Indium(III) Chloride/Chlorotrimethylsilane as a Highly Active Lewis Acid Catalyst System for the Sakurai−Hosomi Reaction

Yoshiyuki Onishi,[a] Takeshi Ito,[a] Makoto Yasuda,[a] and Akio Baba*[a]

Keywords: Allylation / Aldehydes / Indium / Silicon

The indium(III) chloride/chlorotrimethylsilane system acts as a catalyst for the Sakurai–Hosomi reaction between allylsilanes and aldehydes. When γ-substituted allylsilanes such as crotylsilane and prenylsilane are used a high regioselectivity for γ-addition is observed. Smaller amounts of the catalyst (5 mol %) effectively afforded the allylation products, although larger amounts (20 mol %) gave no product whatsoever. Other group 13 Lewis acids such as $AlCl_3$ and $BF_3{\cdot}OEt_2$ did not have catalytic activity even when combined with chlorotrimethylsilane.

Introduction

The synthetic applications of indium compounds have attracted much attention in the last decade.[1] Barbier- or Reformatsky-type reactions using indium species[2] are known to be powerful C−C bond formation methods. A selective addition of allylic dihaloindium, generated by the transmetallation between trihaloindium and allylic tributyltin reagents,[3] has become an important synthetic method. Indium(III) halides have also been used as water-tolerant Lewis acid catalysts for Diels−Alder, aldol and Mannich-type reactions.[4] However, the catalytic use of indium compounds is still limited to a narrow area, in contrast to the extensive use of aluminum or boron compounds, as In^{III} compounds have a lower Lewis acidity than the corresponding Al^{III} or B^{III} compounds.[5]

We have previously reported the reductive Friedel−Crafts reaction of carbonyl compounds catalyzed by In^{III}.[6] Friedel−Crafts benzylation of benzene with benzyl chloride is enhanced remarkably by the combination of a catalytic amount of Me_3SiCl and $InCl_3$.[6b] The Mukaiyama group has also reported an aldol reaction catalyzed by tBuMe$_2$SiCl/InCl$_3$.[7] In this context, we felt that the combination of In^{III} compounds and Me_3SiCl would work as a strong carbonyl-activating "catalyst".

The catalytic allylation of carbonyl compounds by allylsilanes (Sakurai−Hosomi reaction)[8] is a challenging theme because of the difficulty of regenerating the catalyst from the produced homoallylic metal oxides.[9] We wish to report here the characteristic activation of the allylation by the combined catalyst, $InCl_3/Me_3SiCl$.

Results and Discussion

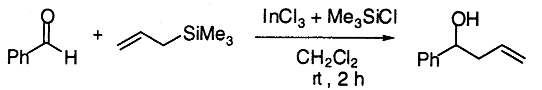
We found that the reaction between benzaldehyde (**1a**) and allyltrimethylsilane (**2a**) depends, rather unusually, on the amount of the combined catalyst $InCl_3/Me_3SiCl$, as shown in Table 1. Based on reported conditions for the catalytic aldol reaction,[7] we performed the first trial of our reaction with 10 mol % of the catalyst. However, the yields of allylated product **3a** were very low (entries 3 and 4); the use of 20 mol % of the catalyst completely depressed the formation of **3a** (entries 1 and 2). Surprisingly, only 5 mol % of the catalyst gave 61% yield (entry 5). The yield was further improved to 81% by changing the order of addition (entry 6): allylsilane was added to a premixed solution of aldehyde and the combined catalyst (Method B). When allyltrimethylsilane and 20 mol % of the combined catalyst was treated at room temperature without benzaldehyde, the complete decomposition of the allylsilane was observed within 2 hours (^{29}Si NMR spectroscopy), and the formation of propene was confirmed by GLC analysis of the gas in the flask. This test strongly suggests that the catalyst activates allylsilane, as neither $InCl_3$ nor Me_3SiCl promote this decomposition on their own.[10] The proton source needed to form propene is not yet known, although a trace amount of water is the most likely candidate. The decomposition of allyltrimethylsilane is considerably slower with only 5 mol % of the catalyst, and this is probably the reason why the yield is improved by loading smaller amounts of the catalyst or by changing the addition order (Method B).

