Manganese-Mediated Reactions in Aqueous Media: Chemoselective Allylation and Pinacol Coupling of Aryl Aldehydes

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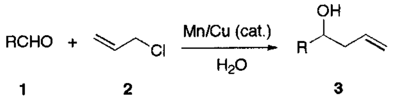
The pursuit of synthetic targets with increasing complexity has resulted in the development of reactions which emphasize chemo-, regio-, diastereo-, and enantioselectivity. In defining strategies and reactions to construct complex molecules, chemoselectivity is required.[1] Metal-mediated carbonyl addition generally has a low chemoselectivity among different carbonyls. Recently, the exploration of aqueous medium metal-mediated reactions[2] has shown the potential for unusual chemoselectivity.[3] Here, we wish to report an unprecedented chemoselectivity related to metal-mediated carbonyl addition between aromatic and aliphatic aldehydes.[4] The allylation of aldehydes[5] mediated by manganese in water in the presence of a catalytic amount of copper shows exclusive selectivity toward aromatic aldehydes. Manganese was found to be equally selective in promoting pinacol-coupling reactions of aryl aldehydes.

The recent interest in aqueous medium metal-mediated carbon−carbon bond formations led to the continuing search for more reactive and selective metal mediators for such reactions. As a starting point, we have studied the use of manganese[6] as a potential useful mediator for metal-promoted reactions. When benzaldehyde was stirred with 1 equiv of allyl chloride and a mixture of manganese−copper[7] in water for 8 h at room temperature, 62% of the corresponding allylation product was isolated.[8] When 3 equiv of allyl chloride and manganese mediator was used, the isolated yield of the allylation product increased to 83%. Interestingly, changing allyl chloride to the usually more reactive allyl bromide decreased the yield of the allylation product (36%) under the same reaction conditions. Such a seemingly abnormal behavior is most likely due to a competing Wurtz-type coupling of the allyl bromide.[9] Throughout the reaction process, no apparent change of pH value (6−7) of the media was observed. The combined use of manganese and copper appears critical. No reaction was observed with either manganese or copper alone as the metal mediator. Only a catalytic amount of copper is required for the reaction. The use of a catalytic amount of Cu(0), Cu(I), or Cu(II) gave the same result. On the other hand, the use of a stoichiometric amount of Cu combined with a catalytic amount of Mn (allyl chloride/Mn/Cu = 3:0.1:3) provided less than 5% of the desired product. The use of a catalytic amount of Mn(II) or Mn(III) in place of Mn metal completely depressed the product formation. Subsequently, a variety of aldehydes were tested with this allylation method (eq 1).

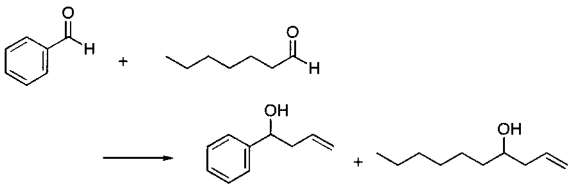


(1)

1 2 3

Selected examples are listed in Table 1. It was found that various aromatic aldehydes were allylated efficiently by allyl chloride and manganese in water. It is noteworthy to mention that aromatic aldehydes bearing halogens were allylated without any problem (entries 9−11). The allylation of a hydroxylated aldehyde was equally successful (entry 12). On the other hand, aliphatic aldehydes are inert under the reaction conditions (entry 15).[10] Such an unusual reactivity difference between an aromatic aldehyde and an aliphatic aldehyde suggests the possibility of an unprecedented chemoselectivity.

To test this hypothesis, competitive studies were carried out between aliphatic and aromatic aldehydes with different methods (eq 2). By using the present combination, a single allylation of benzaldehyde was generated when a mixture of heptaldehyde and benzaldehyde was reacted with allyl chloride. Such a selectivity appears unique; aqueous methodologies mediated by other metals (Zn, Sn, In) all generated a 1:1 mixture of allylation products of both aldehydes. A 1:1 mixture of products was also generated when the allylation was performed with allylmagnesium bromide[11] in ether.



