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Study on the Synergistic Effect and Reusability of Copper Methanesulfonate-Acetic Acid in Diacetoxylation of Aldehydes

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Acylals (geminal diacetates) are used as protecting groups for aldehydes because of their remarkable stability to acidic, basic and neutral media[1]. In addition, acylals have been applied as crosslinking reagents for cellulose in cotton[2] and served as important precursors for the preparation of 1-acetoxydienes for Diels-Alder reactions[3]. Usually, acylals are prepared from aldehydes and Ac_2O in the presence of an acidic catalyst. Different acid catalysts for this conversion have been reported including H_2NSO_3H[4], $LiBF_4$[5], NBS[6], $Bi(NO_3)_3 5H_2O$[7], $InCl_3$[8], $Cu(OTf)_2$[9], PCl_3[10], $Zn(ClO_4)_2 5H_2O$[11], and I_2[12] etc. However, above methods are not satisfied due to the prolonged reaction time, high temperature, and moisture sensitive and non-recoverable catalysts. Many reactions must be carried out in poisonous solvent or under N_2 atmosphere. It is necessary to propose an eco-friendly protocol to replace conventional methods.

Recently, the use of $Cu(CH_3SO_3)_2 \cdot 4H_2O$ (CMS) as water tolerant Lewis acid catalyst in organic synthesis has been paid much attention[13,14]. In the course of further study, we developed CMS-HOAc as an effective combined catalyst for diacetoxylation. In this catalytic system, CMS or HOAc used alone did not induce the reaction (Table 1). A powerful synergistic effect was observed when they were mixed together. Aromatic aldehydes with electron-withdrawing group required longer reaction time than with electron-donating group. In all cases, the reactions proceed moderately and no by-product was detected almost by GC.

Take the diacetoxylation of benzaldehyde as model reaction, the relationship between conversion of benzaldehyde and reaction time was shown in Fig. 1. It clearly revealed that the increasing of HOAc greatly improved the reaction rate. These results demonstrated both CMS and HOAc were indispensable for the reaction. These observations were consistent with the effect of Br nsted acid-assisted Lewis acid catalysis, which produce the active catalytic species (Scheme 1)[15,16]. In this complex, the aldehyde experienced "double activation" through coordination to the Lewis acid Cu^{2+} and through hydrogen bonding with the acid proton. These interactions would facilitate electrophilic attack into the aldehyde. What is more, the CMS with less nucleophilic counter anion $CH_3SO_3^-$ is more cationic, and the high Lewis acidity promotes the desired reaction.

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Table 1 CMS-HOAc combined system catalyzed conversion of aldehydes to acylals

$$RCHO + Ac_2O \xrightarrow[\text{solvent-free r. t.}]{\text{CMS-HOAc}} RCH(OAc)_2$$

Entry	Aldehyde	Time (h)	Yield (%)[a]	
			Cat: CMS	Cat: CMS-HOAc
1	PhCHO	51	–	0[b]
2	PhCHO	1.3	9	94
3	2-ClC_6H_4CHO	8	0	85
4	3-ClC_6H_4CHO	6	0	87
5	2-$CH_3OC_6H_4CHO$	2.5	8	81
6	4-$CH_3OC_6H_4CHO$	2.5	7	78
7	4-$CH_3C_6H_4CHO$	3	6	75
8	CH_3CH_2CHO	7	0	73
9	2-$NO_2C_6H_4CHO$	12	0	80
10	3-$NO_2C_6H_4CHO$	10	0	86
11	4-$NO_2C_6H_4CHO$	12	0	84

[a]Isolated yields after crystallization or column chromatography separation

[b]Only HOAc was used.

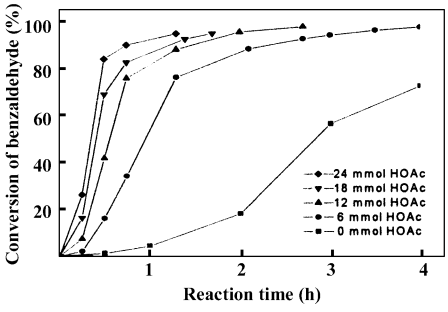
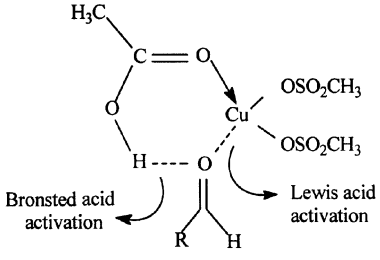


Fig. 1 Conversion of benzaldehyde vs. reaction time in the presence of different amount of HOAc



Scheme 1 "double-activation" of aldehyde

CMS is a blue crystal catalyst, which is insoluble in reactants and products in this reaction. In order to demonstrate whether CMS can be reused, CMS was filtered after the product was extracted by CH_2Cl_2. CMS was reused for six runs in the model reaction of benzaldehyde with Ac_2O, the results were listed in Table 2. A little decrease in product yields may be due to the loss of CMS during filtration.