The catalysts examined for the reaction between p-chlorobenzaldehyde (**1b**) and allyltrimethylsilane (**2a**) are summarized in Table 2. The typical Lewis acids $AlCl_3$ and $BF_3{\cdot}OEt_2$ did not catalyze the reaction, only giving stoichiometric yields of the product (entries 1 and 2). Although neither Me_3SiCl nor $InCl_3$ exhibited any catalytic ability on their own (entries 3−5), their combined use gave **3b** in 87%

---

[a] Department of Molecular Chemistry, Graduate School of Engineering, Osaka University,
2−1 Yamadaoka, Suita, Osaka, 565−0871, Japan
Fax: (internat.) + 81-6-6879/7387
E-mail: baba@ap.chem.eng.osaka-u.ac.jp

Table 1. Effect of the amount of combined catalyst

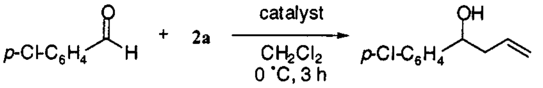


1a **2a** (1.5 equiv) **3a**

Entry	Catalyst (mol %)	Method[a]	Yield (%)
1	20	**A**	0
2	20	**B**	0
3	10	**A**	5
4	10	**B**	15
5	5	**A**	61
6	5	**B**	81

[a] Method **A**: addition order, i) $InCl_3/CH_2Cl_2$, ii) Me_3SiCl, iii) **2a**, iv) **1a**.; method **B**: addition order, i) $InCl_3/CH_2Cl_2$, ii) **1a**, iii) Me_3SiCl, iv) **2a**.

Table 2. Effect of different catalysts



1b **3b**

Entry	Catalyst (mol %)	Yield (%)	Recovery (%)[a]
1	$AlCl_3$ (20)[b]	37	35
2	$BF_3 \cdot OEt_2$ (20)[b]	26	20
3	Me_3SiCl (20)[b]	6	94
4	$InCl_3$ (20)	0	99
5	$InCl_3$ (5)	9	84
6	$InCl_3$ (5) + Me_3SiCl (5)	87	0
7	$InCl_3$ (5) + tBuMe$_2$SiCl (5)	85	0
8[c]	$InCl_3$ (5) + Me_3SiCl (5)	0	72
9	$InCl_3$ (1) + Me_3SiCl (1)	77	0
10	$AlCl_3$ (5) + Me_3SiCl (5)	9	79
11	$BF_3 \cdot OEt_2$ (5) + Me_3SiCl (5)	10	84
12	$TiCl_4$ (5) + Me_3SiCl (5)	9	91

[a] Recovery of **1b**. [b] No allylated product **3b** was obtained with 5 mol % of these catalysts. [c] Allytributylin was used instead of **2a**.

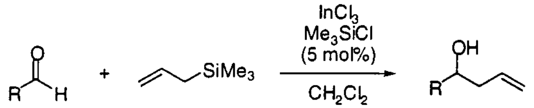
yield (entry 6). It should be noted that even 1 mol % of the combined catalyst afforded an acceptable yield of product (77%, entry 9).

$AlCl_3$, $BF_3 \cdot OEt_2$ and $TiCl_4$ do not catalyze the allylation even in combination with Me_3SiCl (entries 10−12). The reaction with allyltributyltin, which has a higher nucleophilicity than allyltrimethylsilane, resulted in the recovery of **1b** in this combined catalyst system (entry 8). These results strongly indicate a strong interaction between indium and silicon.

