Asian Journal of Chemistry; Vol. 24, No. 6 (2012), 2484-2486

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

One-Pot, Solvent-Free Allylation or Propargylation of Carbonyl Compounds Mediated by the *in situ* Generated Zn-Ag Couple

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(*Received*: 22 April 2011; *Accepted*: 9 January 2012) AJC-10927

Zn-Ag couple which was *in situ* generated by zinc being oxidized with catalytic silver acetate was successfully applied to the one-pot and solvent-free allylation or propargylation of carbonyl compounds, in which high yields, regioselective addition, waste minimization and simple operation can be achieved.

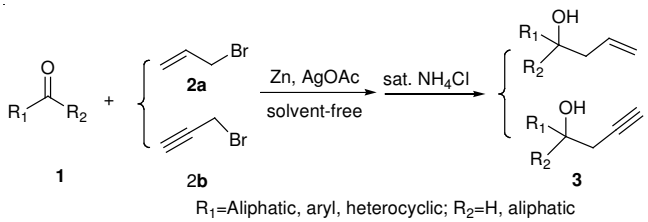
Key Words: Allylation, Propargylation, Zn-Ag couple, One-pot, Solvent-free.

INTRODUCTION

Allylation or propargylation of carbonyl compounds being mediated by some metals which was named the Barbier reaction[1] has been successfully applied recently in the synthesis of various biologically active compounds[2]. So far a variety of metals, such as In[3], Zn[4] and Pb[5] have been reported to be effective in mediating the addition reaction. Among them, zinc, because of its availability and safety, has been demonstrated as a good reagent to mediate the Barbier reaction[4,6]. The latest improvements of the reaction mediated by zinc were achieved by addition of NH_4Cl in this reaction[4a], pre-activation with HCl[6a] or 1,2-dibromoethane[6a], electrochemical protocol[6b,6c]. However, many of these reported methods suffered from one or more shortcomings, such as pre-activation of zinc before reaction[6a], special equipment[6b,6c], unsatisfactory yields, low selectivity for propargylation[7] and the use of solvent. So there is a substantial need to find a new method for integrating the two steps into one-pot form and improving the efficiency of this reaction especially the regioselective addition for propargylation. Herein we report a one-pot, solvent-free allylation or propargylation of carbonyl compounds *via* Barbier reaction mediated by Zn-Ag couple which was *in situ* generated by Zn being oxidized with catalytic AgOAc (**Scheme-I**).

EXPERIMENTAL

Chemicals were reagent, purchased from commercial suppliers and used without further purification. IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer. ^{1}H NMR spectra were obtained on a Bruker Avance DMX 400 MHz in $CDCl_3$ with TMS as an internal standard. ^{13}C NMR spectra were analyzed by a Bruker Avance DMX-500 at 100 MHz. Mass spectra were recorded on a HP5973 at 70 eV.

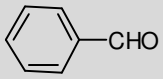
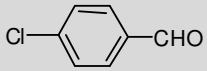
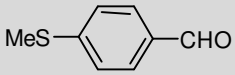
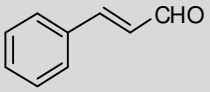
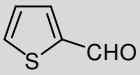
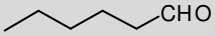
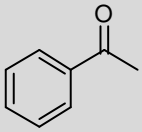
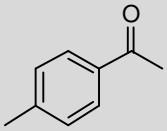
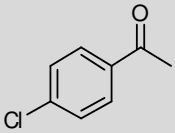
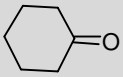


Scheme-1: Allylation or propargylation of carbonyl compounds under SFC mediated by the *in situ* generated Zn-Ag couple

Typical experimental procedure for allylation or propargylation of carbonyl compounds: Commercial fresh zinc powder (15 mmol) and silver acetate (0.30 mmol, 2 % equiv. of zinc) were mixed under nitrogen at room temperature and then stirred for 2 h at 110 ºC. After cooling at 0 ºC, the brown mixture was added carbonyl compounds (10 mmol). Allyl bromide or propargyl bromide (13 mmol.) was added to the mixture over 0.5 h at 0 ºC. 10 mL saturated solution of NH_4Cl was added dropwise after stirring for 2 h. After 3 h, the mixture was extracted with 10 mL ethyl acetate. The separated organic layer was removed in vacuum and the residue was separated by column chromatography (ethyl acetate/petroleum = 1/20) to afford the desired product (Table-1).

