Pinacol coupling of aromatic aldehydes mediated by Zn in aqueous oxalic acid under ultrasound irradiation

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Pinacol coupling of aromatic aldehydes mediated by Zn powder in aqueous oxalic acid gives the corresponding pinacols in 33–83% yields within 2.5 h at r.t. under ultrasound irradiation.

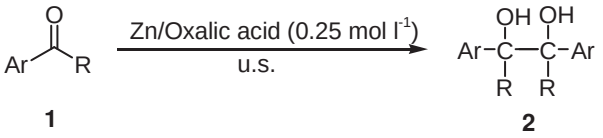
Keywords: pinacol coupling, aromatic aldehyde, ultrasound irradiation

1,2-Diols are very useful synthons for a variety of organic syntheses,[1] and have been used as intermediates for the construction of biologically important natural product skeletons.[2] The formation of 1,2-diols has been attempted using a number of regents such as Mg,[3] Mn,[4] Al,[5] In,[6] transition metal,[7,8] and rare earth metals.[9] However, some of these reductants are expensive or the reduction conditions are critical. These reactions are often also associated with the toxic reagents and heavy metals, which would lead to economic and environmental concerns.

Organic reactions in aqueous media have attracted increasing interest currently because of environmental issues and the understanding of biochemical processes. Water offers many practical and economic advantages as a reaction solvent, including low cost, safe handling and environmental compatibility. Recently, pinacol coupling reactions in aqueous media have been described in the literature.[3,5] However, these methods so far suffer from harsh reaction and work-up conditions, using an excess amount of metal or a long reaction time.

Ultrasound has increasingly been used in organic synthesis in the last three decades. Compared with traditional methods, this technique is more convenient and easily controlled. A large number of organic reactions can be carried out in higher yields, for shorter reaction times and under milder conditions under ultrasound irradiation.[10] Lim et al.[6] reported the reaction of aromatic aldehydes with indium in neutral aqueous media using sonication affording the corresponding diols in moderate to good yields; Basu *et al.* [7] reported the reduction of several aromatic ketones to diols by samarium in the presence of ammonium chloride under sonication at room temperature, and the reaction could be completed within 5 minutes; Mecarova and Toma[11] reported pinacol coupling reactions in aqueous media under ultrasound irradiation and found that ultrasound considerably accelerates the benzaldehydes' conversion. Recently, Liu and Zhang[12] reported pinacol coupling of aromatic carbonyl compounds promoted by Zn powder in dilute hydrochloric acid. Our laboratory has also reported the pinacol coupling of aromatic aldehydes and ketones in aqueous media under ultrasound irradiation.[13-16] To the best of our knowledge, there are no literature examples of pinacol coupling of aromatic aldehydes and ketones using Zn powder in aqueous oxalic acid under ultrasound irradiation. Herein, we wish to report the results of the pinacol coupling of aromatic aldehydes by Zn in aqueous oxalic acid under ultrasound irradiation.

As shown in Table 1 and Scheme 1, pinacol coupling of some aromatic aldehydes was carried out in good yield using Zn powder in aqueous oxalic acid under ultrasound irradiation. It is shown that the yield of pinacol coupling of 2-ClC_6H_4CHO (**1a**) in 0.25 mol l^{-1} aqueous oxalic acid (81%, **2a**[b]) was similar to that in 1 mol l^{-1} aqueous oxalic acid (79%, **2a**[a]).



1 **2**

Scheme 1

Table 1 Pinacol coupling of carbonyl compounds in aqueous oxalic acid under ultrasound irradiation

Entry	Substrates	Isolated yield / %	*dl / meso*	R_f [h]
a	2-ClC_6H_4CHO	79[a] 81[b]	28/72	0.45
b	3-ClC_6H_4CHO	82 83[c] 65[d] 79[e] 78[f] 72[g]	46/54	0.44
c	4-$CH_3C_6H_4CHO$	48 49[c]	56/44	0.29
d	3-BrC_6H_4CHO	79	30/70	0.50
e	2,4-$Cl_2C_6H_3CHO$	78	20/80	0.45
f	$PhCOCH_3$	68	54/46	0.52
g	PhCHO	63	57/43	0.28
h	4-ClC_6H_4CHO	65	43/57	0.22
i	3,4-$(OCH_2O)C_6H_3CHO$	45	55/45	0.22
j	4-$CH_3OC_6H_4CHO$	45	51/49	0.11
k	PhCH=CHCHO	33	50/50	0.16

[a]Using 1 mol l^{-1} oxalic acid as the reaction media. [b]Using 0.25 mol l^{-1} oxalic acid as the reaction media. [c]The reaction time is 5 h. [d]The reaction time is 1 h. [e]The ultrasound irradiation frequency is 40 kHz. [f] The ultrasound irradiation frequency is 59 kHz. [g] The amount of Zn is 0.13 g. [h] Silica gel TLC Eluent: petroleum ether /diethyl ether (V: V = 1:1).

