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In/InCl₃-Mediated 1,2-Addition of Allyl Group to α , β -Unsaturated Carbonyl Compounds

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In/InCl₃-Mediated 1,2-Addition of Allyl Group to α,β-Unsaturated Carbonyl Compounds

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ABSTRACT

In/InC1₃-mediated addition of allyl iodide to α , β -unsaturated carbonyl compounds gave moderate to high yields of 1,2-addition products. The reactions covered acylic and cyclic α , β -unsaturated carbonyl compounds. Indium trichloride was effective for these Barbier-type allylation reactions.

Key Words: Indium; Indium trichloride; 1,2-Addition; Allylation.

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Indium-mediated reactions play a significant role in carbon–carbon bond formation, and are widely applied to prepare homoallylic alcohols. Although much attention has focused on the allylation of carbonyl compounds, to our best knowledge, there are only a few examples of study on 1,2-allylation to α , β -unsaturated carbonyl compounds such as *trans*-cinamaldehyde, 3,7-dimethyl-2,6-octadiene carboxaldehyde.^[1–3] Herein, we wish to report the indium-mediated 1,2-addition of allyl group to α , β -unsaturated carbonyl compounds in the presence of indium trichloride (Sch. 1).

For the examination of allylation of conjugated carbonyl compounds in acyclic system, 1-acetyl cyclohexene was chosen. In general, indiummediated allylations and combination of allylindium and Lewis acid^[4] to carbonyl compounds undergo smoothly in aqueous media via Barbier type reaction.^[5] At the first attempt, however, no reaction occurred in aqueous media such as water, aqueous ethanol, and aqueous THF. In anhydrous THF, 1,2-addition product was only given in 36% yield. Next, several additives such as lanthanium triflate, indium tnflate, cupper triflate, and indium trichloride in the THF solution were examined. Encouragingly, indium trichloride gave the dramatic improvement of reaction yields (89%). La(OTf)₃ is also effective for the reaction to give 71% yield. But In(OTf)₃ and Cu(OTf)₂ were not so effective for the reaction. After a survey of the amount of indium chloride (0.05 to 1 equiv. based on substrate), the highest yield (89%) was obtained by applying 1.0 equiv. of InC1₃.

The results of the 1,2-addition of allyl iodide to the cyclic and acyclic α , β -unsaturated carbonyl compounds using indium and indium trichloride were summarized in Table 1. The reactivities of the α , β -unsaturated carbonyl compounds were dependent upon the nature of the substrate. The reactions of ketones (Entries 1–5) smoothly underwent in THF or DMF solution. However, in the cases of cyclic ketones, the solvent played crucial role. Most of the cyclic compounds gave much-improved yields in DMF than THF except Entries 5 and 6. Especially, 3-methyl-2-cyclo-hexen-l-one (Entry 8), 2-cyclopenten-l-one (Entry 11), and 2-methyl-2-cyclopenten-l-one (Entry 12) did not afford the desired products in THF.



Scheme 1.

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	Substrate		Yield (%)			
Entry		Product	Time (h)	А	Time (h)	В

Table 1. 1,2-Addition of allyl group to α , β -unsaturated carbonyl compounds.^a

Entry	Substrate	Product	Time (h)	А	Time (h)	В
1		HO	1	96	1	61
2	(show	S A	3	90	3	93
3	C C	OH CLOCO	0.5	99	1	85
4	101	OH	4	98	0.5	46
5		OH	1.5	75	4	89
6	Ĉ	HO	2	61	4	75
7	Ŷ	HO	2	92	0.5	30
8		HO	4	54	2	0
9	↓ ↓	OH	4	90	5	44
10	ů	но	2	99	4	77
11	Å	HO	2	61	1	0
12	ů,	HO	1.5	55 ^b	1	0

Method A: Isolated yield using DMF as solvent; Method B: Isolated yield using THF as solvent.

^aAll reactions were carried out in 1.0 mmol scale.

^bThis reaction was carried out at $-5-0^{\circ}$ C.

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In the case of 2-methyl-2-cyclopenten-1-one (Entry 12), the 1,2-addition product could only be obtained under low temperature $(-5-0^{\circ}C)$.

In conclusion, the reaction of allyl iodide to α , β -unsaturated carbonyl compounds using indium and indium trichloride gave moderate to high yields of 1,2-allylation products.

