimethylsilane, 2.4 mmol; acetophenone, 2 mmol; solvent, 10 mL; N₂ atmosphere. ^b Yields and selectivities were determined by GLC and NMR. ^c 11% of *sec*-phenethyl chloride was obtained. ^d 10 mol% of catalyst was used. ^e 45% of *sec*-phenethyl chloride was obtained. ^f 33% of *sec*-phenethyl chloride was obtained.

Table 2. InCl₃-Catalyzed Reductive Friedel-Crafts Alkylation of Various Carbonyls.

$$\text{Me}_2\text{SiClH} \quad \mathbf{1a} + \text{R}^1\text{-C(=O)-R}^2 \quad \mathbf{2a-k} + \text{ArH (excess)} \xrightarrow{\text{InCl}_3 (5 \text{ mol}\%)} \text{R}^1\text{-C(Ar)(R}^2\text{)-H} \quad \mathbf{3a-k}$$

| Entry | R ¹ in 2 | R ² in 2 | ArH | Time /h | Temp /°C | Yield of 3 /% o:m:p ^a |
|-------|----------------------------------------------|---------------------|------|---------|----------|----------------------------------|
| 1 | 2a: Ph | H | PhH | 14 | 25 | 3a: 79 |
| 2b | 2b: <i>n</i> -C ₅ H ₁₁ | H | PhH | 1 | 25 | 3b: 0 |
| 3 | 2c: Ph | Me | PhMe | 1 | 60 | 3c: 99 15:4:81 |
| 10 | 2j: -(CH ₂) ₅ - | Me | PhMe | 3 | 110 | 3j: 92 38:1:61 |
| 11 | 2k: Me | Me | PhMe | 4 | 110 | 3k: 42 |

^a Yields and selectivities were determined by ¹H, ¹³C NMR or GLC. ^b Di-*n*-hexyl ether was obtained quantitatively.

Deoxygenative allylation of aryl ketones

Baba et al. *TL*, **2000**, 41, 2425.

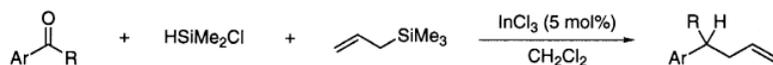
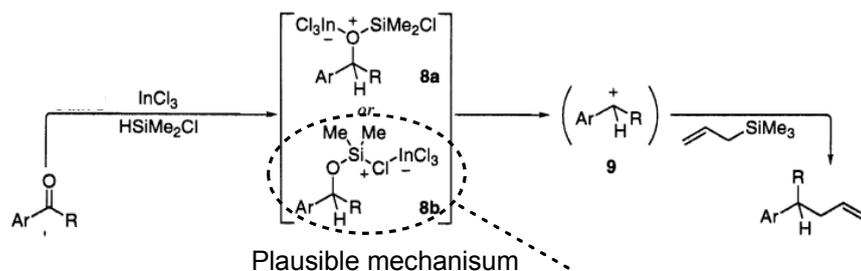


Table 2

| Entry | Ar | R | Conditions | Product | Yield/ % ^a |
|-------|----------------------------------------------------------|------------------------------------|----------------------|---------|-----------------------|
| 1 | Ph | Et | rt, 2 h | 2 | 67 |
| 2 | Ph | Ph | rt, 2 h | 3 | 99 |
| 3 | Ph | CH ₂ CH ₂ Cl | rt, 1 h → 60 °C, 3 h | 4 | 70 |
| 4 | <i>p</i> -Cl-C ₆ H ₄ | Me | rt, 2 h | 5 | 84 |
| 5 | <i>p</i> -EtOCO-C ₆ H ₄ | Me | rt, 1 h → 60 °C, 3 h | 6 | 44 |
| 6 | <i>p</i> -O ₂ N-C ₆ H ₄ | Ph | rt, 1 h → 60 °C, 2 h | 7 | 75 |

^a Yields were determined by GLC.



I think this intermediate is active species.
(See next page.)