A typical reaction procedure is as follows: allyltrimethylsilane (**2a**, 0.33 g, 3.0 mmol) was added at 0 °C to a mixture of dried indium(III) chloride (0.022 g, 0.1 mmol), chlorotrimethylsilane (0.010 g, 0.1 mmol) and benzaldehyde (**1a**, 0.21 g, 2.0 mmol) in dichloromethane (4 mL), and the mixture stirred for 2 hours. After confirming the disappearance of the aldehyde by GLC, the reaction was quenched by addition of a 1 M THF solution of tetra-*n*-butylammonium fluoride (2 mL, 2 mmol) and stirring for 5 minutes.[11] The reaction mixture was then extracted with Et_2O (40 mL) and washed twice with H_2O (50 mL). The organic layer was dried ($MgSO_4$) and the solvents evaporated. Column chromatography of the residue on silica gel (eluting with 9:1 hexane/ether) followed by distillation gave **3a**.

The catalyst system $Me_3SiCl/InCl_3$ was also applied to the allylation of various carbonyl compounds and gave high yields of homoallylic alcohols, as shown in Table 3. Functional groups such as nitro, ester and cyano moieties tolerated the reaction conditions to give products allylated selectively at the carbonyl group, perhaps because of the mild non-protic conditions (entries 1−3). When *p*-methylbenzaldehyde was used as a substrate, the homoallyl alcohol **3f** was obtained in 56% yield, along with 25% of the diallylation compound **3fa**. The methoxy-substituted aldehyde (**1g**) gave only the diallylation product **3ga**. These results indicate that the $Me_3SiCl/InCl_3$ system also possesses a high catalytic ability for the allylation of initially formed homoallyl trimethylsilyl ethers.[12]

Table 3. Allylation of various carbonyl compounds[a]

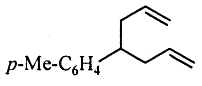


1c-g **2a** **3c-g**

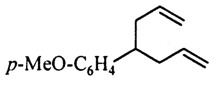
Entry	RCHO	Time (h)	Product	Yield (%)
1	*p*-MeOCO-C_6H_4CHO (**1c**)	1	**3c**	97
2	*p*-NO_2-C_6H_4CHO (**1d**)	1	**3d**	93
3	*p*-CN-C_6H_4CHO (**1e**)	2	**3e**	99
4[b]	*p*-Me-C_6H_4CHO (**1f**)	13	**3f**	56[c]
5[b]	*p*-MeO-C_6H_4CHO (**1g**)	13	–	0[d]
6	*n*HexCHO (**1h**)	1	**3h**	75
7	*t*BuCHO (**1i**)	2	**3i**	78

[a] $InCl_3/Me_3SiCl$/ **1**/**2a** = 0.1:0.1:2.0:3.0 mmol, solvent was 4 mL. [b] The reaction was performed at 0 °C. [c] The diallylation product **3fa** was obtained in 25% yield. [d] The diallylation product **3ga** was obtained in 49% yield.

An aliphatic aldehyde, *n*-heptanal (**1h**), also afforded the expected allylated product **3h** in high yield (entry 6). The reaction with the sterically hindered aldehyde **1i** proceeded cleanly and afforded the homoallylic alcohol **3i** in 78% (entry 7). Only trace amounts of the products were obtained in the allylation of ketones such as acetophenone or benzophenone.

