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Mild and convenient method for acetylation of alcohols with $NaBH_4/Cu(dmg)_2$ system

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ABSTRACT

During the past decades, sodium borohydride as a key reagent has played an important roel in the reduction of organofunctional groups in modern organic synthesis. This reagent is a relatively mild reducing agent and mostly used for the reduction of aldehydes and ketones in protic solvents. It is also know that the reducing capability of $NaBH_4$ greatly could be accelerated by using many of additives. Therefor, controlling the reducing power of sodium borohydride has been one of the main interests for organic chemists in many years. Transformation of alcohol to the corresponding acetates is typically carried out using $NaBH_4/Cu(dmg)_2$ in refluxing ethyl acetate in high to excellent yields.

KEYWORDS

Alcohol;
Acetate;
Sodium borohydride;
(dimethylglyoximato)
Copper(II);
Ethyl acetate.

INTRODUCTION

The conversion of alcohols to esters is an important synthetic transformation that has received considerable attention[1,2]. Conversion of an alcohol to the corresponding acetate is typically carried out using acetic anhydride or acetyl chloride in the presence of pyridine or triethylamine as a catalyst[3,4]. 4-(Dimethylamino) pyridine is known to cause a remarkable rate acceleration in the reaction[5]. In addition to catalysis by tertiary amines, Lewis acids have also been reported to catalyze the acetylation of alcohols. Examples include TMSCl[6], $MgBr_2$[7], $Sc(AcO)_3$-$(CF3SO_2)_2NH$[8], $TiCl_4$ + $AgClO_4$[9], $CoCl_2$[10], as well as $Sn(OTf)_2$, $Cu(OTf)_2$ and $In(OTf)_3$[11-13]. A highly efficient catalyst, $Sc(OTf)_3$, was introduced by Yamamoto[14]. However most of the reported methods suffer from one or more of the following disadvantages: long reaction time, vigorous reaction conditions, the occurance of side reactions and unavailability of the reagents, as well as poor yields of the desired product. Thus, there is still a demand to develop new and mild methods for the acetylation of alcohols in the presence of inexpensive and bench top reagents[15-17].

Transformation of alcohols to acetyl esters is one of the most important methods which has been received considerable attentions in organic synthesis specially in protection of functional groups. This goal was carried out in the presence of various reagents in acetic anhydride as a source of acetyl moiety[18,19]. However most of the reported methods suffer from one or more disadvantages such as using Ac_2O as an acidic and high boiling solvent, long reaction times, vigorous reaction conditions, occurrence of side reactions, unavailability of the reagents and poor yields of the desired products. Thus, there is still a demand to develop new and mild methods to convert alcohol to acetyl esters in the presence of inexpensive and bench top reagents[20,21]. Herein, we wish to report a clean, simple and efficient protocol for acetylation of alcohols using $NaBH_4/Cu(dmg)_2$ sys-

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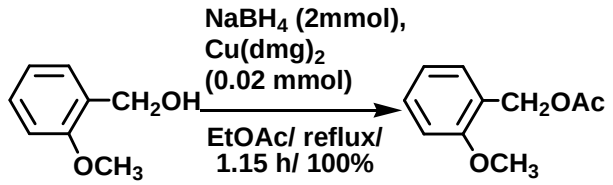
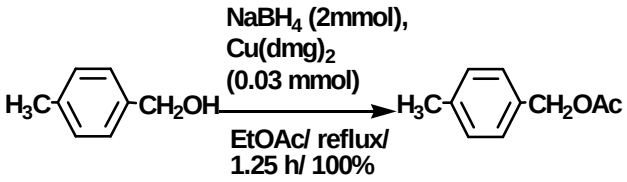
tem in refluxing EtOAc.



Scheme 1



Scheme 2

EXPERIMENTAL

General

All reagents and substrates were purchased from commercial sources with the best quality and were used without further purification. IR and ^1H NMR spectra were recorded on Thermo Nicolet Nexus 670 FT–IR and 300 MHz BrukerAvance spectrometers, respectively. The products were characterized by a comparison with authentic samples (melting or boiling points) and their ^1H NMR or IR spectra. All yields refer to isolated pure products. TLC was applied for the purity determination of substrates, products and reaction monitoring over silica gel 60 F254 aluminum sheet.