The combination of InCl₃ and chlorosilane show high Lewis acidity. Baba et al. also achieved catalytic Sakurai-Hosomi reaction using InCl₃-Me₃SiCl. cf) *Eur. J. Org. Chem.* **2002**, 1578., *Tetrahedron*. **2002**, 58, 8227. And catalytic Mukaiyama aldol reaction was reported. cf) Mukaiyama et al. *Chem. Lett.* **1991**, 20, 949.

Deoxygenative allylation of alcohols

Baba et al. *ACIE*. 2004, 43, 1414.

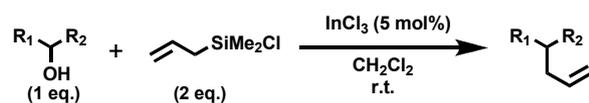


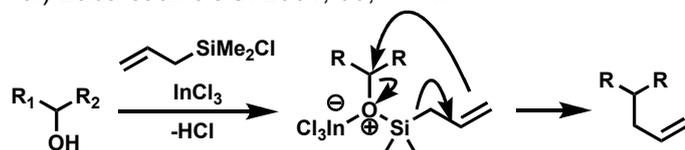
Table 2: Allylation of alcohols 2 with allylsilane 1 catalyzed by InCl₃.^[a]

| Entry | Alcohol | t [min] | Product | Yield [%] |
|---------------------|-----------------------|---------|---------|-----------|
| 1 | 2a: R=H | 10 | 3a | 80 |
| 2 | 2b: R=Me | 10 | 3b | 86 |
| 3 | 2c: R=Cl | 10 | 3c | 92 |
| 4 | 2d: R=NO ₂ | 10 | 3d | 80 |
| 5 | 2e: R=MeO | 10 | 3e | 82 |
| 13 ^[b] | 2j | 180 | 3j | 52 |
| 14 ^[d] | 2k | 60 | 3k | 66 |
| 15 | 2l | 180 | 3l | 59 |
| 16 ^[d,e] | 2m | 60 | 3m | 56 |

[a] The reactions were carried out in dichloromethane (1 mL) with allylsilane 1 (2.0 mmol), alcohol 2 (1.0 mmol), and InCl₃ (0.05 mmol) at RT unless otherwise stated. [b] Allylsilane 1 (3.0 mmol), dichloromethane (2 mL). [c] Allylsilane 1 (3.0 mmol), dichloroethane (2 mL), 80 °C. [d] Allylsilane 1 (4.0 mmol). [e] Bu₄NF was added during the workup.

First estimated mechanism

cf) Baba et al. *JOC*. 2001, 66, 7741.



But in a case of R₁=R₂=Ph, HCl and intermediate were not observed on NMR.

And also the reaction was proceeded in the cases of using trimethylsilyl.

Baba et al. *Synlett*. 2005, 11, 1737.

Table 1 Optimization of the Lewis Acid-Catalyzed Allylation with Allyltrimethylsilane^a

| Entry | Catalyst (mol%) | Solvent | Yield (%) |
|-------|---------------------------------------------------|---------|-----------|
| 1 | InCl ₃ (5) + Me ₃ SiCl (10) | Hexane | 13 |
| 2 | InCl ₃ (5) + Me ₃ SiBr (10) | Hexane | 77 |

^a All reactions were carried out in a solvent (1 mL) with allylsilane 2 (2.0 mmol), 1a (1.0 mmol), and a catalyst (0.05 mmol) at r.t. for 2 h.

Baba et al. *Chem. Commun*. 2008, 6396.

Table 1 Effect of catalysts in the coupling reaction of benzhydrol 1a with (*E*)-2-phenyl-1-trimethylsilyl ethylene 2a^a

| Entry | Catalyst | Yield (%) |
|-------|-----------------------------------|-----------|
| 1 | None | 0 |
| 2 | InCl ₃ | 91 |
| 3 | InBr ₃ | 85 |
| 4 | BiCl ₃ | 56 |
| 5 | BiBr ₃ | 82 |
| 6 | BF ₃ ·OEt ₂ | 7 |
| 7 | AlCl ₃ | 5 |
| 8 | TiCl ₄ | 20 |
| 9 | Sc(OTf) ₃ | 33 |
| 10 | Yb(OTf) ₃ | 8 |

^a Alcohol: 1 mmol, alkenylsilane: 2 mmol, catalyst: 5 mol%: ClCH₂CH₂Cl: 1 mL.

