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Facile chemoselective carbonyl allylation of chalcones with allyltributylstannane catalyzed by CuI

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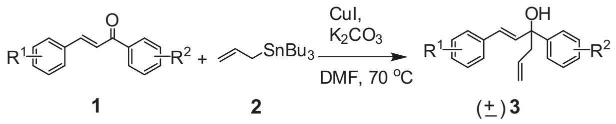
ABSTRACT

Chemoselective allylation of carbonyl functionality of chalcones with allyltributylstannane was accomplished in the presence of CuI as catalyst. This reaction works well in DMF at 70 °C with exclusive formation of 1,2-addition product. Interesting feature of this reaction is that no conjugate addition product was produced. Various types of chalcones undergo carbonyl allylation in excellent yield.

The chemoselective functionalization of organic compounds is synthetically important, both in the laboratory and in industry. Allylation of carbonyl compounds is a useful method for the synthesis of homoallylic alcohols,[1] which has been widely applied in the synthesis of natural products and other complex targets.[2] In general, addition of allyl metals to α,β-unsaturated ketones such as chalcones, leads to conjugate addition of allyl metals to chalcones, which is referred to as the Sakurai-type Michael reaction.[3] In many cases, a mixture of 1,4-and 1,2-addition products was formed during the reaction with predominant formation of the 1,4-product. In 2001, Lee[3a] has successfully studied the regioselectivity on the reactions of α,β-enones with allyl indium reagents generated in situ by the reaction of allyl iodide with indium metal in the presence of chlorotrimethylsilane (TMSCl). They found that the regioselectivity (1,4-addition vs 1,2-addition) is dependent on the type of substrate used. Kelly and Gilheany[4] investigated the effect of $InCl_3$ on the addition of Grignard reagents to chalcones, where they found that the presence of 5 mol % $InCl_3$ can significantly alter the amount of 1,2-addition product. But the reaction needs 16 h for completion. Cho and co-workers[5] reported indium mediated 1,2-addition of allyl iodide to α,β-unsaturated carbonyl compounds. In this method, they used indium trichloride as an activator along with indium powder to accomplish the reaction. Very recently, Li et al.[6] reported a Barbier-type allylation method by using Mg powder under solvent-free condition where in case of chalcones, 1,2-addition products were obtained regioselectively in good yields.

To our knowledge, there are only a few reports of allylation reaction of chalcones with exclusive formation of 1,2-addition product.[4–6] In continuation of our investigations on various allylation reactions[7] and CuI catalyzed reactions,[7e–g,8] we present herein a new method for chemoselective carbonyl allylation of chalcones with allyltributylstannane using CuI as catalyst in the presence of K_2CO_3 in DMF medium (Scheme 1).

In a typical reaction, chalcones (1 mmol), allyltributylstannane (1 mmol), K_2CO_3 (1 mmol), and CuI (10 mol %) were added successively in DMF (1.5 mL) at room temperature. The reaction was monitored by TLC. The results are presented in Table 1. Initial experiment without K_2CO_3 failed to produce any product both at room temperature (Table 1, entry 1) and at 70 °C (Table 1, entry 2). Another experiment without CuI also produced negative result both at room temperature and at 70 °C (Table 1, entries 3 and 4, respectively). When the reaction was examined using both K_2CO_3 (1 mmol) and CuI (10 mol %), it produced 48% of the 1,2-addition product after 24 h at room temperature (Table 1, entry 5). The reaction with increasing the concentration of the catalyst gradually increases the yield of the reaction up-to 62%. However, the reaction rate as well as yield of the product increased significantly, when the temperature of the reaction was increased from room temperature to 70 °C. In this case, the reaction produced corresponding alcohol in 62% yield just after 10 h of reaction. An improvement



Scheme 1. 1,2-Allylation of chalcones.