Representative spectroscopic data for the compounds: 1-Phenylbut-3-en-1-ol (compound **3a**) colourless oil. IR (neat, ν_{max}, cm^{-1}): 3402, 3074, 3028, 2970, 2929, 1641, 1493, 1454, 1364, 1228, 1052; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.18 (s,

TABLE-1
ALLYLATION OR PROPARGYLATION OF CARBONYL COMPOUNDS WITH **2a**

Entry	Substrate (1)	**2**	Product[b]	Yield[c] (%)
1		**2a**	**3a**	90
2		**2b**	**3b**	89
3		**2a**	**3c**	92
4		**2a**	**3d**	89
5		**2a**	**3e**	82
6		**2a**	**3f**	90
7		**2b**	**3g**	88
8		**2a**	**3h**	75
9		**2a**	**3i**	87
10		**2b**	**3j**	85
11		**2a**	**3k**	87
12		**2b**	**3l**	86
13		**2a**	**3m**	85
14		**2b**	**3n**	91
15		**2a**	**3o**	81
16		**2b**	**3p**	82

[a]Reaction conditions: zinc powder (15 mmol) and AgOAc (0.30 mmol) (2h, 110 ºC), **1** (10 mmol), **2a** or **2b** (13 mmol., added slowly at 0 ºC). [b]All products were characterized by IR, ^{1}H NMR, ^{13}C NMR and MS. Representative spectroscopic data for the compounds were presented in reference **8**. [c]Isolated yields after column chromatography.

1H), 2.49-2.54 (m, 2H), 4.71-4.74 (dd, *J* = 7.4, 5.5 Hz, 1H), 5.13-5.19 (m, 2H), 5.76-5.86 (m, 1H), 7.27-7.36 (m, 5H); ^{13}C NMR($CDCl_3$, 100 MHz): 43.76, 73.30, 118.28, 125.80, 127.48, 128.37, 134.45, 143.87; MS (EI) m/z: 148 (M^+), 147(M^+-1), 131, 115, 107, 91, 79.

1-Phenylbut-3-yn-1-ol (compound **3b**) colourless oil. IR (neat, ν_{max}, cm^{-1}): 3294, 3063, 3031, 2911, 2119, 1955, 1603, 1494, 1454, 1422, 1317, 1202, 1050; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.07-2.09 (t, *J* = 2.6 Hz, 1H), 2.41 (s, 1H), 2.64-2.66 (dd, *J* = 6.3, 2.5 Hz, 2H), 4.86-4.89 (t, *J* = 6.0 Hz, 1H), 7.29-7.41 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): 29.38, 70.91, 72.29, 80.66, 125.73, 127.95, 128.41, 142.44; MS(EI) m/z: 146 (M^+), 115, 107, 79, 77, 55, 51.

(E)-1-Phenylhexa-1,5-dien-3-ol (compound **3e**) colourless oil. IR (neat, ν_{max}, cm^{-1}): 3365, 3077, 3026, 2978, 2905, 1641, 1600, 1493, 1448, 1435, 1239, 1029; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.01(s, 1H), 2.38-2.51(m, 2H), 4.36-4.41(q, *J* = 6.2 Hz, 1H), 5.18-5.23 (m, 2H), 5.84-5.93 (m, 1H), 6.25-6.30(dd, *J* =15.9, 6.3 Hz), 6.62-6.66(d, *J* = 15.9 Hz, 1H), 7.25-7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): 41.98, 71.70, 118.35, 126.46, 127.61, 128.54, 130.32, 131.61, 134.04, 136.68; MS (EI) m/z: 174 (M^+), 141, 133, 115, 105, 102.

1-(Thiophen-2-yl)but-3-yn-1-ol (compound **3g**) pale yellow oil. IR (neat, ν_{max}, cm^{-1}): 3291, 3106, 3089, 2911, 2108, 1608, 1529, 1423, 1382, 1315, 1198, 1038; ^{1}H NMR ($CDCl_3$): δ = 2.07 (t, *J* = 2.5 Hz, 1H), 2.60 (s, 1H), 2.71-2.73(q, *J* = 7.1, 2.9 Hz, 2H), 5.06-5.09 (t, *J* = 6.1 Hz, 1H), 6.91-7.01(m, 2H), 7.23-7.24 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 29.49, 68.47, 71.47, 80.04, 124.09, 124.92, 126.65, 146.11; MS(EI) m/z: 152 (M^+), 133, 113, 85, 58, 51.