EXPERIMENTAL

¹H NMR spectra were obtained on Varian Gemini 300 and Bruker Avance 300 spectrometers. Chemical shifts were reported in ppm. Infrared spectra were obtained on Perkin Elmer 16FPC FT-IR spectromter. GC/MS spectra were obtained on Hewlett Packard 5890. Analytical thin layer chromatographies (TLC) were carried out on precoated silica gel plates (Merck Kieselgel 60F254, layer thickness 0.25 mm). Flash column chromatography was conducted with silica gel 60 (Merck, 230–400 mesh).

Typical Experimental Procedure

Method A: 2-Cyclohex-l-enyl-pent-4-en-2-ol (5): A mixture of 1-acetyl-1-cyclohexene (128 mg, 1 mmol), allyl iodide (183 µL, 2 mmol), indium powder (171 mg, 1.5 mmol), and indium trichloride (226 mg, 1 mmol) in freshly distilled tetrahydrofuran (2 mL) was stirred at room temperature for 4 h. The reaction mixture was quenched with 0.5 mL of 1 N HCl, then filtered through celite and it was washed with ethyl acetate. The filtrate was neutralized with saturated sodium bicarbonate solution (pH = 6), then organic layer was washed with brine, dried over anhydrous magnesium sulfate. Then the solvent was evaporated off under reduced pressure. The residue was purified on neutral alumina (ether:hexane = 1:10 to 1:5) to give 148 mg (89%) of product as a light yellow oily compound. Rf = 0.36(EtOAc:Hexane = 1:6). ¹H NMR (300 MHz, CDC1₃): δ 5.77–5.66 (m, 2H), 5.11 (m, 2H), 2.25 (dd, J = 8.4 Hz, 1H), 2.05 (m, 4H), 1.62 (m, 4H), 1.29 (s, 3H) ppm. ¹³C NMR (75 MHz, CDC1₃): δ 142.39, 134.53, 120.54, 118.98, 74.55, 45.42, 27.49, 25.46, 25.28, 23.46, 22.75 ppm. MS (m/e): 148 (M⁺-H₂O), 125 (base peak); IR (KBr): 3388, 2932, 1658, $1372, 918 \,\mathrm{cm}^{-1}.$

1-Allyl-2-methyl-cyclopent-2-enol (12): A mixture of 2-methyl-2-cyclopenten-1-one (98 mg, 1 mmol), allyl iodide (183 μ L, 2 mmol),

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indium powder (171 mg, 1.5 mmol), and indium trichloride (221 mg, 1mmol) in freshly distilled *N*,*N*-dimethylforamide (2 mL) was stirred at $-5-0^{\circ}$ C for 1.5 h. The reaction mixture was quenched with 0.5 mL 1 N HCl, then filtered through celite and the celite, pad was washed with ethyl acetate. The organic layer was neutralized with saturated sodium bicarbonate solution (pH = 6), then rewashed with brine, dried over anhydrous magnesium sulfate. Then the solvent was evaporated off in vacuum. The residue was purified on neutral alumina (dilute with ether: hexane = 1:10, 1:5) to give 76 mg (55%) as a light yellow oily compound. Rf = 0.35 (EtOAc:hexane = 1:6). ¹H NMR (300 MHz, CDC1₃): δ 5.78 (m, 1H), 5.50 (s, 1H), 5.17–4.99 (m, overlap, 2H), 2.46–2.09 (m, 3H), 1.82 (m, 1H), 1.69 (s, 3H), 1.62 (m, 2H) ppm.

Method B: 2-Cyclohex-1-enyl-pent-4-en-2-ol (5): A mixture of 1-acetyl-1-cyclohexene (128 mg, 1 mmol), allyl iodide (183 μ L, 2 mmol), indium powder (171 mg, 1.5 mmol) and indium trichloride (226 mg, 1 mmol) in *N*,*N*-dimethylforamide (2 mL) was stirred at room temperature for 1.5 h. The reaction mixture was quenched with 0.5 mL of 1 N HCl, then filtered through celite and it was washed with ethyl acetate. The filtrate was neutralized with saturated sodium bicarbonate solution (pH = 6), then organic layer was washed with brine, dried over anhydrous magnesium sulfate. Then the solvent was evaporated off under reduced pressure. The residue was purified on neutral alumina (ether:hexane = 1:10 to 1:5) to give a light yellow oily compound (148 mg, 89%).

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