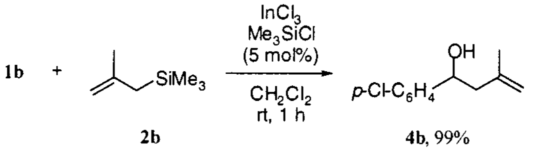


3fa

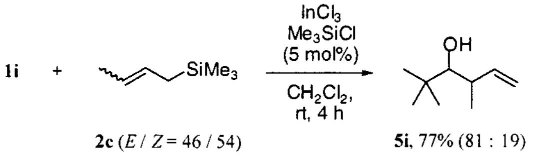


3ga

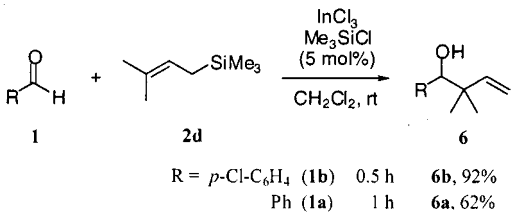
The results of the allylation with substituted allylsilanes are shown in Equations (1)−(3), as the reaction with substituted allylsilanes are very rare.[13] The β-methylated allylsilane **2b** reacted with *p*-chlorobenzaldehyde (**1b**) to give **4b** quantitatively [Equation (1)]. When γ-substituted allylsilanes [crotyltrimethylsilane (**2c**) and trimethylprenylsilane (**2d**)], which have lower reactivity than **2a** and **2b** because of their steric hindrance,[14] were used, the addition readily took place with highly γ-selective C−C bond formation.[15] These results emphasize that the combination of $InCl_3$ and Me_3SiCl has opened up a new catalytic system for selective carbonyl-group allylation.



(1)



(2)



(3)

Conclusion

We have shown that the combined system $InCl_3/Me_3SiCl$ exhibits a high catalytic activity for the Sakurai−Hosomi reaction using various substrates, including aromatic and aliphatic aldehydes. The use of small amounts of the catalyst is effective for allylation. Substituted allylsilanes were also applied to this catalytic reaction and gave the allylated products with inversion of the allylic unit in a highly selective manner.

Experimental Section

General Remarks: IR spectra were recorded as thin films on a HORIBA FT-720 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with a JEOL JNM-GSX-270 spectrometer (at 270 and 67.9 MHz, respectively), with TMS as internal standard. Mass spectra were recorded on a JEOL JMS-DS303 or a Shimadzu GCMS-QP2000A spectrometer. GLC analyses were performed on a Shimadzu GC-14A with FID using a 15 m × 0.25 mm column packed with TC-1701. Column chromatography was performed on silica gel (Fuji Silysia BW 200). Bulb-to-bulb distillation (kugelrohr) was accomplished in a Sibata GTO-250RS at the oven temperature and pressure indicated. Yields were determined by GLC or ^1H NMR spectroscopy using internal standards.

Dichloromethane was distilled from CaH_2. The substituted allysilanes **2c** and **2d** were prepared from the corresponding vinyl bromides and trimethylsilylmethylmagnesium chloride by known methods. The allylsilanes **2a** and **2b**, aldehydes **1a**−**1i**, $InCl_3$, Me_3SiCl, $tBuMe_2SiCl$ and TBAF (1.0 M solution in THF) are commercially available.

General Procedure for the Synthesis of Homoallylic Alcohols from 1a−i: The allylsilane **2a**−**d** (3.0 mmol) was added under nitrogen to a mixture of $InCl_3$ (0.2 mmol), Me_3SiCl (0.4 mmol) and aldehydes **1b**−**i** (2.0 mmol) in dichloromethane (4 mL) and this solution was stirred for the appropriate time at ambient temperature. The resultant mixture was quenched with a 1.0 M solution of TBAF in THF and then extracted with Et_2O (40 mL) and washed twice with H_2O (50 mL). The organic layer was dried ($MgSO_4$) and the solvents evaporated. Column chromatography of the evaporated residue on silica gel (eluting with a 9:1 hexane/ether mixture) and distillation gave pure products.

Product data: The spectroscopic data of the products **3a**−**i**,[9b,16−19] **3fa**, [9b] **3ga**,[9b] **4b**,[21] **5i**,[21] and **6a**[17] were in excellent agreement with reported compounds.

1-(4-Chlorophenyl)-2,2-dimethylbut-3-en-1-ol (6b): Prepared by the typical procedure from **1b** (2 mmol) and **2d** (3 mmol). B.p.: 70 °C/ 1×10^{-1} Torr. ^1H NMR (270 MHz, $CDCl_3$): δ = 7.30−7.20 (m, 4 H, aromatics), 5.87 (dd, J = 17.58 Hz, 10.74 Hz, 1 H, 3-H), 5.15 (dd, J = 10.74 Hz, 0.98 Hz, 1 H, 4-H-*trans*), 5.07 (dd, J = 17.58 Hz, 0.98 Hz, 1 H, 4-H-*cis*), 4.40 (d, J = 2.92 Hz, 1 H, 1-H), 2.07 (d, J = 2.92 Hz, 1 H, OH), 0.99 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3). ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 144.66 (C-3), 139.11 (1-Ph), 133.08 (4-Ph), 129.07 (arom. CH), 127.61 (arom. CH), 114.28 (C-4), 79.87 (C-1), 42.24 (C-2), 24.33 (CH_3), 20.77 (CH_3). IR (neat): $\tilde{\nu}$ = 3467 (OH), 1635 (C=C). HRMS (CI, 70 eV): calculated ($C_{12}H_{17}ClO^+$) 211.0890 [M + H+]; found 211.0885. $C_{12}H_{16}ClO$ (182.6516): calcd. C 68.40, H, 7.18; found C 68.20, H, 7.39.