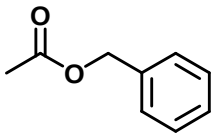
Preparation of catalyst (dimethylglyoximato) copper (II)

Dimethylglyoxime and $Cu(OAc)_2.H_2O$ were added into absolute ethanol to get brown precipitates of $Cu(dmg)_2$[4].

Reduction of alcohols to acetates with $NaBH_4/Cu(dmg)_2$ system in ethyl acetate; typical procedure

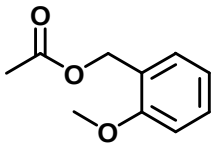
In a round-bottom flask (10 mL) equipped with a magnetic stirrer, a mixture of benzyl alcohol (0.106 g, 1 mmol) in EtOAc (2mL) was prepared. $Cu(dmg)_2$ (0.02mmol) was then added and the resulting mixture was stirred for 2 min at room temperature. Afterward, $NaBH_4$ (2 mmol) was added and the mixture was continued to stirring for 1.10 h. TLC monitored the progress of the reaction (eluent, CH_2Cl_2/Et_2O:5/2). The mixture was extracted with CH_2Cl_2 (3 × 8 mL), dried over anhydrous Na_2SO_4. Evaporation of the solvent affords the pure benzyl acetate in 96% yield (TABLE 1, entry 1).

Selected data for Benzyl acetate (1)



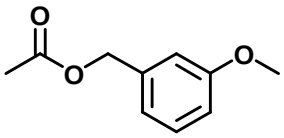
FT-IR (cm^{-1}): 3066, 2954, 1742, 1455, 1381, 1230, 1027, 748, 699. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): δ 2.12 (s, 3H, CH_3CO), 5.13 (s, 2H, CH_2) 7.38 (s, 5H, Ar). ^{13}C NMR (62.5 MHz, DMSO-d6, δ ppm): δ 21.01, 66.32, 126.98, 128.26, 128.57, 135.93, 170.92.

Selected data for 2-Methoxybenzyl acetate (2)



FT-IR (cm^{-1}): 2940, 2839, 1739, 1665, 1496, 1465, 1381, 1248, 1029, 755. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): δ 2.12 (s, 3H, CH_3CO), 3.86 (s, 3H, CH_3O), 5.18 (s, 2H, CH_2), 6.94 (m, 2H, Ar), 7.31 (q, *j* 7.5 Hz, 2H, Ar). ^{13}C NMR (62.5 MHz, DMSO-d6, δ ppm): δ 21.06, 55.42, 61.75, 110.48, 120.42, 124.23, 129.59, 129.76, 157.54, 171.02.

Selected data for 3-Methoxybenzyl acetate (3)

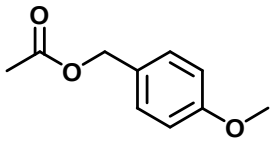


FT-IR (cm^{-1}):2950, 2839, 1741, 1600, 1460, 1378, 1232, 1161, 1038, 784, 694.^1H NMR (300 MHz, $CDCl_3$, δ ppm):δ 2.12 (s, 3H, CH_3CO), 3.83 (s, 3H, CH_3O), 5.10 (s, 2H, CH_2), 6.87 (d, *j* 2.1 Hz, 1H, Ar), 6.91 (d, *j* 3.9 Hz, 1H, Ar), 6.95 (d,*j* 7.5 Hz, 1H, Ar), 7.30 (t, *j* 7.8 Hz, 1H, Ar). ^{13}C NMR (62.5 MHz, DMSO-d6, δ ppm):δ 20.97, 55.22, 66.15, 113.69, 113.73, 120.39, 129.62, 137.46, 159.76, 170.81.

