A remarkable catalytic activity of [Cu(NCMe)$_2$(PPh$_3$)$_2$]BF$_4$ in conjugate addition of organomanganese reagents to α,β-unsaturated ester, enone and allyl chloride

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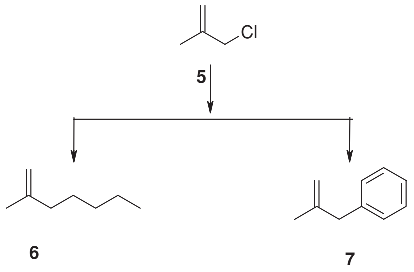
A simple and convenient method of conjugate addition of alkyl and aryl organomanganese reagents to α,β-unsaturated ester and enone and allyl chloride in presence of Cu(I) salts is described. Conjugated products result with [Cu(NCMe)$_2$(PPh$_3$)$_2$]BF$_4$ as a catalyst along with chlorosilane as an accelerator at –10 to 0 °C.

Keywords: organomanganese reagent, conjugate addition, chlorosilane

Conjugate addition reactions have recently been developed extensively either by using a Cu(I) catalysed reaction of Grignard reagents[1] or a stoichiometric amount of dialkylcuprates.[2] The Cu(I) salts have been used as efficient catalysts for conjugate addition of Grignard reagents to carbonyl compounds[3] by using RCu–BF$_3$[4] or a combination of mixed cuprate with Me$_3$Si–Cl–acetylide and Me$_3$Si–Cl.[5] Introduction of an alkyl group to unsaturated esters requires a large excess of Grignard reagents. It has been also reported that Cu(II) salts can also be used as a catalyst in conjugate addition reactions,[6] but there is need of Me$_3$Si–Cl or Me$_3$Si–Cl/HMPA to act as efficient catalyst.

During our efforts to perform conjugate addition of phenyl manganese bromide to ethyl (2E)-but-2-enoate, we found that Me$_3$Si–Cl greatly improved the conjugate addition yield (see Table 1). In the presence of [Cu(NCMe)$_2$(PPh$_3$)$_2$]BF$_4$ catalyst, there was introduction of a phenyl group almost quantitatively by using 2 equiv. of Me$_3$Si–Cl (entry 1). The same reaction, when performed without Me$_3$Si–Cl, gave only 46 % yield (entry 5). Moderate yields were obtained with other Cu(I) catalysts. The introduction of the phenyl group resulted quantitatively with 10 mol % CuI catalyst and 1.2 equiv. of Me$_3$Si–Cl (entry 3). When the reaction was performed with CuCN catalyst, moderate conjugation resulted (entry 4).

During studies on Me$_3$Si–Cl accelerated conjugate addition of organomanganese reagents to (2E)-1,3-diphenylprop2-en-1-one, we found that Me$_3$Si–Cl has not much improved the quantitative yield (see Table 2, entries 1 and 2). However, a moderate yield was observed with CuCN catalyst (entry 3). The introduction of a phenyl group resulted quantitatively with CuI catalyst in presence of 2 equiv. of Me$_3$Si–Cl (entry 4). Performing the reaction in presence of CuCN + 2LiCl catalyst gave no quantitative improvement in the yield (entry 5).



Scheme 1

3-chloro-2-methyl prop-1-ene, **5** was treated with *n*BuMnBr in THF at –10 °C, to afford alkylated product as a colourless liquid **6** up to 96 % when the reaction was performed in presence of [Cu(NCMe)$_2$(PPh$_3$)$_2$]BF$_4$ catalyst (Scheme 1). When the same alkylation reaction was performed in Et$_2$O at –5 °C and 10 mol % CuCN catalyst, the yield dropped to 79 %. However, the presence of Me$_3$Si–Cl as an accelerator and 10 mol % of CuI catalyst resulted in quantitative alkylation (74%) in Et$_2$O at –18 °C.

We have explored the catalytic activity of [Cu(NCMe)$_4$]BF$_4$ catalyst in substitution of **5** with PhMnBr. We found better substitution in presence of 2 equiv. of Me$_3$Si–Cl, to afford yellow orange coloured product **7** in 87 % yield. The structures of **6** and **7** were confirmed by spectroscopical data (see Experimental).