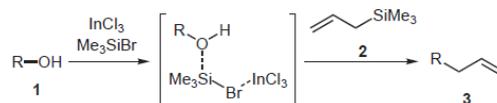
Table 3: Allylation of alcohols 2 with trimethylsilyl nucleophiles catalyzed by InCl₃.^[a]

| Entry | Silane | Alcohol | t [h] | Product | Yield [%] |
|------------------|--------|---------|-------|---------|-----------|
| 1 | 7 | 2a | 3 | 3a | 99 |
| 2 ^[b] | 7 | 2a | 3 | 3a | 0 |
| 4 ^[c] | 7 | 2g | 3 | 3g | 87 |
| 5 | 8 | 2a | 3 | 9a | 100 |
| 6 | 10 | 2a | 3 | 11a | 64 |
| 7 | 10 | 2g | 3 | 11g | 72 |
| 8 ^[c] | 10 | 2g | 3 | 11g | 81 |
| 9 | 12 | 2a | 3 | 13a | 64 |
| 10 | 12 | 2g | 6 | 13g | 55 |

[a] The reactions were carried out in 1,2-dichloroethane (2 mL) with silane (2.0 mmol), alcohol 2 (1.0 mmol), and InCl₃ (0.05 mmol) at 80 °C. [b] InCl₃ was not added. [c] Silane (3.0 mmol).

Same mechanism?

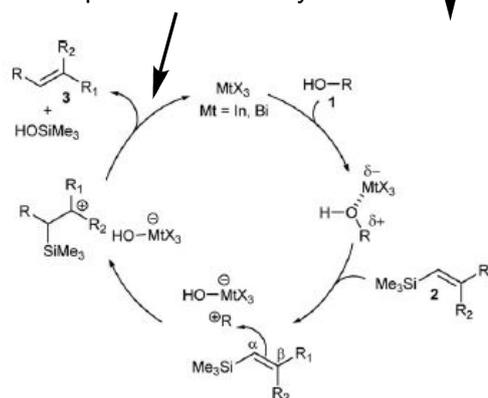
Lewis acidity of trimethylsilylhalides
Me₃SiCl < Me₃SiBr < Me₃SiI



Scheme 1 Plausible mechanism

Similar mechanism?

Indium has lower oxophilicity than Al, B etc. So this process proceeds smoothly.



Scheme 1 Plausible mechanism.

Deoxygenative halogenation of ketones

Baba et al. JACS, 2002, 124, 13690.

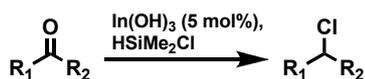
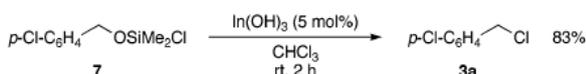


Table 2. In(OH)₃-Catalyzed Deoxygenative Chlorination of Various Carbonyls **1** by HSiMe₂Cl (**2b**)^a

| entry | carbonyls | T/°C | t/h | product | yield/% |
|----------------|-----------|------|-----|---------|-----------------|
| 1 | | rt | 5.5 | | 90 |
| 2 ^b | | rt | 5.5 | | 60 |
| 11 | | 60 | 3 | | 0 ^e |
| 12 | | rt | 3 | | 11 |
| 13 | | 60 | 3 | | 92 |
| 14 | | 60 | 2 | | 76 ^f |
| 15 | | rt | 2 | | 64 |
| 17 | | rt | 3.5 | | 46 |
| 18 | | 0 | 0.3 | | 78 |

