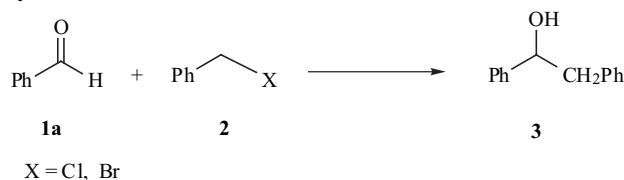


Table 1. Benzylation of Benzaldehyde under Various Conditions



Entry	X	Condition ^[a]	Yield (%) ^[b] /Time (h)
1	Br	Zn	0/12
2	Br	Zn/CdCl ₂ ^[c]	5 ^[f] /12
3	Br	CdCl ₂	0/12
4	Br	Cd	0/24
5	Br	Mg/CdCl ₂	-[g], [h]/24
6	Br	Al/CdCl ₂	-[g]/24
7	Br	Zn/CdCl ₂ ^[d]	56/3
8	Br	Zn/CdCl ₂	65/3
9	Cl	Zn/CdCl ₂	84/3
10	Br	Zn/SnCl ₂	5/3
11	Br	Zn/BiCl ₃	0/3
12	Br	Zn/InCl ₃	0/3
13	Br	Zn/CdCl ₂ /InCl ₃ ^[e]	80/3
14	Cl	Zn/CdCl ₂ /InCl ₃ ^[f]	92/3
15	Cl	Zn/CdCl ₂ /BiCl ₃ ^[f]	65/3
16	Cl	Zn/CdCl ₂ /SnCl ₂ ^[f]	72/3

^[a] 2.0 equiv. of zinc powder and 1.0 equiv. of Lewis acid unless noted

^[b] Isolated yield

^[c] 0.1 equiv. of CdCl₂ based on benzaldehyde

^[d] 0.5 equiv. of CdCl₂ based on benzaldehyde

^[e] 0.5 equiv. of InCl₃ based on benzaldehyde

^[f] 0.1 equiv. of InCl₃, BiCl₃, SnCl₂ based on benzaldehyde

^[g] Pinacol coupling product was observed

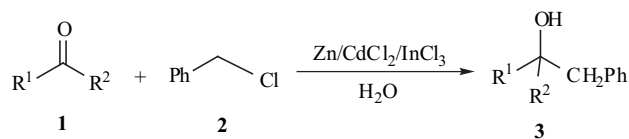
^[h] Determined by GC-MS

chloride (2.0 mmol), Zn powder (2.0 mmol), CdCl₂ (1.0 mmol), and InCl₃ (0.1 mmol) in water (5.0 mL) was stirred at room temperature for a period as shown in Table 2. Then the mixture was extracted with ethyl acetate and the organic layer was dried over anhydrous MgSO₄ for 2 h. The organic solvent was removed under reduced pressure. The residue was purified by column chromatography to afford pure product, which was characterized by IR, MS, ¹H and ¹³C NMR spectra.

As shown in Table 2, all the aromatic aldehydes were benzylated effectively to afford the desired product in high yields (entries 1-11, Table 2). The aromatic aldehydes with hydroxyl group were successfully employed in this reaction without protection (entries 10, 11, Table 2), yielding the corresponding 1,2-diaryl-ethanols. The conjugated aliphatic aldehyde was also benzylated in good yield (entry 12). However, the reaction of aliphatic aldehydes afforded only the corresponding products in poor yields (entries 13 and

14). The ketones could not be benzylated these conditions (entries 15-17) since they are less reactive than the aldehydes.

The different reactivity of aldehydes and ketones suggests a useful chemo-selectivity of this benzylation reaction in water [9]. So an equimolecular mixture of an aromatic aldehyde and a ketone was used in the benzylation reaction mediated by Zn/CdCl₂/InCl₃ in water. As shown in Table 3, all the reactions yielded the 1,2-diaryl alcohols exclusively from the aldehydes while the ketones were not benzylated (entries 1, 2, 3). The chemo-selectivity was studied when aldehyde and ketone functional groups are in the same molecule. When using this tri-metal system, the benzylation of 4-acetylbenzaldehyde (**1r**) afforded exclusively the product (**3r**) in 94% yield without any reaction on the ketone moiety (Eq. 1). These results indicated that Zn/CdCl₂/InCl₃ could selectively mediate the benzylation of an aldehyde in the presence of a ketone.