It has been reported that ketones can be easily obtained in high yields by acylation of organomanganese reagent[7] in the

Table 1 Conjugate addition of phenyl manganese bromide reagents to (2E)-but-2-enoate

Entry[a]	[Cu][b]	Additives/equiv.	Temp./°C	Yield/%
1	[Cu(NCMe)$_2$(PPh$_3$)$_2$]BF$_4$	Me$_3$Si–Cl (2)	–5	78
2	[Cu(NCMe)$_4$]BF$_4$	Me$_3$Si–Cl (3)	–5	58[c]
3	CuI	Me$_3$Si–Cl (1.2)	–15	68
4	CuCN	–	–5	60
5	[Cu(NCMe)$_2$(PPh$_3$)$_2$]BF$_4$	–	–5	46

[a]All reactions were performed in Et$_2$O on 1 mmol scale for 1 h.
[b]10 mol % of catalyst was used.
[c]Yield of the conjugation addition product in THF solvent.

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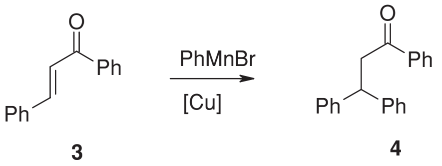
Table 2 Conjugate addition of phenyl manganese bromide reagent to (2E)-1,3-diphenylprop2-en-1-one



Entry[a]	[Cu][b]	Additives/equiv.	Temp./°C	Yield/%
1	[Cu(NCMe)2(PPh3)2]BF4	Me3Si–Cl (1)	0	69
2	[Cu(NCMe)2(PPh3)2]BF4	–	0	63
3	CuCN	–	–10	59
4	CuI	Me3Si–Cl (2)	–18	61
5	CuCN + 2 LiCl	–	–5	58

[a]All reactions were performed in Et2O on 1 m mol scale for 1 h.
[b]10 mol % of catalyst was used.

presence of a catalytic amount of CuCl and iron (III) acetylacetonate. In order to get better acylation of **8** (Scheme 2), a very low temperature is required. Therefore, we have tried to perform these reactions under optimum conditions in acylation reactions. We found that there was better acylation with $[Cu(NCMe)_2(PPh_3)_2]BF_4$ catalyst to form **9** (94 % yield) and the reaction can be carried out at 0 °C. The same reaction, when performed with 10 mol % Cu $(OAc)_2$ at –5 °C resulted in only 54 % acylated product in THF.

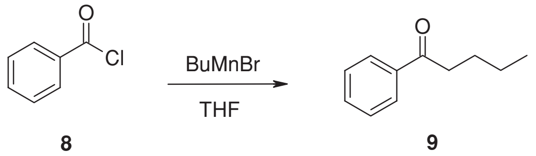
At present, the role of $[Cu(NCMe)_2(PPh_3)_2]BF_4$ species in these conjugate addition reactions is not clear, but the reaction mechanism might be different from the reaction catalysed by Cu(I). At any event, the results described here may open a new entry to organomanganese (I) species as promising reagents for 1,4-addition reactions.

Results and discussion

These results showed that $[Cu(NCMe)_2(PPh_3)_2]BF_4$ complex is a better catalyst than CuCN, CuI and $[Cu(NCMe)_4]BF_4$ in conjugate addition of organomanganese reagents to α,β-unsaturated carbonyl compounds. Reactions can be performed under mild conditions and conjugated yields are high. There is no need to use a large excess of the reagent to perform this transformation in a synthetically acceptable yield. Among Cu(I) species briefly examined, the $[Cu(NCMe)_2(PPh_3)_2]BF_4$ complex has exhibited the most efficient catalytic activity.