Table 2 Reuse of CMS for synthesis of benzylidene diacetate[a]

Run	Yield (%)[b]
1	94
2	91
3	90
4	88
5	87
6	85

[a]Reaction time 1.3 h, HOAc 12 mmol

[b]Yields were analysed by GC.

In conclusion, we have demonstrated the mixing CMS and HOAc leads to a powerful synergistic effect for the conversion of aldehydes to acylals. The advantages of the new combined catalyst are simple operation, mild condition and inexpensive, no corrosive and reusable catalyst, which provide an atom economic and environmentally friendly procedure.

Experimental

Melting points were determined by using RY-1 micro melting point apparatus and were uncorrected. GC analysis was carried out on a Perkin Elmer Auto System XL Gas Chromatograph. Infrared spectra were recorded on Spectrum GX series Fourier Transform instrument of Perkin Elmer. ^1H NMR spectra were recorded on Bruker ARX-300 spectrometer in $CDCl_3$ using TMS as an internal standard. Elemental analyses were carried

out on EA 2400II elemental analyzer (Perkin-Elmer). The preparation of CMS has been described in our previous research[13]. In this experiment, CMS is the same size for it has been grounded in agate mortar before use.

Typical procedures for the preparation of acylals: Aldehyde 15 mmol, Ac_2O 30 mmol, CMS 0.3 mmol, and HOAc 12 mmol were added to a 30 mL conical flask. The mixture was magnetic stirred at room temperature for an appropriate time (minitored by GC). After the reaction, most of the mixture solidified gradually, 20 mL CH_2Cl_2 was added to dissolve the solid product. The organic layer was washed twice with saturated $NaHCO_3$ solution (20 mL), dried (Na_2SO_4) and evaporated to yield the almost pure product. The product was purified further by crystallization from cyclohexane or by flash column chromatography on silica gel (ethyl acetate/hexane, 1:9 as the eluent). All the acylals were characterized by IR, ^1H NMR and elemental analysis.

Entry **2**: white crystal, m. p. 44 ~ 45 C. IR (KBr) ν: 1 760, 1 510, 1 440, 1 250,1 220, 1 010 cm^{-1}; ^1H NMR δ: 7.69 (s, 1H, CH), 7.55-7.51 (m, 2H, ArH), 7.42-7.40 (m, 3H, ArH), 2.14 (s, 6H); Anal. Calcd. For $C_{11}H_{12}O_4$: C, 63.46; H, 5.81; O, 30.74. Found: C, 63.49; H, 5.82; O, 30.72.

Entry **3**: white crystal, m. p. 55 ~ 57 ℃. IR (KBr) ν: 1 749, 1 445, 1 366, 1 237, 1 199, 1 015, 995 cm^{-1}; ^1H NMR δ: 8.21 (s, 1H, CH), 8.07-8.04 (m, 1H, ArH), 7.73-7.70 (m, 2H, ArH), 7.73-7.59 (m, 1H, ArH), 2.14 (s, 6H); Anal. Calcd. For $C_{11}H_{11}O_4Cl$: C 54.45; H, 4.57; O, 26.37. Found: C, 54.48; H, 4.56; O, 26.38.

Entry **4**: white crystal, m. p. 64 ~ 66 ℃. IR (KBr) ν: 3 060, 3 020, 1 760, 1 605, 1 480, 1 210, 1 010 cm^{-1}; ^1H NMR δ: 7.50 (s, 1H, CH), 7.45-7.34 (m, 4H, ArH), 2.10 (s, 6H); Anal. Calcd. For $C_{11}H_{11}O_4Cl$: C 54.45; H, 4.57; O, 26.37. Found: C, 54.44; H, 4.58; O, 26.35.