When prolonging the reaction time from 2.5 h to 5 h, the yield of pinacol increased from 82%(**2b**) to 83% (**2b**[c]). However, on decreasing the reaction time from 2.5 h to 1 h, the yield of pinacol decreased from 82% to 65% (**2b**[d]).

The effect of Zn powder on the pinacol coupling of 3-ClC_6H_4CHO (**1b**) has been investigated. Using 3 mmol or 2 mmol Zn in 0.25 mol l^{-1} aqueous oxalic acid under 25 kHz ultrasound irradiation for 2.5 h, the yields of pinacol were 82% (**2b**) and 72% (**2b**[g]) respectively. Ultrasound irradiation frequency has little effect on this reaction system. For example, pinacol coupling of 3-ClC_6H_4CHO (**1b**) under 25 kHz, 40 kHz or 59 kHz irradiation, the yield of pinacol was 82% (**2b**), 79% (entry **2b**[e]) and 78% (**2b**[f]), respectively. So, the reaction conditions we chosen were: 0.25 mol l^{-1} aqueous oxalic acid, 25 kHz irradiation frequency, 0.195 g (3 mmol) Zn powder.

Electron-withdrawing groups in the aromatic ring of aromatic aldehydes (**1a**, **1b**, **1d, 1e**) increase the reactivity. In contrast, the aromatic aldehydes with electron–donating groups (**1c**, **1j**) show less reactivity. The steric hindrance

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around the carbonyl group (**1i**) inhibits the coupling reaction. No coupling of 3-ClC_6H_4CHO (**1b**) took place when Zn powder was replaced by Mg or Al powder.

In the present system, high yields of pinacol could be obtained when the substrates are 2,4-$Cl_2C_6H_3CHO$ (78%) and 4-ClC_6H_4CHO (65%) compared with the reaction system using aqueous H_2NSO_3H and H_3PO_4 [17] (the corresponding yields are 54% and 42% using H_2NSO_3H, 42% and 34% using H_3PO_4, respectively) after 2.5 h ultrasound irradiation. When the substrate is $PhCOCH_3$, the yield of pinacol is 68% compared with the yield of 16% in $Mg/MgCl_2$ aqueous[18] under ultrasound irradiation. The pinacol coupling reaction can form *dl* and *meso* stereoisomers. In the present process, higher amounts of *meso* stereoisomer are obtained (**2a**, **2d**, **2e**) or in other cases the amount is nearly 50%.

In summary, ultrasound irradiation can efficiently prompt pinacol coupling of some aromatic aldehydes in acidic aqueous media. The main advantages of the present procedure are the milder reaction conditions, inexpensive catalyst and operational simplicity.

Experimental

Liquid aldehydes were distilled before use. IR spectra were recorded on a Bio-Rad FTS-40 spectrometer (KBr). MS were determined on a VG-7070E spectrometer (EI, 70 eV). ^{1}H NMR spectra were measured on a Bruker AVANCE 400 (400 MHz) spectrometer using TMS as internal standard and $CDCl_3$ as solvent. Sonication was performed in a Shanghai Branson-CQX ultrasonic cleaner (with a frequency of 25kHz and a nominal power 250W) and an SK 250 LH ultrasonic cleaner (with a frequency of 40kHz, 59kHz and a nominal power 250W, Shanghai Kudos ultrasonic instrument Co., Ltd). The reaction flasks were located in the maximum energy area in the cleaner, where the surface of reactants is slightly lower than the level of the water. The reaction temperature was controlled by addition or removal of water from the ultrasonic bath.

General procedure for the pinacol coupling of aromatic aldehydes in aqueous oxalic acid under ultrasound irradiation: A 10 ml Pyrex flask was charged with the desired aldehyde (1 mmol), Zn powder (0.195 g, 3 mmol) and $H_2C_2O_4$ (0.25 mol l^{-1}, 5 ml). The mixture was irradiated in the water bath of an ultrasonic cleaner under air at 25–30°C for 2.5 h. After the completion of the reaction, the resulting suspension was filtered to remove the Zn powder and the filtrate was extracted with ethyl acetate (3×15 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous magnesium sulfate for 12 h and filtered. Ethyl acetate was evaporated under reduced pressure to give the crude product, which was separated by column chromatography on silica (200–300 mesh), eluted with petroleum ether or a mixture of petroleum ether and diethyl ether. All the products were confirmed by comparing their R_f values on TLC with that of the authentic samples from previous studies, and IR, MS, ^{1}H NMR and spectroscopic data.[15-19]

2a: ^{1}H NMR: δ 2.66 (2H, s, OH, *meso*), 2.76 (2H, s, OH, *dl*), 5.39 (2H, s, CH, *dl*), 5.63 (2H, s, CH, *meso*), 7.17–7.70 (16H, m, Ph–H). *m/z* (%): 282 (1), 165 (47), 141 (89), 113 (13), 107 (14), 77 (100), 51 (38). IR (KBr) ν_{max} : 3100–3500.

