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Pinacol Coupling Reaction of Benzaldehyde Mediated by TiCl_3 -Zn in Basic Media under Ultrasound Irradiation

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Abstract: Pinacol coupling of benzaldehyde mediated by TiCl_3 -Zn in basic media under ultrasound irradiation can lead to the corresponding pinacol rapidly. The optimum reaction condition is chosen.

Key words: Pinacol coupling, low valent titanium, basic media, ultrasound

Introduction

The pinacol coupling, which was described in 1859, is still a useful tool for the synthesis of vicinal diols¹. 1, 2-Diols have been used as intermediates for the construction of biologically important natural product skeletons and asymmetric ligands for catalytic asymmetric reaction². In particular, the pinacol coupling has been employed as a key step in the construction of HIV-protease inhibitors³. The formation of 1, 2-diol has been attempted using a number of reagents such as Mg⁴, Mn⁵, Al⁶, In⁷, and so on.

Low valent titanium is a highly reactive reagent for carbonyl-coupling reactions⁸. In 1973, Mukaiyama firstly reported that TiCl_4 -Zn reduced aromatic aldehydes and ketones to produce pinacols in high yield⁹, but the stereoselectivity was not reported. In 1982, Clerici reported pinacol coupling of aromatic aldehydes and ketones promoted by aqueous TiCl_3 in basic media¹⁰.

Ultrasound (u.s) has increasingly been used in organic synthesis. Mearová¹¹ reported the pinacol coupling reaction in aqueous media under u.s and found that ultrasound considerably accelerated the benzaldehyde conversion. Our laboratory has also reported the pinacol coupling of aromatic aldehydes and ketones in aqueous media under u.s¹². Herein, we wish to report the result of the pinacol coupling of benzaldehyde by TiCl_3 -Zn in aqueous NaOH under ultrasound irradiation (**Scheme 1**).

Scheme 1 Pinacolization of benzaldehyde under ultrasound irradiation

Experimental

Benzaldehyde was distilled before use. IR spectra were recorded on Bio-Rad FTS-40 spectrometer (KBr). MS were determined on a VG-7070E spectrometer (EI, 70 eV). ¹H NMR spectra were measured on Bruker AVANCE 400 (400 MHz) spectrometer using TMS as internal standard and CDCl_3 as solvent. Sonication was performed in Shanghai Branson-CQX ultrasonic cleaner (with a frequency of 25kHz and a nominal power 250W) and SK 250 LH ultrasonic cleaner (with a frequency of 40 kHz and a nominal power 250 W; 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 ultrasonic bath.

Procedure for the pinacol coupling of benzaldehyde under u.s

A 50 ml round flask was charged with Zn power (1.8 mmol) and 15% TiCl_3 solution (1.5 mmol). The mixture was irradiated in the water bath of an ultrasonic cleaner at r.t., after 15 minutes, a solution of benzaldehyde (1 mmol) in 2mL EtOH was added, and then the 10% NaOH solution (4.5 ml) was added. After the completion of the reaction, the mixture 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 MgSO_4 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 a mixture of petroleum ether and diethyl ether. 1, 2-diphenyl-1, 2-ethanediol was confirmed by MS, IR, ¹H NMR spectral data.

Compound 2: ¹H NMR: δ 2.28 (2H, s, OH, *meso*), 2.92 (2H, s, OH, *dl*), 4.73 (2H, s, CH, *dl*), 4.85 (2H, s, CH, *meso*), 7.14-7.45 (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 cm^{-1} .

Results and Discussion

Low valence titanium has stronger reducing power in basic media. As shown in **Table 1**, the effect of the amount of 10% NaOH has been investigated. Without addition of the aqueous NaOH solution, **2** was obtained in 41% yield within 60 min (Entry **a**). Increasing the amount of NaOH, the yield of **2** increased to 48%, 52%, 58% and 59% respectively (Entry **b**, **c**, **d** and **e**).

The molar ratio of TiCl_3 to Zn had some effect on the reaction. When the molar ratio of TiCl_3 to Zn was 1:1, the yield of **2** was obtained in 58%. Changing the molar ratio of TiCl_3 to Zn to 1:0.8, 1:1.2, 1:1.4, 1:1.6 and 1:3, the yield of **2** were 55%, 66%, 66%, 68% and 69% respectively (Entry **f**, **g**, **h**, **i**, **j**). When the molar ratio of TiCl_3 to Zn was 1:1.2, **2** had good yield.