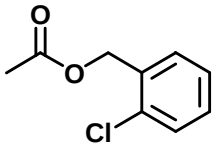
Selected data for 4- Methoxybenzyl acetate (4)

FT-IR (cm^{-1}):2957, 2838, 1738, 1613, 1516,

1242, 1177, 1031, 824.[1]H NMR (300 MHz, $CDCl_3$, δ ppm):δ 2.08 (s, 3H, CH_3CO), 3.81 (s, 3H, CH_3O), 5.05 (s, 2H, CH_2), 6.90 (d, *j* 8.1 Hz, 2H, Ar), 7.30 (d, *j* 7.2 Hz, 2H, Ar).[13]C NMR (62.5 MHz, DMSO-d6, δ ppm):δ 21.04, 55.27, 66.11, 113.94, 128.57, 130.09, 159.66, 170.91.

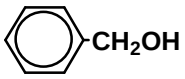
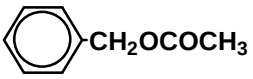
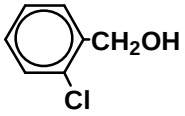
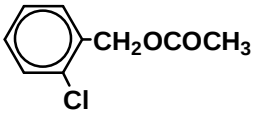
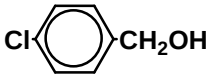
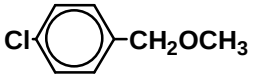
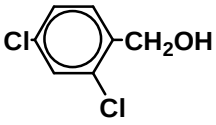
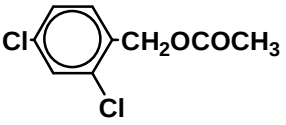
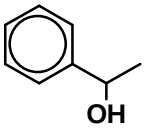
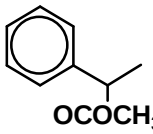
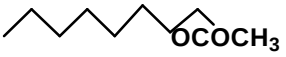
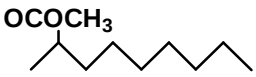
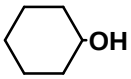
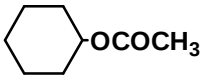
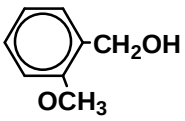
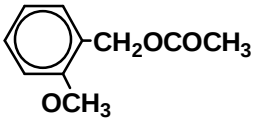
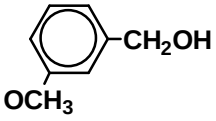
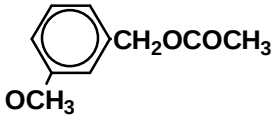
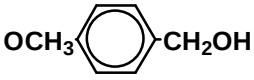
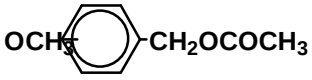
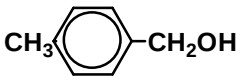
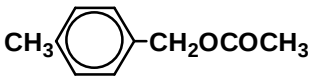


Selected data for 2-Chlorobenzyl acetate (5)



FT-IR (cm^{-1}):3068, 2931, 1743, 1444, 1380, 1233, 1034, 755. [1]H NMR (300 MHz, $CDCl_3$, δ ppm):δ 2.15 (s, 3H, CH_3CO), 5.23 (s, 2H, CH_2), 7.37 (m, 4H, Ar).[13]C NMR (62.5 MHz, DMSO-d6, δ ppm):δ 20.872, 63.638, 126.939, 128.246, 128.710,

TABLE 1 : Acetylation of alcohols with $NaBH4/Cu(dmg)_2$ systema

Entry	Substrate	Product	Molar ratio[b]	Time (h)	Yield (%)[c]
1			1:2:0.02	1.10	96
2			1:2:0.05	2	96
3			1:2:0.05	2	91
4			1:2:0.05	2.25	94
5			1:2:0.06	3	93
6			1:2:0.05	2.15	91
7			1:2:0.06	2.30	95
8			1:2:0.1	2.15	94
9			1:2:0.02	1.15	98
10			1:2:0.03	1.25	95
11			1:2:0.05	1.45	96
12			1:2:0.03	1.25	93

[a]All reactions were carried out in refluxing EtOAc (2 ml); [b]Molar ratio as Subs./$NaBH4/Cu(dmg)_2$; [c]Isolated yields.