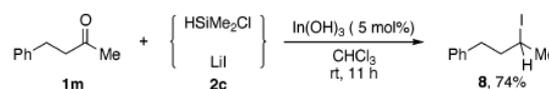
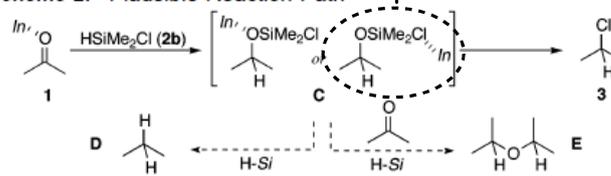
^a All reactions were carried out with carbonyls **1** (2.0 mmol), chlorosilane **2b** (2.4 mmol), and In(OH)₃ (0.1 mmol) in chloroform (4 mL). ^b InCl₃ was used instead of In(OH)₃. ^c Chlorosilane **2b** (4.4 mmol) was used. ^d (4-Methoxyphenyl)ethane (**5**) was obtained in 38% yield. ^e The ether (PhCH₂CH₂)₂O (**6**) was obtained in 70% yield. ^f Cis/trans = 12/88.



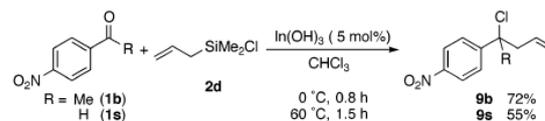
-> Silyl ether is intermediate.

I think this is active species.

Scheme 2. Plausible Reaction Path



Iodination



Chloroallylation

Deoxygenative chlorination of alcohols

Baba et al. JACS. 2004, 126, 7186.

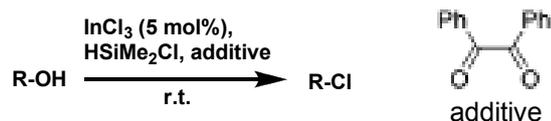


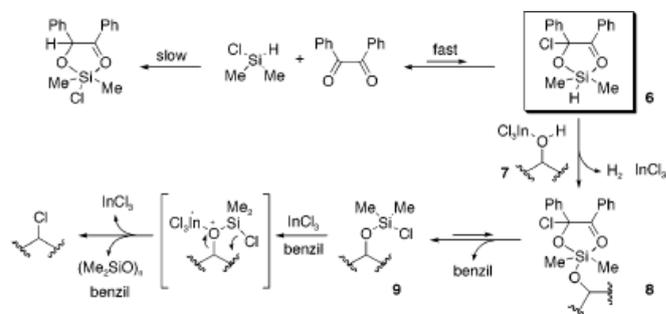
Table 2. Chlorination of Various Alcohols^a

| entry | alcohol | time/h | product | yield/% |
|-------|---------|-----------------|---------|-----------------------------|
| 1 | | 1b , 8 | | 3b , 74 ^b |
| 2 | | 1c , 15 | | 3c , 59 |
| 5 | | 1f , 9 | | 3f , 100 |
| 9 | | 1j , 24 | | 3j , 0 |
| 10 | | 1k , 1 | | 3k , 80 |
| 11 | | 1l , 2.5 | | 3l , 92 |
| 12 | | 1m , 0.7 | | 3m , 83 |
| 13 | | 1n , 24 | | 3n , 97 |
| 14 | | 1o , 1.5 | | 3o , 77 |
| 15 | | 1p , 2.5 | | 3p , 91 ^d |
| 16 | | 1q , 0.1 | | 3q , 96 |

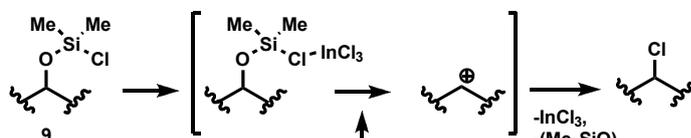
^a All entries were carried out at room temperature in CH₂Cl₂ with 5 mol % of InCl₃, 1.1 equiv of HSiMe₂Cl and 1.0 equiv of benzil. ^b Rearrangement products (regio isomers) were observed in 23% yield. ^c dr = 1:1. ^d <2% ee. ^e 2-Phenylpropane was obtained in 49% yield. ^f Premixing of HSiMe₂Cl and MeOH (1.0 equiv) followed by the addition of **1r**.