Acknowledgments

This work was supported by a Grant-in Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, of the Japanese Government.

---

[1] [1a] P. Cintas, *Synlett* **1995**, 1087−1096. [1b] C.-J. Li, T.-H. Chan, *Tetrahedron* **1999**, *55*, 11149−11176. [1c] K. K. Chauhan, C. G. Frost, *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015−3019. [1d] G. Babu, P. T. Perumal, *Aldrichimica Acta* **2000**, *33*, 16−22.

[2] [2a] S. Araki, H. Ito, Y. Butsugan, *J. Org. Chem.* **1988**, *53*, 1831−1833. [2b] L-C. Chao, R. D. Rieke, *J. Org. Chem.* **1975**, *40*, 2253−2255. [2c] C.-C. Li, T.-H. Chan, *Tetrahedron Lett.* **1991**, *32*, 7017−7020. [2d] T.-P. Loh, X.-R. Li, *Angew. Chem.* **1997**, *109*, 1029−1031; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 980−982.

[3] [3a] J. A. Marshall, K. W. Hinkle, *J. Org. Chem.* **1995**, *60*, 1920−1921. [3b] M. Yasuda, T. Miyai, I. Shibata, A. Baba, R. Nomura, H. Matsuda, *Tetrahedron Lett.* **1995**, *36*, 9497−9500.

[4] [4a] T. P. Loh, J. Pei, M. Lin, *Chem. Commun.* **1996**, 2315−2316. [4b] G. Babu, P. T. Perumal, *Tetrahedron Lett.* **1997**, *38*, 5025−5026. [4c] S. Kobayshi, T. Busujima, S. Nagayama, *Tetrahedron Lett.* **1998**, *39*, 1579−1582. [4d] T.-P. Loh, L.-L. Wei, *Tetrahedron Lett.* **1998**, *39*, 323−326 and also ref.[1]

[5] G. A. Olah, S. Kobayashi, M. Tashiro, *J. Am. Chem. Soc.* **1972**, *94*, 7448−7461.

[6] [6a] T. Miyai, Y. Onishi, A. Baba, *Tetrahedron Lett.* **1998**, *39*, 6291−6294. [6b] T. Miyai, Y. Onishi, A. Baba, *Tetrahedron* **1999**, *55*, 1017−1026.

[7] T. Mukaiyama, T. Ohno, J. S. Han, S. Kobayashi, *Chem. Lett.* **1991**, 949−952.

[8] [8a] A. Hosomi, H. Sakurai, *Tetrahedron Lett.* **1976**, 1295−1296. [8b] A. Hosomi, *Acc. Chem. Res.* **1988**, *21*, 200−206.

[9] [9a] A. Hosomi, A. Shirahata, H. Sakurai, *Tetrahedron Lett.* **1978**, 3043−3046. [9b] A. P. Davis, M. Jaspars, *J. Chem. Soc., Perkin Trans. 1* **1992**, 2111−2118. [9c] G. Kaur, K. Manju, S. Trehan, *Chem. Commun.* **1996**, 581−582. [9d] D. R. Gauthier Jr., E. M. Carreira, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2363−2365. [9e] V. K. Aggarwal, G. P. Vennall, *Synthesis* **1998**, 1823−1826. [9f] A. Marx, H. Yamamoto, *Angew. Chem. Int. Ed.* **2000**, *39*, 178−181. [9g] K. Ishihara, M. Mouri, Q. Gao, T. Maruyama, K. Furuta, H. Yamamoto, *J. Am. Chem. Soc.* **1993**, *115*, 11490−11495. [9h] N. Komatsu, M. Uda, H. Suzuki, T. Takahashi, T. Domae, M. Wada, *Tetrahedron Lett.* **1997**, *38*, 7215−7218. [9i] X. Fang, J. G. Watkin, B. P. Warner, *Tetrahedron Lett.* **2000**, *41*, 447−449. [9j] M. W. Wang, Y. J. Chen, D. Wang, *Synlett* **2000**, 385−387.