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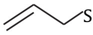
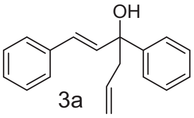
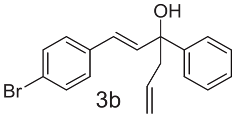
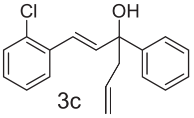
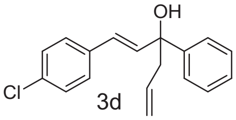
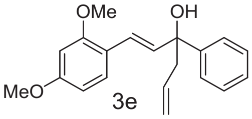
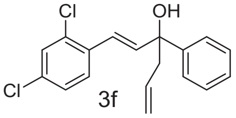
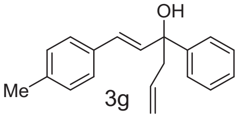
Table 1
Allylation of chalcones by allyltributylstannane using CuI as catalyst

Entry	Chalcone (mmol)	SnBu$_3$ (mmol)	Base (mmol)	Solvent (1.5 mL)	Catalyst (mmol)	Temp (°C)	Time (h)	Yield[a] (%)
1	1	1	—	DMF	CuI (0.10)	rt	24	0
2	1	1	—	DMF	CuI (0.10)	70	10	0
3	1	1	K_2CO_3 (1)	DMF	—	rt	24	0
4	1	1	K_2CO_3 (1)	DMF	—	70	10	0
5	1	1	K_2CO_3 (1)	DMF	CuI (0.10)	rt	24	48
6	1	1	K_2CO_3 (1)	DMF	CuI (0.15)	rt	24	52
7	1	1	K_2CO_3 (1)	DMF	CuI (0.20)	rt	24	61
8	1	1	K_2CO_3 (1)	DMF	CuI (0.25)	rt	24	62
9	1	1	K_2CO_3 (1)	DMF	CuI (0.10)	50	10	55
10	1	1	K_2CO_3 (1)	DMF	CuI (0.10)	70	10	62
11	1	1	K_2CO_3 (1)	DMF	CuI (0.15)	70	10	73
12	1	1	K_2CO_3 (1)	DMF	CuI (0.20)	70	10	77
13	1	1	K_2CO_3 (1)	DMF	CuI (0.25)	70	5	85
14	1	1.1	K_2CO_3 (1)	DMF	CuI (0.25)	70	5	90
15	1	1.2	K_2CO_3 (1)	DMF	CuI (0.25)	70	5	95
16	1	1.2	K_2CO_3 (1)	H_2O	CuI (0.25)	70	5	0
17	1	1.2	K_2CO_3 (1)	CH_3CN	CuI (0.25)	70	5	10
18	1	1.2	K_2CO_3 (1)	Toluene	CuI (0.25)	70	5	0
19	1	1.2	K_2CO_3 (1)	DMSO	CuI (0.25)	70	5	10
20	1	1.2	K_2CO_3 (1)	EtOAc	CuI (0.25)	70	5	5
21	1	1.2	Na_2CO_3 (1)	DMF	CuI (0.25)	70	5	20
22	1	1.2	$NaHCO_3$ (1)	DMF	CuI (0.25)	70	5	15
23	1	1.2	NaOAc (1)	DMF	CuI (0.25)	70	5	18
24	1	1.2	Cs_2CO_3 (1)	DMF	CuI (0.25)	70	5	0
25	1	1.2	DMAP (1)	DMF	CuI (0.25)	70	5	0
26	1	1.2	K_2CO_3 (1)	DMF	$CuSO_4{\cdot}5H_2O$(0.25)	70	12	0
27	1	1.2	K_2CO_3 (1)	DMF	$Cu(NO_3)_2{\cdot}3H_2O$(0.25)	70	12	0

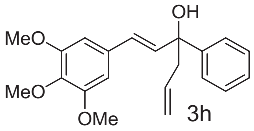
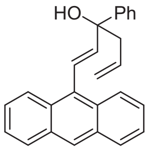
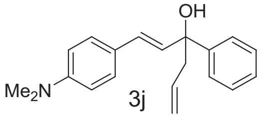
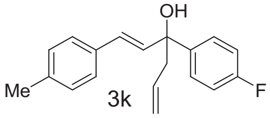
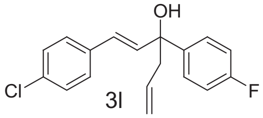
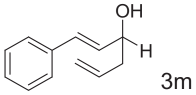
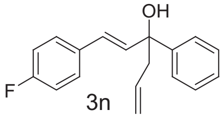
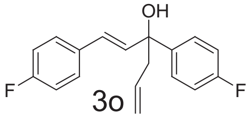
[a] Isolated yield.