Experimental

Proton spectra were recorded in $CDCl_3$ solution on a JEOL JNM-GX 270 M Hz spectrometer while tetramethylsilane (TMS, 0.00 ppm) was used as reference for ^1H NMR spectra. The IR spectra were recorded on a Perkin Elmer FTIR spectrometer. Merck silica gel (230–400 mesh) was used for column chromatography, and thin-layer chromatography (TLC) was run on Merck precoated silica gel 60-F_{254} plates. Concentrations of the Grignard reagent were determined by titration. All reactions were carried out in flame-dried glassware under a N_2 atmosphere, unless stated otherwise. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl solution. $[Cu(NCMe)_4]BF_4$ and $[Cu(NCMe)_2(PPh_3)_2]BF_4$ was prepared according to literature procedures. Copper (I) Iodide (98 %) and CuCN (99 %) were purchased from Lancaster Synthesis. Me_3Si–Cl was used without further purification.



Scheme 2

Preparation of $[Cu(NCMe)_2(PPh_3)_2]BF_4$: PPh_3 (0.83 g), freshly prepared $[Cu(NCMe)_4]BF_4$ (0.50 g) and CH_2Cl_2 (15 ml) was added and the suspension stirred for 30 min until a colourless solution was obtained. Then Et_2O (40 ml) was added and again the contents stirred for another 15 min. After cooling at 0 °C for 1 h the colourless crystals formed which after filtration and drying in desiccators gave the desired white crystalline solid compound. Yield: (89 %).

IR (KBr): 3051, 2935, 2342, 2270, 1599, 1479, 1434, 1364, 1183, 1169, 1095, 1059, 998, 745, 695, 517 cm^{-1}

^1H NMR (200 M Hz, δ, $CDCl_3$): 2.11 (s, 6H, 2 × CH_3), 7.16–7.40 (m, 30 H, Ar–H) ppm.

Li_2MnCl_4: Manganese (II) chloride, (1 M) and lithium chloride (2 M) were vacuum dried in oven at 120 °C for 3 hours and then Na dried THF was added to form 'Li_2MnCl_4'. Organomanganese reagents are prepared by adding Grignard reagent to the complex prior to use.

Ethyl 3-phenylbutanoate (**2**): To a cooled solution of Li_2MnCl_4 (10 mmol, 10ml, 1 M) was added phenyl magnesium bromide (12 mmol, 9 ml, 1.3 M) and the mixture was stirred for 30 min at 0 °C to form the organomanganese reagent. Then $[Cu(NCMe)_2(PPh_3)_2]BF_4$, 1 mol % and Me_3Si–Cl (2 equiv., 1.2 ml) was added and reaction mixture was stirred for a further 30 min at –5 °C. Then ethyl (2E)-but-2-enoate (10 mmol, 1.2 ml) in dry THF (2 ml) was added dropwise over 5 min. After completion of reaction (confirmation by TLC), the reaction mixture was poured into 10 ml 10 % aq. NH_4Cl and extracted with Et_2O (20 ml) After evaporating the solvent the crude yellow liquid was purified on a silica column.

IR (KBr): 1718, 1701, 1599, 1493, 1376, 1260, 1216, 1020, 757, cm^{-1}

^1H NMR (270 M Hz, δ, $CDCl_3$): 1.25 (t, *J*=7 Hz, 3H, CH_3), 1.49 (d, 3H, *J*=4.8 Hz CH–CH_3), 1.89 (d, 2H, *J*=6.7 Hz, CH_2COO–), 4.89–4.93 (q, *J*=7 Hz, 2H, –CH_2–CH_3), 6.80–6.90 (m, 1H, Ar–CH), 7.1–7.3 (m, 5H, Ar–H) ppm.

1,3,3-triphenylpropan-1-one (**4**): To a cooled solution of Li_2MnCl_4 (5 mmol, 5 ml, 1 M) phenyl magnesium bromide (15 mmol, 11 ml, 1.3 M) was added and stirred for 30 min to form a black brown suspension of the organomanganese reagent. Then $[Cu(NCMe)_2(PPh_3)_2]BF_4$, 1 mol % and Me_3Si–Cl (2 equiv., 1.2 ml) was added and reaction mixture was stirred for a further 30 min at 0 °C. Then (2E)-1,3-diphenylprop2-en-1-one (5 mmol, 1.040 g) in 5 ml dry THF was slowly added over 20 min. The progress of reaction was confirmed by TLC. After completion of reaction, the reaction mixture was poured into 10 ml 10 % aq. NH_4Cl and extracted with ether. After evaporating the solvent, the crude product was purified by column chromatography using pet ether: ethyl acetate is 90: 10 proportions to give a pale yellow oil.