[10] The decomposition of allyltrimethylsilane indicates that the combined catalyst interacts with allylsilanes. On the contrary, we observed the color change of the solution from colorless to yellowish orange by mixing $InCl_3$/Me_3SiCl and benzaldehyde in dichloromethane. This result indicates an interaction between the combined catalyst and benzaldehyde.[22,23] Although the activation mechanism of the combined catalyst system is not clear yet at this stage, we assume that the combined catalyst interacts with both the aldehyde and the allylsilane.

[11] We verified that tetra-*n*-butylammonium fluoride (TBAF) worked only as the quenching reagent of silyl ethers to alcohols.

[12] We have previously reported that activated silyl ethers are receptive to nucleophilic attack by allylsilane,[24] hydrosilane,[25] and aromatics.[6] Diallylation of *p*-methylbenzaldehyde and *p*-methoxybenzaldehyde was reported in the $Sc(OTf)_3$-catalyzed Sakurai−Hosomi reaction.[9e]

[13] There are only two reports of a catalytic Sakurai−Hosomi reaction using a substituted allylsilane.[9b,9g]

[14] β-Substituted allylsilanes possess considerably higher nucleophilicity than allyltrimethylsilane, see: G. Hagen, H. Mayr, *J. Am. Chem. Soc.* **1991**, *113*, 4954−4961.

[15] When we examined the reaction between **2a** and trimethylprenylsilane (**2d**) with $Sc(OTf)_3$ or $YbCl_3$ catalysts in a comparison to the reported conditions,[9e,9i] **6a** was obtained in only 26% and 5% yields, respectively.

[16] T. Akiyama, J. Iwai, M. Sugano, *Tetrahedron* **1999**, *55*, 7499−7508.

[17] A. Hosomi, S. Kohra, K. Ogata, T. Yanagi, Y. Tominaga, *J. Org. Chem.* **1990**, *55*, 2415−2420.

[18] P. Jones, P. Knochel, *J. Org. Chem.* **1999**, *64*, 186−195.

[19] A. S. Pilcher, P. DeShong, *J. Org. Chem.* **1996**, *61*, 6901−6905.

[20] J. M. Watson, J. L. Irvine, R. M. Roberts, *J. Am. Chem. Soc.* **1973**, *95*, 3348−3356.

[21] K. Iseki, S. Mizuno, Y. Kuroki, Y. Kobayashi, *Tetrahedron* **1999**, *55*, 977−988.

[22] The coordination of a Lewis acid to allyltributylstannane is known, see: J. M. Blackwell, W. E. Piers, M. Parves, *Org. Lett.* **2000**, *2*, 695−698.

[23] No transmetallation occurred between the combined catalyst and allyltrimethylsilane, because TMSCl was not observed in the mixture of allyl-TMS, $InCl_3$ and TBDMSCl. On the contrary, facile transmetallation between $InCl_3$ and allyltributyltin has been reported.[3]

[24] M. Yasuda, Y. Onishi, T. Ito, A. Baba, *Tetrahedron Lett.* **2000**, *41*, 2425−2428.

[25] [25a] T. Miyai, M. Ueba, A. Baba, *Synlett* **1999**, 182−184. [25b] M. Yasuda, Y. Onishi, M. Ueba, T. Miyai, A. Baba, *J. Org. Chem.* **2001**, *66*, 7741−7744.

Received October 22, 2001
[O01502]