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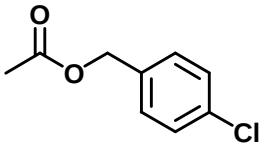
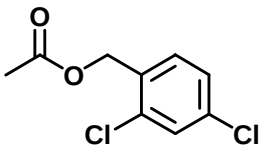
129.563, 133.653, 170.695.

Selected data for 4-Chlorobenzyl acetate (6)



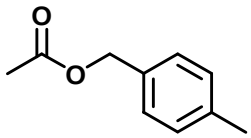
FT-IR (cm^{-1}):2954, 1739, 1493, 1379, 1363, 1228, 1092, 1032, 806, 531.^{1}H NMR (300 MHz, $CDCl_3$, δ ppm):δ 2.11 (s, 3H, CH_3CO), 5.08 (s, 2H, CH_2), 7.32 (q, j= 6, 4H, Ar). ^{13}C NMR (62.5 MHz, DMSO-d6, δ ppm):δ 20.93, 65.43, 128.74, 129.66, 134.14, 134.45, 170.73.

Selected data for 2,4-Dichlorobenzyl acetate (7)



FT-IR (cm^{-1}):2927, 1746, 1591, 1472, 1374, 1229, 1035, 843, 744.^{1}H NMR (300 MHz, $CDCl_3$, δ ppm):δ 2.13 (s, 3H, CH_3CO), 5.17 (s, 2H, CH_2), 7.33 (m, 3H, Ar).^{13}C NMR (62.5 MHz, DMSO-d6, δ ppm):δ 20.78, 62.944, 127.184, 129.44, 130.67, 132.31, 134.39, 134.71, 170.49.

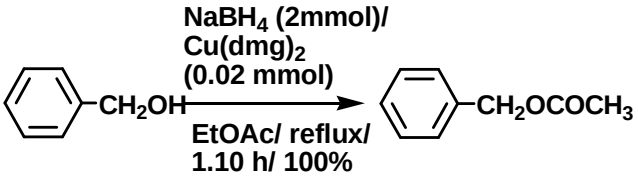
Selected data for 4-Methylbenzyl acetate (8)



FT-IR (cm^{-1}):3027, 2954, 1741, 1518, 1451, 1379, 1230, 1024, 805, 551, 481.^{1}H NMR (300 MHz, $CDCl_3$, δ ppm):δ 2.11 (s, 3H, CH_3CO), 2.38 (s, 3H, CH_3), 5.01 (s, 2H, CH_2), 7.19 (d, *j* 8.1 Hz, 2H, Ar), 7.28 (d, *j* 8.1 Hz, 2H, Ar). ^{13}C NMR (62.5 MHz, DMSO-d6, δ ppm):δ 21.02, 21.18, 66.25, 128.43, 129.24, 132.96, 138.10, 170.91.

RESULT AND DISCUTION

In course of our studies to explore more potentialities of Cu $(dmg)_2$ in organic synthesis, we found that acetylation of benzyl alcohol by $NaBH_4$/Cu $(dmg)_2$ system in ethyl acetate could be carried out. The optimization experiments resulted that conversion of 1 mmol benzyl alcohol to benzyl acetate was carried out perfectly with 2 mmol $NaBH_4$ and 0.02mmol of Cu $(dmg)_2$ in refluxing EtOAc within 1.10 h. This result prompted us to investigate the capability of this system for acetylation of various aliphatic and benzylic alcohols to their corresponding acetates under the optimized conditions. The results of this investigation are summarized in Table 1. As shown, all reactions were completed with 2 mmol of $NaBH_4$ and 0.02-0.1 mmol of Cu $(dmg)_2$ within 1.10-2.30 h to give the corresponding acetates in 91-98% yields (Scheme).



Scheme

CONCLUSION

In conclusion, we have developed an efficient and excellent yielding method for the acetylation of alcohols with ethyl acetate under mild reaction conditions. The reactions are clean and no detectable by-product was found. The products are obtained good to high yields and the procedure is easy.

ACKNOWLEDGMENTS

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