Reactivity: tertiary > secondary > primary (NR.)

Scheme 2. Plausible Reaction Course

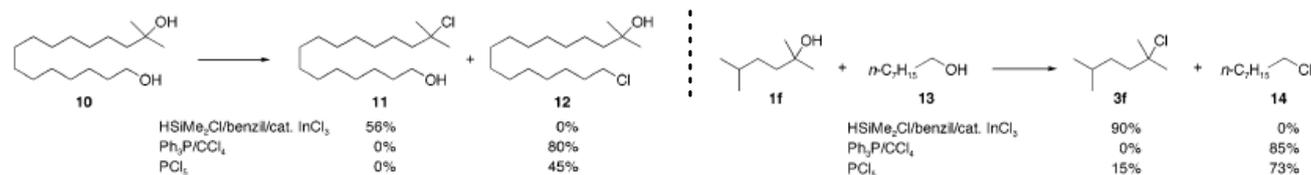


But according to this result, I propose other mechanism.



Does benzil play some role?

Scheme 3. Competitive Reaction between Tertiary and Primary Alcohols



2-2. Coupling reaction with silyl enol ethers

Baba et al. *Org. Lett.* **2007**, *9*, 4931.

Baba et al. *Tetrahedron.* **2009**, *65*, 5462.

Table 1. Effect of Catalysts^a

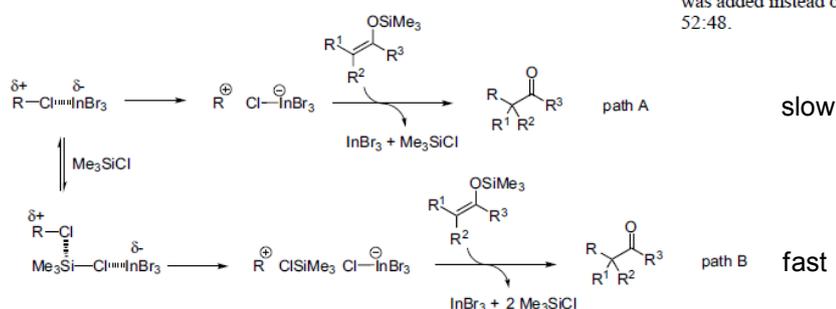
| entry | catalyst | yield (%) |
|-------|-----------------------------------|-----------|
| 1 | none | 0 |
| 2 | InBr ₃ | 99 |
| 3 | InCl ₃ | 9 |
| 4 | ZnBr ₂ | 39 |
| 5 | ZnCl ₂ | 6 |
| 6 | BF ₃ ·OEt ₂ | 0 |
| 7 | AlCl ₃ | 0 |
| 8 | TiCl ₄ | 0 |
| 9 | BiBr ₃ | 0 |

^a Alkyl chloride 1a (1 mmol), silyl enolate 2a (1.5 mmol), catalyst (0.05 mmol), and CH₂Cl₂ (1 mL).

Table 2. InBr₃-Catalyzed Reaction of Alkyl Halides with Silyl Enolates^a

| entry | chloride | silyl enolate 2 | time (h) | product 3 | yield (%) |
|-------------------|-----------------------------------------------------|-----------------|----------|-----------|-----------------|
| 1 | Ph-CH ₂ -Cl (1b) | 2a | 2 | 3ba | 83 |
| 5 | EtO-C(=O)-CH ₂ -CH ₂ -Cl (1f) | 2a | 3 | 3fa | 82 |
| 6 | Ph-CH=CH-Cl (1g) | 2a | 1 | 3ga | 91 |
| 9 ^{c, d} | Ph-CH ₂ -Cl (1j) | 2b | 2 | 3jb | 99 |
| 10 ^c | Ph-CH ₂ -Cl (1j) | 2c | 2 | 3jc | 83 ^e |
| 11 ^d | Ph-CH ₂ -Cl (1k) | 2d | 2 | 3kd | 94 |
| 12 ^d | Ph-CH ₂ -Cl (1k) | 2e | 2 | 3ke | 47 |

^a Alkyl chloride 1 (1 mmol), silyl enolate 2 (1.5 mmol), InBr₃ (0.05 mmol), and CH₂Cl₂ (1 mL). ^b Silyl enolate 2 (3 mmol). ^c InCl₃ (0.05 mmol) was added instead of InBr₃. ^d Silyl enolate 2 (2 mmol). ^e Diastereomer ratio: 52:48.