Table 1 Effects of the reaction condition on pinacolization of benzaldehyde under u.s

Entry	Molar ratio of PhCHO:TiCl ₃ : Zn	10%NaOH (mL)	Frequency (kHz)	Time (min)	Isolated yield (%)	
					2	3
a	1:1:1	0	25	60	41	18
b	1:1:1	1	25	40	48	21
c	1:1:1	2	25	25	52	18
d	1:1:1	3	25	25	58	26
e	1:1:1	4	25	25	59	18
f	1:1:0.8	3	25	25	55	24
g	1:1:1.2	3	25	25	66	13
h	1:1:1.4	3	25	25	66	16
i	1:1:1.6	3	25	25	68	12
j	1:1:3	3	25	25	69	23
k	1:1.2:1.44	3.6	25	25	72	16
l	1:1.5:1.8	4.5	25	25	78	12
m	1:2:2.4	6	25	25	76	16
n	1:2.5:3	7.5	25	25	77	15
o	1:1.5:1.8	4.5	40	25	58	9
p	1:1.5:1.8	4.5	Stir.	25	51	8

Moreover, the effect of the molar ratio of C₆H₅CHO to TiCl₃ was investigated. Changing the molar ratio of C₆H₅CHO to TiCl₃ to 1:1.2 and 1:1.5, the yields of the 1, 2-diols increased to 72% and 78% respectively (Entry **j**, **k**). When the molar ratio of C₆H₅CHO to TiCl₃ increased to 1:2 and 1:2.5, the yields of the 1, 2-diols were 76% and 77% respectively (Entry **m**, **n**), which were similar to 78%. When the molar ratio of C₆H₅CHO to TiCl₃ was 1:1.5, **2** had good yield.

We also investigated the effect of frequency of ultrasound irradiation and stirring on the reaction. While under 40 KHz ultrasound irradiation and stirring, the yields of 1, 2-diol were 58% and 51% respectively (entry **o**, **p**), which are lower than 78% (entry **l**, the yield of **2** under 25 KHz ultrasound irradiation). It is clear that ultrasound can accelerate the pinacolization, and the higher yield can be obtained when the frequency of ultrasound irradiation was 25 kHz.

From the results we obtained, the optimum reaction conditions we chose were: C₆H₅CHO (1 mmol), TiCl₃ (1.5mmol), Zn (1.8 mmol) and 10% NaOH solution (4.5 mL), ultrasound irradiation under 25 kHz.

The pinacol coupling reaction can form *dl* and *meso* stereoisomers. In the reaction system, the ratio of *dl* and *meso* of **2** is about 3/2.

Conclusion

Pinacol coupling of benzaldehyde mediated by TiCl₃-Zn in basic media under ultrasound irradiation can lead to the corresponding pinacol rapidly. When the molar ratio of C₆H₅CHO:TiCl₃: Zn was

1:1.5:1.8, the mount of 10% NaOH was 4.5 mL, and the frequency of ultrasound irradiation was 25 kHz, the yield of pinacol coupling of benzaldehyde was 78%. The ratio of *dl* and *meso* of 1, 2-diol was about 3/2.

References

- 1 Robertson G M *Comprehensive Organic Synthesis*, Ed. Trost, B M Pergamon: New York, 1991.
- 2 Seyden-Penne J *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, John Wiley & Sons, New York, 1995.
- 3 (a) Kammermeier B, Beck G, Jacobi D and Jendralla, H *Angew Chem Int Ed Engl* 1994, **33**, 685-687; (b) Reetz M T and Griebenow N *Liebigs Ann.* 1996, **1996**(3), 335-348.
- 4 Zhang W C and Li C J *J Org Chem*, 1999, **64**, 3230-3236.
- 5 Rieke R D and Kim S H *J Org Chem*, 1998, **63**, 5235-5239.
- 6 Khurana J M and Sehgal A, *J Chem Soc, Chem Commun*, 1994, 571.
- 7 Lim H J, Keum G, Kang S B, Chung B Y and Kim Y *Tetrahedron Lett*, 1998, **39**, 4367-4368.
- 8 McMurry J E, *Chem Rev*, 1989, **89** (7), 1513-1524.
- 9 Mukaiyama T, Sato T and Hanna J, *Chem Lett*, 1973, (10), 1041-1044.
- 10 Clerici A and Porta O *Tetrahedron Lett*, 1982, **23** (34), 3517-3520.
- 11 Mæroková M and Toma C *Green Chem*, 1999, 257-259.
- 12 (a) Zang H J, Li J T, Ning N, Wei N and Li T S *Indian J Chem*, 2002, **41B**, 1078-1080. (b) Yang J H, Li J T, Zhao J L and Li T S *Synth. Commun.* 2004, **34**, 993. (c) Li J T, Chen Y X, Yang J H and Li T S, *J Chem Research*. 2004, (7), 494.