(2)

An intramolecular discrimination study has also been carried out on a compound bearing both aromatic and aliphatic carbonyl groups; a complete chemoselectivity

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[1] Trost, B. M. *Science* **1985**, *227*, 908.

[2] For reviews, see: Li, C. J. *Tetrahedron* **1996**, *52*, 5643. Chan, T. H.; Isaac, M. B. *Pure Appl. Chem.* **1996**, *68*, 919. Li, C. J. *Chem. Rev. (Washington, D.C.)* **1993**, *93*, 2023. Lubineau, A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741.

[3] Yanagisawa, A.; Inoue, H.; Morodome, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 10356. Petrier, C.; Eihorn, J.; Luche, J. L. *Tetrahedron Lett.* **1985**, *26*, 1449.

[4] For studies toward effecting the selectivity of carbonyl addition between ketones and aldehydes, see: Reetz, M. T.; Wenderoth, B. *Tetrahedron Lett.* **1982**, *23*, 5259. Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179. Naruta, Y.; Ushida, S.; Maruyama, K. *Chem. Lett.* **1979**, 919; see also ref 3.

[5] For a recent review, see: Yamamoto, Y. *Chem. Rev. (Washington, D.C.)* **1993**, *93*, 2207.

[6] For recent studies on manganese-mediated reactions, see: Cahiez, C.; Laboue, B. *Tetrahedron Lett.* **1989**, *30*, 7369. Hiyama, T.; Obayashi, M.; Nakamura, A. *Organometallics* **1982**, 1, 1249. Cahiez, G.; Alami, M. *Tetrahedron Lett.* **1989**, *30*, 7373; **1990**, *31*, 7423. Furstner, A.; Brunner, H. *Tetrahedron Lett.* **1996**, *37*, 7009. Takai, K.; Ueda, T.; Ikeda, N.; Moriwake, T. *J. Org. Chem.* **1996**, *61*, 7990−7991. Takai, K.; Ueda, T.; Hayashi, T.; Moriwake, T. *Tetrahedron Lett.* **1996**, *37*, 7049−7052.

[7] Commercially available manganese and copper powders were used directly without pretreatment.

[8] Some allyl chloride was lost during the reaction due to its low boiling point.

[9] Kasatkin, A. N.; Tsypyshev, O. Y.; Romanova, T. Y.; Tolstikov, G. A. *Organomet. Chem. USSR* **1989**, *2*, 830.

[10] Such a reactivity difference may be originated from the difference in reductive potentials of aliphatic and aromatic aldehydes. A related selectivity was recently observed in the allylation of carbonyl compounds with an allylmanganese reagent in organic solvent; see: Cahiez, G. *An. Quim.* **1995**, *91*, 561. We thank the reviewer for pointing out this reference to us.

[11] Wakefield, B. J. *Organomagnesium Methods in Organic Chemistry*; Academic Press: New York, 1995.

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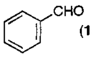
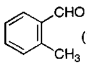
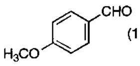
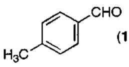
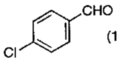
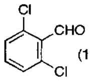
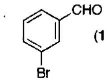
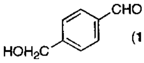
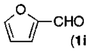
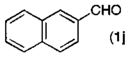
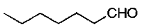
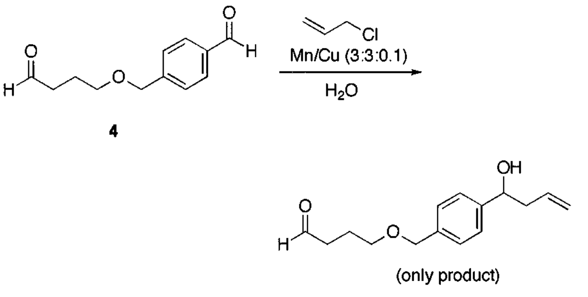
Table 1. Allylation of Aldehydes Mediated by Mn–Cu in Aqueous Medium