Scheme 3. Plausible mechanism.

First, reaction goes on path A. Then, TMSCl is generated and reaction is accelerated by path B.

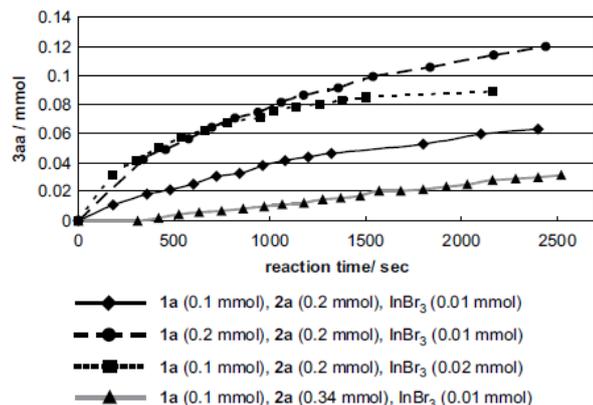
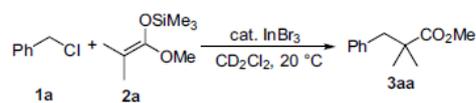


Figure 2. Effects of amounts of reactants and catalyst for the reaction rate.

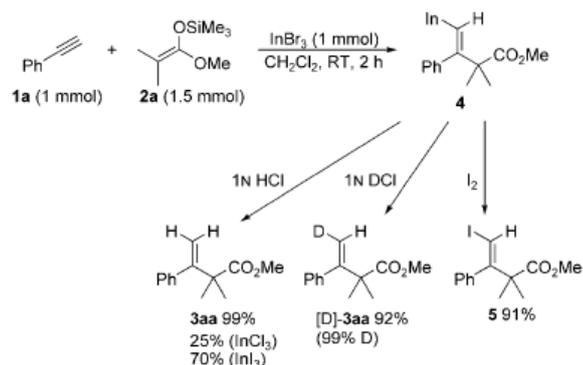
When the amount of 1a or InBr₃ was doubled, the reaction rate was increased.
->The generation carbocation step is rate-determining step.

When the amount of 2a was increased, the reaction rate was decreased.
->The coordination of the oxygen atom on the silyl enol ether deactivates the catalytic activity of InBr₃.
This is the reason why the strong Lewis acids showed no activity.

3. C=C or C≡C bond activation

3.1 C≡C bond activation

Baba et al. *ACIE*. 2009, 48, 4577.



Scheme 1. Reaction with InBr_3 , alkyne **1a**, and ketene silyl acetal **2a**.

Table 1: Additions of ketene silyl acetal **2a** to various alkynes.^[a]

| Entry | Alkyne | R ¹ | Product | Yield [%] ^[b] |
|-------|-----------|------------------------------------|------------|--------------------------|
| 1 | 1b | 4-MeC ₆ H ₄ | 3ba | 94 (80) ^[c] |
| 2 | 1c | 4-tBuC ₆ H ₄ | 3ca | 71 |
| 3 | 1d | 4-ClC ₆ H ₄ | 3da | 99 (97) ^[c] |
| 4 | 1e | C ₆ H ₁₃ | 3ea | 71 |
| 6 | 1g | | 3ga | 83 (82) ^[c] |