2b: ^{1}H NMR: δ 3.29 (4H, b, OH), 4.56 (2H, s, CH, *dl*), 4.74 (2H, s, CH, *meso*), 6.87–7.36 (16H, m, Ph–H). *m/z* (%): 263 (1.2), 251 (1.6), 178 (4.6), 165 (4.6), 141 (100), 113 (23.8), 77 (71.0). IR (KBr) ν_{max} : 3260–3318.

2c: ^{1}H NMR: δ 2.31(12H, s, CH_3), 2. 60 (4H, s, OH), 4.69 (2H, s, CH, *dl*), 4.75 (2H, s, CH, *meso*), 7.04–7.26 (16H, m, Ph–H). *m/z* (%): 242 (1.2), 195 (6), 121 (100), 107 (12), 77 (13). IR (KBr) ν_{max} : 3280–3450.

2d: ^{1}H NMR: δ 2.36 (2H, s, OH, *meso*), 2.93 (2H, s, OH, *dl*), 4.65 (2H, s, CH, *dl*), 4.81 (2H, s, CH, *meso*), 6.97–7.46 (16H, m, Ph–H). *m/z* (%): 325 (6), 186 (16), 157 (8), 107 (7), 77 (100), 51 (13). IR (KBr) ν_{max} : 3200–3500.

2e: ^{1}H NMR: δ 3.46 (4H, s, OH), 5.15 (2H, s, CH, *dl*), 5.47(2H, s, CH, *meso*), 7.10–7.26 (12H, m, Ph–H). *m/z* (%): 352 (1), 305 (1.4), 233 (10), 175 (100), 145 (10), 111 (25), 77 (15). IR (KBr) ν_{max} : 3320–3400.

2f: ^{1}H NMR: δ 1.46 (6H, s, CH_3, *dl*), 1.53 (6H, s, CH_3, *meso*), 2.52 (2H, s, OH, *meso*), 2.68 (2H, s, OH, *dl*), 7.03–7.36 (20H, m, Ph–H). *m/z* (%): 225 (4), 206 (4), 181 (32), 165 (9), 121 (100), 105 (12), 77 (11), 43 (80). ν_{max} : 3100–3600.

2g: ^{1}H NMR: δ 2.20 (2H, s, OH, *meso*), 2.83 (2H, s, OH, *dl*), 4.72 (2H, s, CH, *dl*), 4.84 (2H, s, CH, *meso*), 7.14–7.32 (20H, m, Ph–H). *m/z* (%)**:** 214 (1), 180 (7.6), 167 (12.5), 149 (6.0), 107 (93.8), 79 (100), 77 (73.8). IR (KBr) ν_{max} : 3200–3480.

2h: ^{1}H NMR: δ 2.87 (4H, s, OH), 4.63 (2H, s, CH, *dl*), 4.84 (2H, s, CH, *meso*) 7.02–7.26 (16H, m, Ph–H). *m/z* (%): 276 (14), 249 (32), 155 (100), 111 (8). IR (KBr) ν_{max} : 3380–3420.

2i: ^{1}H NMR (DMSO as solvent): δ 4.44 (4H, s, OH), 5.14 (2H, s, CH, *dl*), 5.27 (2H, s, CH, *meso*), 5.96 (8H, s, CH_2), 6.52–6.82 (12H, m, Ph–H). *m/z* (%): 302 (1), 284 (2.5), 268 (5.0), 255 (11.8), 151 (100), 123 (32), 93 (77.1), 65 (39.0). IR (KBr) ν_{max} : 3100–3600.

2j: ^{1}H NMR: δ 2.95 (4H, s, OH), 3.75 (12 H, s, OCH_3, *dl*), 3.79 (12 H, s, OCH_3, *meso*), 4.64 (2H, s, CH, *dl*), 4.72 (2H, s, CH, *meso*), 6.84–7.52 (16H, m, Ph–H). *m/z* (%): 276 (14), 249 (32), 155 (100), 111 (8). IR (KBr) ν_{max} : 3300–3600.

2k: ^{1}H NMR: δ 1.79 (4H, s, OH), 4.44 (2H, s, –CH–OH, *dl*), 4.63 (2H, s, –CH–OH, *meso*), 6.29 (4H, t, –CH=CH–), 4.63 (2H, s, –CH=CH–), 6.94–7.13 (20H, m, Ph–H). *m/z* (%): 282 (1), 266 (15), 221 (12), 177 (24), 162 (26), 151 (30), 135 (23), 120 (70), 85 (38), 77 (17), 57 (100). IR (KBr) ν_{max} : 3300–3500.

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