Non-1-en-4-ol (compound **3h**) colourless oil. IR (neat, ν_{max}, cm^{-1}): 3346, 3077, 2956, 2930, 2859, 1641, 1487, 1430, 1378, 1125, 1029; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.88-0.91(t, *J* = 6.7 Hz, 3H), 1.30-1.48 (m, 8H), 1.71 (s, 1H), 2.11-2.18 (m, 1H2), 2.27-2.33 (m, $1H_2$), 3.61-3.63 (m, 1H), 5.11-5.15 (m, 2H), 5.78-5.88 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.92, 22.54, 25.26, 31.79, 36.73, 41.87, 70.66, 117.83, 134.89; MS(EI) m/z: 125, 111, 100, 83, 77.

2-*p*-Tolylpent-4-yn-2-ol (compound **3l**) colourless oil. IR(neat, ν_{max}, cm^{-1}): 3440, 3026, 2976, 2923, 2118, 1982, 1608, 1514, 1455, 1374, 1274, 1232, 1094; ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.66 (s, 3H), 2.07-2.09 (t, *J* = 2.5 Hz, 1H), 2.38 (s, 3H), 2.46 (s, 1H), 2.68-2.81 (qd, *J* = 16.7, 2.5 Hz, 2H), 7.19-7.21(d, *J* = 8.0 Hz, 2H), 7.40-7.42(d, *J* = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 20.97, 29.21, 34.55, 71.64, 73.08, 80.55, 124.62, 128.91, 136.69, 143.40; MS (EI) m/z: 175(M^+ + 1), 157, 135, 119, 115, 91, 77.

2-(4-Chlorophenyl)pent-4-yn-2-ol (compound **3n**) colourless oil. IR (neat, ν_{max}, cm^{-1}): 3445, 3048, 2977, 2931, 2113, 1985, 1597, 1491, 1455, 1399, 1272, 1093, 1012; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.62(s, 3H), 2.04-2.06 (t, *J* = 2.4 Hz, 1H), 2.42 (s, 1H), 2.63-2.75 (qd, *J* = 16.7, 2.4 Hz, 2H), 7.30-7.32 (d, 2H), 7.39-7.42 (d, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 29.17, 34.50, 71.99, 72.93, 79.97, 126.26, 128.31, 132.92, 144.78; MS (EI) m/z: 195 (M^+ + 1), 177, 155, 139.

1-(Prop-2-ynyl)cyclohexanol (compound **3p**) colourless oil. IR (neat, ν_{max}, cm^{-1}): 3309, 2934, 2849, 2120, 1946, 1446, 1361, 1304, 1242, 1149, 1112; ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.21-1.27 (m, 10H), 1.83 (s, 1H), 2.04-2.05 (t, *J* = 2.5 Hz, 1H), 2.32(d, *J* = 2.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 22.08, 25.51, 32.78, 36.67, 70.39, 71.36, 80.61; MS(EI) m/z: 139 (M^+ + 1), 138, 129, 123, 121, 99, 81, 72.

RESULTS AND DISCUSSION

First, to evaluate the effects of different Zn-Ag couples in the reaction, a series condensation of **2a** (13 mmol) and benzaldehyde (10 mmol) under SFC at 0 ºC as a model were studied when Zn (15 mmol) was *in situ* oxidized by catalytic amount of different metal salts such as $FeCl_2$, $Pb(OAc)_2$, $SnCl_2$, AgOAc at 110 ºC for 2 h. Although the yield was only 68 % when the reaction was carried out with no metal salts being added, the yields under these conditions reached 75, 83, 78 and 90 %, respectively. Among these results, Zn-Ag couple which was generated by zinc reacting with silver acetate had the best effect. So we further extended the generality of the reaction to coupling various carbonyl compounds with allyl or propargyl bromide under SFC using 2 % mol. of silver acetate for *in situ* generated Zn-Ag couple (Table-1).

The results in Table-1 show that the allylation of various carbonyl compounds can precede in high yields by this method. For propargylation, the reported isomerized products homoallenyl alcohols[4,7] could not be detected from ^1H and ^{13}C NMR in present reaction, so it is believed that the reaction was regioselective besides productive (Table-1, entries 2, 7, 10, 12, 14, 16). Either allyl or propargyl bromide, the yields of alcohols from coupling with aromatic carbonyl compounds were higher than with aliphatic carbonyl compounds under the same reaction conditions.

Conclusion

In summary, we described an efficient, one-pot and green method to couple carbonyl compounds with allyl or propargyl bromide under solvent-free conditions mediated by Zn-Ag couple which was *in situ* generated by Zn being oxidized with catalytic AgOAc. The main advantages of this method are as follows: excellent yields (the yields rise to 75-92 % for allyl bromide and rise to 82-91 % for propargyl bromide), easy operation, regioselective addition for propargylation and avoidance of organic solvents.

ACKNOWLEDGEMENTS

The work was supported by the National Natural Science Foundation of China (20976160).

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