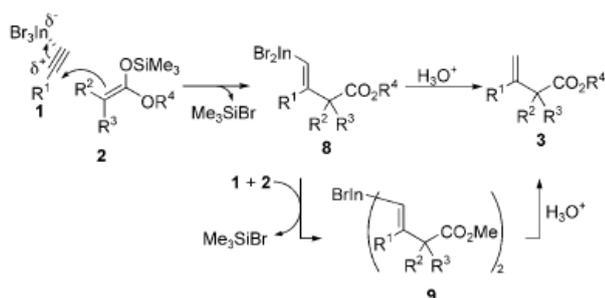
[a] Reaction conditions: **1** (1.0 mmol), **2a** (1.5 mmol), InBr_3 (1.0 mmol), CH_2Cl_2 (1 mL), RT, 2 h. [b] Yields were determined by ¹H NMR analysis. [c] Yield of product in a reaction using 0.5 mmol of InBr_3 .

In some cases, the reactions were proceeded by 50 mol% indium catalyst.

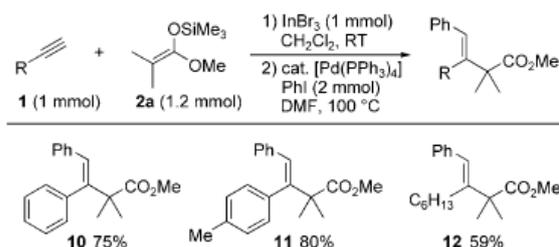
Table 2: Additions of various ketene silyl acetals to alkyne **1a**.^[a]

| Entry | Silyl ketene acetal | R ¹ | R ² | R ³ | Product | Yield [%] ^[b] |
|-------|--------------------------|------------------------------------|----------------|----------------|------------|--------------------------|
| 2 | 2c | -(CH ₂) ₅ - | - | Me | 3ac | 99 |
| 3 | 2d ^[c] | Me | Ph | Me | 3ad | 98 |
| 4 | 2e ^[d] | H | <i>n</i> Bu | Me | 3ae | 58 |
| 6 | 2g | H | H | Me | 3ag | 0 ^[f] |

[a] Reaction conditions: **1a** (1.0 mmol), **2** (1.5 mmol), InBr_3 (1 mmol), CH_2Cl_2 (1 mL), room temperature, 2 hours. [b] Yields were determined by ¹H NMR analysis. [c] *E/Z* = 66:34. [d] *E/Z* = 89:11. [e] *E/Z* = 70:30. [f] **2g** isomerized to a corresponding α -silyl ester.



Scheme 2. Plausible mechanism.



Scheme 4. One-pot addition/coupling reaction. DMF = *N,N*-dimethylformamide.

By using Pd catalyst, one-pot addition / coupling reactions were achieved.

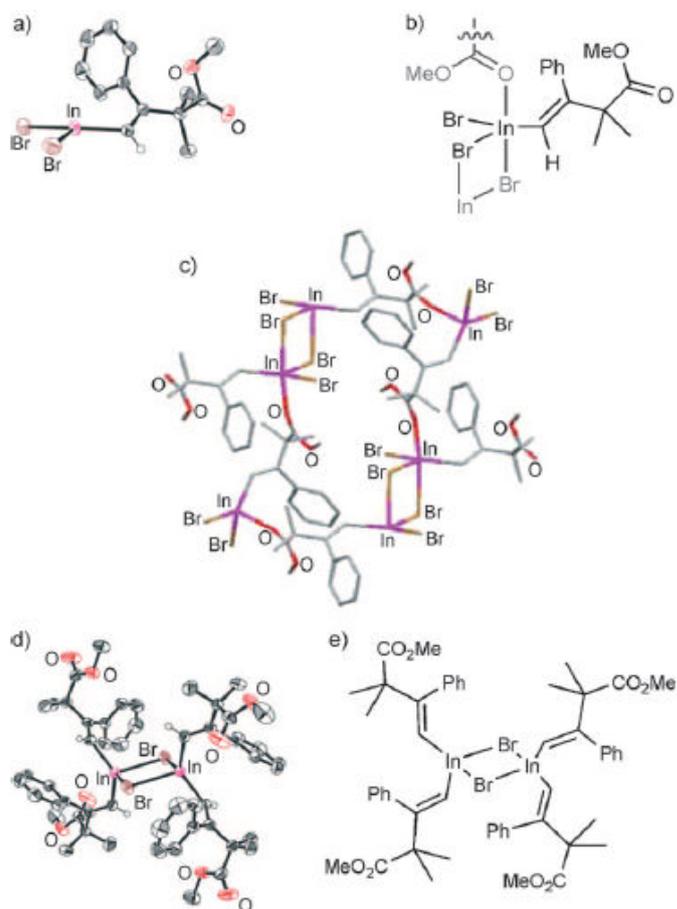
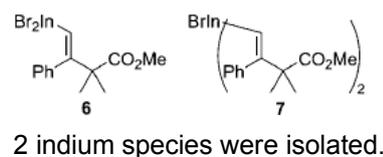