Table 2. Benzylation of Various Carbonyl Compounds Using Zn/CdCl₂/InCl₃ in Water

Entry	R1	R2	Yield (%) ^[a] /Time (h)
1	Ph (1a)	H	92/3
2	4-benzo[3,4]dioxole (1b)	H	87/4
3	α-Naphth (1c)	H	82/4
4	α-Furan (1d)	H	95/3
5	4-Cl-Ph (1e)	H	93/4
6	4-Me-Ph (1f)	H	88/4
7	4-MeO-Ph (1g)	H	83/4
8	2-Cl-Ph (1h)	H	95/4
9	2-MeO-Ph (1i)	H	85/4
10	2-OH-Ph (1j)	H	76/3
11	2-OH-5-MeO-Ph (1k)	H	78/3
12	PhCHCH (1l)	H	75/5
13	H (1m)	H	30/6
14	CH ₃ (CH ₂) ₅ (1n)	H	25/6
15	Ph (1o)	Me	0/6
16	4-Cl-Ph (1p)	Me	0/6
17	4-MeO-Ph (1q)	Me	0/6

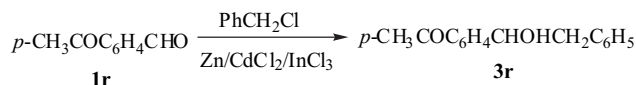
[a] Isolated yield

Table 3. Benzylations of a Mixture of Different Aldehydes and Ketones Using Zn/CdCl₂/InCl₃ in Water^[a]

Entry	Substrate	Product	Yield (%) ^[b] /Time(h)
1	1a, 1o	3a	85/3
2	1e, 1p	3e	87/4
3	1g, 1q	3g	82/4

[a] Standard procedure unless noted

[b] Isolated yield



Eq. (1).

The recycling of the mediation system was studied since cadmium compound is toxic. In order to recover CdCl₂ and InCl₃, the reaction mixture was extracted with ethyl acetate and the organic layer was washed with water for 3 times. Then the combined aqueous layers were concentrated. ICP-MS determination of cadmium amount in the organic layer showed that more than 99.99% cadmium was in the aqueous phase. The reactivity of recovered CdCl₂ and InCl₃ was

investigated. To the recovered CdCl₂ and InCl₃ were added 1.0 mmol of benzaldehyde, 2.0 mmol of benzyl chloride and 2.0 mmol of zinc powder. Then the reaction mixture was allowed to stir at room temperature for 3 h. The reaction mixture was treated in the same manner as mentioned above and the yield was determined by the analysis of ¹H NMR and GC-MS. As indicated in the table below, recovered CdCl₂ and InCl₃ with added Zn can effectively mediate the benzylation reaction even after several recycles. Thus, the toxic reagent in this system is not only completely recovered but also efficiently re-used.

Table 4. The Recycling of CdCl₂ and InCl₃^[a]

Recycle time	1	2	3	4
Reaction yield	89	88	84	78

[a] Yields were determined by ¹H NMR and GC-MS

CONCLUSION

In conclusion, this study has demonstrated that the benzylations of aldehydes in water is achieved by using a novel tri-metal system (Zn/CdCl₂/InCl₃). This tri-metal system can selectively mediate the benzylation of an aldehyde in the presence of a ketone. CdCl₂ and InCl₃ are easily recycled and used in this reaction without further purification.

ACKNOWLEDGEMENTS

The authors are grateful to National Nature Science Foundation of China (No.50073021) and National Nature Science Foundation of Anhui Province (No. 01046301) for their support.

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