

Manganese-Mediated Carbon–Carbon Bond Formation in Aqueous Media: Chemoselective Allylation and Pinacol Coupling of Aryl Aldehydes

Chao-Jun Li,* Yue Meng, and Xiang-Hui Yi

Department of Chemistry, Tulane University, New Orleans, Louisiana 70118

Jihai Ma and Tak-Hang Chan*

Department of Chemistry, McGill University, Montreal, PQ, Canada H3A 2K6

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The use of manganese as a mediator for allylations and pinacol couplings in aqueous media was investigated. The combination of manganese and copper is found to be a highly effective mediator for the allylation of aryl aldehydes in water. Such a combination is found to be more reactive than other previously reported metals in aqueous media. No reaction was observed with either manganese or copper alone as the mediator. Only a catalytic amount of copper is required for the proceeding of the reaction. The uses of Cu(0), Cu(I), and Cu(II) as the copper source are all effective. The use of a catalytic amount of manganese combined with a stoichiometric amount of copper led to the failure of the reaction. Allyl chloride is found to be more effective than allyl bromide for the corresponding reaction. The use of substituted allyl halides gave a mixture of regio- and diastereoisomers. Aromatic aldehydes reacted chemoselectively in the presence of aliphatic aldehydes. An exclusive selectivity was also observed when both an aliphatic and an aromatic aldehyde functionalities are present in the same molecule. In the presence of acetic acid or ammonium chloride, manganese was found to effect the pinacol-coupling reaction in water. The reaction proceeds selectively with aryl aldehydes.

Introduction

The pursuit of synthetic targets with increasing complexity has resulted in the development of reactions which emphasize chemo-, regio-, diastereo-, and enantioselectivity. In the defining of strategies and reactions to construct complex molecules, chemoselectivity is required.¹ Metal-mediated carbonyl addition generally has a low chemoselectivity among different carbonyls. To effect such a selectivity, previous efforts have shown that it is possible to alkylate an aldehyde in the presence of a ketone with certain selectivity.² Recently the exploration of aqueous medium metal-mediated reactions³ has shown the potential for unusual chemoselectivity. Under such reaction conditions, aldehydes have been shown to be allylated selectively in the presence of ketones by tin reagents.⁴ A considerable challenge is to effect a high chemoselectivity between different aldehydes. Recently we reported a complete chemoselectivity related to metal-mediated carbonyl addition between aromatic and aliphatic aldehydes.⁵ The allylation of aldehydes mediated

by manganese in water in the presence of a catalytic amount of copper shows exclusive selectivity toward aromatic aldehydes. Manganese was found equally selective in promoting pinacol-coupling reactions of aryl aldehydes in the presence of acetic acid or ammonium chloride. Here we report the detailed study on this subject.

Results and Discussion

The recent interest in aqueous medium metal-mediated carbon–carbon bond formation led to the continuing search for more reactive and selective metal mediators for such reactions. Among the reactions, allylations⁶ of carbonyl compounds are studied most extensively.⁷ Metals such as tin, zinc, and indium have been found effective for such transformations. The searching for a more reactive metal mediator could prove difficult, since metals, such as sodium and magnesium, tend to react with water. Metals that rapidly form an oxide shell would not be suitable for mediating carbonyl nucleophilic addition either. When one looks at the reductive potentials of various metals, as well as their reactivity toward water, manganese stands out as a promising candidate. While manganese has a much more negative reductive potential ($E^\circ = -1.18$ eV), pure manganese is not attacked by water. Previously, manganese and manganese-based reagents have been used in a variety of organic trans-

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(2) For early 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. The use of organomanganese reagents was found to give a high selectivity, see: Cahiez, G.; Figadere, B. *Tetrahedron Lett.* **1986**, *26*, 4445.

(3) For recent reviews, see: Li, C. J. *Tetrahedron* **1996**, *52*, 5643. Chan, T. H.; Isaac, M. B. *Pure Appl. Chem.* **1996**, *68*, 919. Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; John Wiley & Sons: New York, 1997. Lubineau, A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741. Li, C. J. *Chem. Rev.* **1993**, *93*, 2023.

(4) 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.