entry	substrates	conditions	product	yield (%)
1	 (1a)	A	2a	83
2	(1a)	B	2a	62
3	(1a)	C	2a	36
4	(1a)	D	2a	0
5	(1a)	E	2a	0
6	 (1b)	A	2b	72
7	 (1c)	A	2c	74
8	 (1d)	A	2d	62
9	 (1e)	A	2e	81
10	 (1f)	A	2f	68
11	 (1g)	A	2g	51
12	 (1h)	A	2h	66
13	 (1i)	A	2i	59
14	 (1j)	A	2j	54
15	 (1k)	A	2k	0

Reaction conditions: A: allyl chloride/Mn/Cu (3:3:0.1); B: allyl chloride/Mn/Cu (1:1:1); C: allyl bromide/Mn/Cu (1:1:1); D: allyl chloride/Mn (3:3); E: allyl chloride/Cu (3:3).

was observed in which the reaction occurs exclusively on the aromatic carbonyl (eq 3).



4

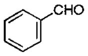
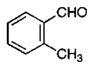
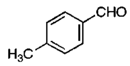
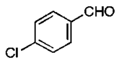
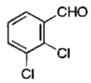
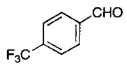
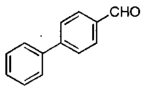
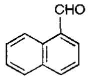
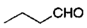
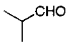
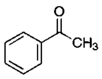
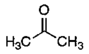
(only product)

5

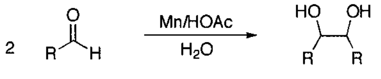
(3)

The pinacol-coupling reaction is another fundamental reaction in organic chemistry.[12] The pinacol-coupling reaction in water mediated by Ti(III) has been extensively studied.[13] Other metals such as Zn–Cu have been also found to promote this reaction under ultrasonic radiation in aqueous acetone.[14] When benzaldehyde was reacted with manganese in the presence of a catalytic amount of acetic acid in water, the corresponding pinacol-coupling product was obtained smoothly. Other aryl aldehydes (eq 4) were coupled similarly (Table 2). On the other hand, aryl and aliphatic ketones appeared to be inert under the same reaction conditions, and only the reduced product was obtained with aliphatic aldehydes.

Table 2. Pinacol-Coupling of Aldehydes Mediated by Mn in Aqueous Medium

entry	substrates	product	yield (%)^a	threo:erythro^b
1		6a	74	44:56
2		6b	70	56:44
3		6d	62	56:44
4		6e	90	51:49
5		6f	85	48:52
6		6g	quantitative	59:41
7		6h	92	55:45
8		6i	84	56:44
9		reduced		
10		reduced		
11		no reaction		
12		no reaction		

The reactions were carried out with carbonyl compound (1 mmol), manganese (2.5 mmol) and acetic acid (0.1 mmol) in water (3 mL) at r.t. for 16 hrs. a: isolated yields; b: measured by ^{1}H NMR.


$$2\ RCHO \xrightarrow[H_2O]{Mn/HOAc} RCH(OH)CH(OH)R \qquad (4)$$

6

In conclusion, manganese is highly effective for mediating aqueous medium carbonyl allylations and pinacol-coupling reactions. This metal offers a higher reactivity (compared with previously reported ones) and a complete chemoselectivity toward aromatic aldehydes in the allylation of carbonyl compounds and in pinacol coupling.

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Supporting Information Available: Experimental procedures for the allylation and pinacol-coupling reactions and complete characterization of all new compounds reported herein (2 pages).

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(12) For a recent review, see: Wirth, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 61–63.

(13) For recent publications, see: Gansauer, A. *J. Chem. Soc., Chem. Commun.* **1997**, 457–458. Barden, C.; Schwartz, J. *J. Am. Chem. Soc.* **1996**, *118*, 5484–5485.

(14) Delair, P.; Luche, J. L. *J. Chem. Soc., Chem. Commun.* **1989**, 398.