Entry **5**: white crystal, m. p. 73 ~ 75 ℃. IR (KBr) ν: 3 020, 2 980, 1 761, 1 605, 1 495, 1 465, 1 370, 1 245, 1 200, 1 050, 995, 950, 760 cm^{-1}; ^1H NMR δ: 8.02 (s, 1H, CH), 7.49-6.91 (m, 4H, ArH), 3.82 (s, 3H), 2.12 (s, 6H); Anal. Calcd. For $C_{12}H_{14}O_5$: C, 60.50; H, 5.92; O, 33.58. Found: C, 60.53; H, 5.91; O, 33.57.

Entry **6**: white crystal, m. p. 62 ~ 64 ℃. IR (KBr) ν: 2 940, 1 765,1 645, 1 520, 1 400, 1 245, 1 210 cm^{-1}; ^1H NMR δ: 7.45 (s, 1H, CH), 7.34 (d, 2H, ArH), 6.74 (d, 2H, ArH), 3.80 (s, 3H), 2.14 (s, 6H); Anal. Calcd. For $C_{12}H_{14}O_5$: C, 60.50; H, 5.92; O, 33.58. Found: C, 60.47; H, 5.91; O, 33.59.

Entry **7**: white crystal, m. p. 80 ~ 82 ℃. IR (KBr) ν: 2 928, 1 770, 1 368, 1 244, 1 206, 1 068, 960 cm^{-1}; ^1H NMR δ: 7.65 (s, 1H, CH), 7.43 (d, 2H, ArH), 7.20 (d, 2H, ArH), 2.32 (s, 3H), 2.09 (s, 6H); Anal. Calcd. For $C_{12}H_{14}O_4$: C, 64.85; H, 6.35; O, 28.80. Found: C, 64.91; H, 6.33; O, 28.79.

Entry **8**: colorless liquid, b. p. 71 ~ 73 ℃/18 torr. IR (KBr) ν: 3 000, 1 760, 1 460, 1 432, 1 246, 1 204, 1 115, 1 061, 1 014, 966 cm^{-1}; ^1H NMR δ: 6.72 (t, 1H, CH), 2.10 (s, 6H, $2COCH_3$), 1.40-2.13 (m, 2H, CH_2), 1.02 (t, 3H, CH_3); Anal. Calcd. for $C_7H_{12}O_4$: C, 52.49; H, 7.55; O 39.96. Found: C, 52.52; H, 7.53; O, 39.93.

Entry **9**: off-white crystal, m. p. 82 ~ 84 ℃. IR (KBr) ν: 2 938, 1 765, 1 354, 1 260, 1 202, 972 cm^{-1}; ^1H NMR δ: 8.21 (s, 1H, CH), 8.08-8.05 (m, 1H, ArH), 7.69-7.62 (m, 2H, ArH), 7.65-7.57 (m, 1H, ArH), 2.15 (s, 6H); Anal. Calcd. for $C_{11}H_{11}NO_6$: C, 52.18; H, 4.38; O, 37.91. Found: C, 52.14; H, 4.39; O, 52.17.

Entry **10**: off-white crystal, m. p. 62 ~ 64 ℃. IR (KBr) ν: 2 954, 1 760, 1 530, 1 376, 1 247, 1 210, 1 010, 815, 670 cm^{-1}; ^1H NMR δ: 8.4 (s, 1H, CH), 8.27 (dd, 1H, ArH), 7.83 (d, 1H, ArH), 7.74 (s, 1H, ArH), 7.62 (t, 1H, ArH), 2.17 (s, 6H); Anal. Calcd. for $C_{11}H_{11}NO_6$: C, 52.18; H, 4.38; O, 37.91. Found: C, 52.15; H, 4.40; O, 37.92.

Entry **11**: off-white crystal, m. p. 122 ~ 124 ℃. IR (KBr) ν: 1 763, 1 610, 1 530, 1 350, 1 234,

1 204, 1 062, 1 012, 978 cm^{-1}; ^1H NMR δ: 8.27 (d, 2H, CH), 7.74 (s, 1H, CH), 7.71 (d, 2H), 2.17 (s, 6H); Anal. Calcd. for $C_{11}H_{11}NO_6$: C, 52.18; H, 4.38; O, 37.91. Found: C, 52.14; H, 4.39; O, 37.93.

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甲基磺酸铜-醋酸催化醛的双乙酰化反应的协同效应及重复使用性研究

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摘　要:甲基磺酸铜-醋酸作为协同催化体系, 在室温条件下催化醛生成相应的 1,1-双乙酸酯取得了较高收率. 反应结束后, 甲基磺酸铜可被回收重复使用, 重复使用多次未见明显失活.

关　键　词:双乙酸酯; 甲基磺酸铜; 协同效应; 重复使用