(5) For a preliminary communication of this work, see: Li, C. J.; Meng, Y.; Yi, X. H.; Ma, J. H.; Chan, T. H. *J. Org. Chem.* **1997**, *62*, 8632. Yi, X. H.; Meng, Y.; Ma, J. H.; Chan, T. H.; Li, C. J. Presented at the 215th ACS Meeting, Dallas, TX 1998 (ORGN 237).

(6) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.

formations in organic solvents.⁸ Manganese is also an abundant element which makes manganese-based syntheses practical.

At the starting point, we examined the allylation reaction of various carbonyl compounds. In terms of the relative reactivity, the reaction between allyl chloride and an aldehyde can generally be used as a marker of relative effectiveness for different methods. When benzaldehyde was stirred with allyl chloride and manganese in water overnight at room temperature, no apparent reaction was observed. The addition of aqueous 1 N HCl or saturated NH₄Cl to activate the metal lead to complicated mixtures. Additionally, several aqueous buffer solutions (NH₄Cl–NaOH, Na₂HPO₄, and NaH₂PO₄) were examined as the reaction solvents and no significant improvement was observed. A different approach was subsequently considered. The activation of zinc with copper through the formation of a zinc–copper couple is a well-known process.⁹ When benzaldehyde was stirred with 1 equiv of allyl chloride and a mixture of manganese–copper in water for 8 h at room temperature, 62% of the corresponding allylation product was isolated. Because of the low boiling point of allyl chloride, part of it was lost during the reaction process. When 3 equiv of allyl chloride and manganese mediator was used, the isolated yield of the allylation product increased to 83%.

Thereupon, various combinations of manganese and copper were examined to determine the roles that they played in the reaction process (Table 1). The combined use of manganese and copper appears critical. It is interesting to note that 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.

(7) For examples with various metal-mediators, see the following. Sn: Nokami, J.; Wakabayashi, S.; Okawara, R. *Chem. Lett.* **1984**, 869. Uneyama, K.; Matsuda, H.; Torii, S. *Tetrahedron Lett.* **1984**, 25, 6017. Zn: Petrier, C.; Luche, J. L. *J. Org. Chem.* **1985**, 50, 910. Einhorn, C.; Luche, J. L. *J. Organomet. Chem.* **1987**, 322, 177. Mattes, H.; Benezra, C. *Tetrahedron Lett.* **1985**, 26, 5697. Wilson, S. R.; Guazzaroni, M. E. *J. Org. Chem.* **1989**, 54, 3087. In: Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, 32, 7017. Chan, T. H.; Li, C. J. *J. Chem. Soc., Chem. Commun.* **1992**, 747. Araki, S.; Jin, S. J.; Idou, Y.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1992**, 65, 1736. Kim, E.; Gordon, D. M.; Schmid, W.; Whitesides, G. M. *J. Org. Chem.* **1993**, 58, 5500. Paquette, L.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, 118, 1931. Li, C. J.; Chen, D. L.; Lu, Y. Q.; Haberman, J. X.; Mague, J. T. *J. Am. Chem. Soc.* **1996**, 118, 4216. Wang, R.; Lim, C. M.; Tan, C. H.; Lim, B. K.; Sim, K. Y.; Loh, T. P. *Tetrahedron: Asymmetry* **1995**, 6, 1825. Bi: Wada, M.; Ohki, H.; Akiba, K. Y. *Bull. Chem. Soc. Jpn.* **1990**, 63, 1738; *J. Chem. Soc., Chem. Commun.* **1987**, 708. Katritzky, A. R.; Shobana, N.; Harris, P. A. *Organometallics* **1992**, 11, 1381. Minato, M.; Tsuji, J. *Chem. Lett.* **1988**, 2049. Ge: Akiyama, T.; Iwai, J. *Tetrahedron Lett.* **1997**, 38, 853. For manganese-mediated allylations in organic solvent, see: Hiyama, T.; Obayashi, M.; Nakamura, A. *Organometallics* **1982**, 1, 1249. Cahiez, G.; Chavant, P. Y. *Tetrahedron Lett.* **1989**, 30, 7373 and the patents cited therein (the addition of a small amount of a metal salt, e.g., ZnCl₂, CdCl₂, and HgCl₂, enhanced the reactivity of manganese in aprotic solvent).