Table 2
Allylation of various chalcones using CuI as catalyst[a]

Entry	R^1	R^2	Time(h)	Product[b]	Yield[c](%)
1	Ph	Ph	5	 3a	95
2	4-Br-Ph	Ph	7	 3b	92
3	2-Cl-Ph	Ph	6	 3c	90
4	4-Cl-Ph	Ph	6	 3d	92
5	2,4-DiOMe-Ph	Ph	7	 3e	90
6	2,4-DiCl-Ph	Ph	6	 3f	80
7	4-Me-Ph	Ph	7	 3g	80

(continued on next page)

Table 2 (*continued*)

Entry	R^1	R^2	Time(h)	Product[b]	Yield[c](%)
8	3,4,5-TriOMe-Ph	Ph	6	 3h	92
9	Anthracene	Ph	7	 3i	82
10	4-N,N-DiMe-Ph	Ph	5	 3j	77
11	4-Me-Ph	4-F-Ph	6	 3k	83
12	4-Cl-Ph	4-F-Ph	7	 3l	77
13	Ph	H	5	 3m	88
14	4-F-Ph	Ph	6	 3n	85
15	4-F-Ph	4-F-Ph	8	 3o	72

[a] Reaction condition: chalcones, 1 mmol; allyltributylstannane, 1.2 mmol; CuI, 25 mol %; solvent, 1.5 mL; time, 5–8 h; 70 °C.

[b] All products were characterized by IR, ^{1}H NMR, ^{13}C NMR, and GCMS.

[c] Isolated yield after chromatographic purification.

in the yield of up-to 95% was observed when the amount of allylating agent was increased from 1 to 1.2 equiv and the concentration of the catalyst was increased up-to 25 mol % (Table 1, entry 15). When we examined the reaction with Cu (II) salts (Table 1, entries 26 and 27), no product formation was observed after 12 h. The reaction was also examined using different solvents such as H_2O, CH_3CN, toluene, DMSO, and ethyl acetate (Table 1, entries 17–20). While the use of CH_3CN, DMSO, and ethyl acetate produced low yield, the reaction was found inactive in water and toluene. DMF was found to be the only solvent to produce high yield of the product. Furthermore, we have carried out the reaction using different bases (Table 1, entries 21–25) and K_2CO_3 was found to be the best choice with 95% yield (Table 1, entry 15). The marked difference in reactivity with Na_2CO_3, K_2CO_3, and Cs_2CO_3 may be due to highly moisture sensitive nature of Na_2CO_3 as well as less polarizing power of Cs_2CO_3. Finally, the use of 25 mol % of CuI, 1.2 equiv of allyltributylstannane, and 1 equiv of K_2CO_3 was found to be optimum to realize the best yield of the product.

Having established the optimized reaction conditions,[9] a variety of chalcones were investigated under the same reaction conditions. The results are summarized in Table 2. In general, this procedure[9] works well for different substituted chalcones to produce the corresponding allylated alcohols in excellent yield. Most important observation of the reaction is that 1,2-addition is predominant over 1,4-addition. We did not observe any byproduct under this particular reaction condition. The absence of 1,4-addition product suggested that, there is no possibility of *trans*-metallation, as this will lead to predominant formation of conjugate addition product.[10] Hence, there is a possibility of involvement of a different kind of mechanism, where direct carbonyl allylation might have taken place. Further experiments are underway in our laboratory to investigate the mechanistic pathway and will be reported in due course.

In conclusion, we have developed a method for chemoselective allylation of chalcones with exclusive formation of 1,2-addition product. 25 mol % of CuI is required to complete conversion of the desired product. All types of chalcones undergo carbonyl allylation in very high yield. Further studies on the relation between the 1,2 and 1,4-selectivity and delineating the scope of the reaction are in progress.

Acknowledgment

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.06.037.

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9. *General procedure:* To a solution of chalcones (1 mmol) and allyltributylstannane (1.2 mmol) in dry DMF (1.5 mL), CuI (25 mol %) and K_2CO_3 (1 mmol) were added successively. The mixture was then heated at 70 °C under nitrogen atmosphere. On completion of reaction, the undissolved materials are filtered out and the residue was washed with diethyl ether. The mixture was extracted with diethylether (3 × 25 mL) and the combined organic extract was thoroughly washed with water (3 × 25 mL), dried over anhydrous Na_2SO_4 and the solvent was removed to afford the crude product. The crude product was purified by column chromatography over silica gel (230–400 mesh) using ethylacetate:petroleum ether (5:95) as eluent.
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