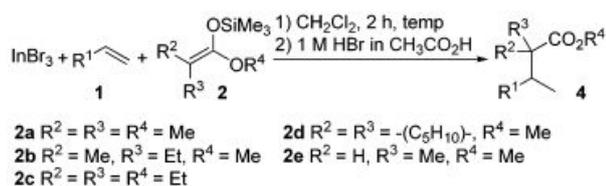
Figure 2. Molecular structure of **6** (a, b, and c) and **7** (d and e).



2 indium species were isolated.

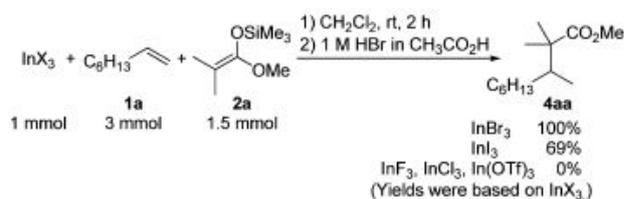
3.2 C=C bond activation

Table 1. Scope and Limitations of Alkenes **1** and Silyl Ketene Acetals **2**^a



| entry | 1 | 2 | temp | yield (%) ^g | |
|-----------------|--------------------------------------------------------------|-----------|-----------|------------------------|----------------------------|
| 4 | | | | | |
| 1 | 4-XC ₆ H ₄ CH=CH ₂ X = H | 1b | 2a | rt | 4ba 100 |
| 2 ^b | OMe | 1c | 2a | -20 °C | 4ca 100 |
| 3 ^c | Me | 1d | 2a | rt | 4da 100 |
| 4 | Cl | 1e | 2a | rt | 4ea 95 |
| 5 | NO ₂ | 1f | 2a | 80 °C | 4fa 0 |
| 7 | Ph(CH ₂) ₃ CH=CH ₂ | 1h | 2a | rt | 4ha 70 |
| 8 | | 1i | 2a | rt | 4ia 36 |
| 9 ^d | | 1j | 2a | rt | 4ja 93 |
| 13 ^d | 1b | 2b | rt | | 4bb 81 ^e |
| 14 ^d | 1b | 2c | rt | | 4bc 69 |
| 15 ^d | 1b | 2d | rt | | 4bd 73 |
| 16 ^d | 1b | 2e | 50 °C | | 4be 61 ^f |

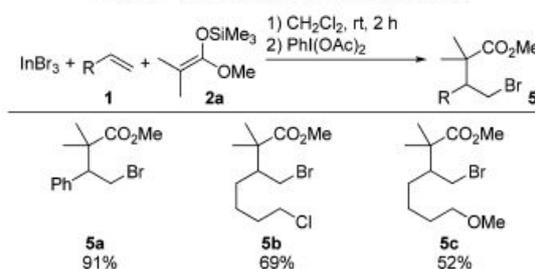
Scheme 1. Effect of Indium Trihalides



InF₃, InCl₃, In(OTf)₃ are too hard.

So they are trapped by oxygen atom of keten silyl acetal.

Scheme 4. Bromination of Alkylindium



4. Summary

- The combination of indium halide and silyl species shows high Lewis acidity.



- Low oxophilicity of indium enables various reactions.