IR (KBr): 1677, 1594, 1494, 1448, 1375, 1262, 1026, 748, 703, 685, cm^{-1}

^1H NMR (300 M Hz, δ, $CDCl_3$): 3.70 (d, *J*=7.3 Hz, –CH_2CO), 4.83 (t, 1H, CH–$(Ph)_2$), 7–8 (m, 15H, Ar–H) ppm.

2-methylhept-1-ene (**6**): To a cooled solution of Li_2MnCl_4 (2 mmol, 2 ml, 1 M), Butyl magnesium bromide (2.2 mmol, 1.8 ml, 1.2 M) was added and stirred for 30 min to form the organomanganese reagent. Then 0.5 mol of $[Cu(NCMe)_2(PPh_3)_2]BF_4$ catalyst was added and the reaction mixture again stirred for 30 min. Then Me_3Si–Cl (2 equiv.) and 3-chloro-2-methylprop-1-ene (2mmol, 0.181 g) were added. After completion of reaction, the mixture was quenched with dil HCl and extracted with diethyl ether. After evaporation of the solvent, a colourless liquid was obtained.

IR (KBr): 1825, 1648, 1452, 1392, 992, 918, 709 cm^{-1}.

^{1}H NMR (200 M Hz, δ, $CDCl_3$): 0.9 (t, 3H, CH_3), 1.2–1.5 (m, 4H, 2×CH_2), 1.7 (s, 3H, CH_3), 2.0 (t, 2H, CH_2), 4.7 (d, 2H, $=CH_2$) ppm.

(2-methylprop-2-enyl) benzene (**7**): To a previously flushed three necked flask, Li_2MnCl_4 (10 mmol, 10 ml, 1M), and 10 mol % of $[Cu(NCMe)_4]BF_4$ were added and stirred at 0 °C for 15 min. 3-chloro-2-methylprop-1-ene (20 mmol, 1.81 gm, 2.0 ml) and $Me_3Si–Cl$ (40 mmol, 5.2 ml) in 10 ml THF were added and stirred for 30 min. Then phenyl magnesium bromide (20 mmol, 14.2 ml, 1.4 M) in dry THF (10 ml) was added dropwise over 20 min with stirring. The completion of reaction was confirmed by TLC. The reaction mixture was hydrolysed with dil HCl and extracted with Et_2O (3 × 20 ml). Purification on a silica gel column gave the pure yellow orange liquid, B.p. 188 °C

IR (KBr) : 3072, 1820, 1640, 1450, 1390, 995, 915, 710 cm^{-1}.

^{1}H NMR (200 MHz, δ, $CDCl_3$) : 1.3 (s, 3H, CH_3), 1.58 (s, 2H, CH_2), 4.9 (d, *J*=2Hz, $=CH_2$), 7.4–7.6 (m, 5H, Ar H) ppm.

1-phenyl pentan-1-one (**9**): To a cooled solution of Li_2MnCl_4 (25 mmol,25 ml, 1 M) was added butyl magnesium bromide (25 mmol, 17 ml, 1.4 M) and the mixture was stirred for 45 min at 0 °C. Then 0.5 mol % $[Cu(NCMe)_2(PPh_3)_2]BF_4$ catalyst was added and stirring continued for another 30 min. Benzoyl chloride (25 mmol, 2.9 ml) in 10 ml dry THF was added dropwise over 20 min and stirred. After completion of reaction, few drops of conc. HCl were added and extracted with Et_2O. After evaporation of solvent gave the solid colourless product was obtained.

IR (KBr) : 1687, 1598, 1584, 1453, 1422, 1326, 1291, 1179, 1127, 1026, 933, 707 cm^{-1}.

^{1}H NMR (200 MHz, δ, $CDCl_3$): 0.94–1.0(t, *J*=3H, CH_3), 1.42–1.53 (m, 2H, CH_2), 1.71–1.76 (quint. 2H, CH_2), 4.29–4.38 (t, *J*=2H, CH_2), 7.3–8.0 (m, 5H, Ar H) ppm.

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