(8) For other recent studies on manganese mediated reactions, see: Cahiez, C.; Laboue, B. *Tetrahedron Lett.* **1989**, 30, 7369. Cahiez, C.; Laboue, B. *Tetrahedron Lett.* **1989**, 30, 7369. 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. Coulton, S.; Hanlon, P. J.; Rogers, N. H. *J. Chem. Soc., Perkin 1* **1982**, 729. Friour, G.; Cahiez, G.; Normant, F. *J. Synthesis* **1985**, 50. Furstner, A.; Shi, N. *J. Am. Chem. Soc.* **1996**, 118, 12349. Tang, J.; Yorimitsu, H.; Oshima, K. *Tetrahedron Lett.* **1997**, 38, 9019. Kakiya, H.; Inoue, R.; Oshima, K. *Tetrahedron Lett.* **1997**, 38, 3275. Vaughan, W. S.; Gu, H. H.; McDaniel, K. F. *Tetrahedron Lett.* **1997**, 38, 1885. Inoue, R.; Shinokubo, H.; Koichiro, O. *J. Org. Chem.* **1998**, 63, 910. Takai, K.; Kaihara, H.; Ikeda, N. *J. Org. Chem.* **1997**, 62, 8612. Hojo, M.; Aihara, H.; Akira, H. *J. Org. Chem.* **1997**, 62, 8610. Takai, K.; Ueda, T.; Moriwake, T. *J. Org. Chem.* **1997**, 62, 8728.

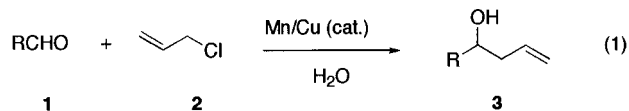
(9) Smith, R. D.; Simmons, H. E. *Org. Synth.* **1961**, 41, 72.

Table 1. Allylation of Benzaldehyde Mediated by Mn–Cu in Water

entry	allyl halide	mediator (equiv)	catalyst (equiv)	yield (%) ^a
1	allyl chloride	Mn (3)	no	0
2	allyl chloride	Cu (3)	no	0
3	allyl chloride	Mn (3)	Cu (0.1)	83
4	allyl chloride	Mn (3)	Cu (3)	(95)
5	allyl chloride	Mn (3)	CuCl (0.1)	(92)
6	allyl chloride	Mn (3)	CuCl ₂ (0.1)	(92)
7	allyl chloride	Cu (3)	Mn (0.1)	(5)
8	allyl chloride	Cu (3)	MnCl ₂ (0.1)	0
9	allyl chloride	Cu (3)	Mn(OAc) ₃ (0.1)	0
10	allyl bromide	Mn (3)	Cu (0.1)	36

^a Isolated yields; yields estimated by ¹H NMR in parentheses.

The uses 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 (3:0.1:3 allyl chloride/Mn/Cu) 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. Different allyl halides were also tested as the allyl moiety. Interestingly, changing allyl chloride to the usually more reactive allyl bromide decreased the yield of the allylation product (36%) under the same reaction conditions. In addition, considerable amounts of byproducts (e.g., reduction and pinacol coupling) were observed when allyl bromide was used instead of allyl chloride. Such a seemingly abnormal behavior is most likely due to a competing Wurtz-type coupling of the allyl bromide, which was confirmed recently during a separate study by one of us.¹⁰ Allyl chloride appeared less effective for the Wurtz-coupling, which provided better a yield of allylation. Throughout the reaction process, no apparent change of pH value (6–7) of the media was observed. Subsequently, a variety of aldehydes were tested with this allylation method (eq 1), and the results are listed in Table 2.



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 various halogens were allylated without any problem (entries 5–7 and 13–15). The allylations of a hydroxylated aldehyde and a cyano-substituted aldehyde, as well as cinnamaldehyde, were equally successful (entries 8, 16, and 12). On the other hand, aliphatic aldehydes are inert under the reaction conditions (entry 11).¹¹ The result could be attributed to the difference in reductive potentials between aliphatic and aromatic aldehydes. Such an unusual reactivity difference between an aromatic aldehyde and an aliphatic aldehyde suggests the possibility of a useful chemoselectivity.

(10) Ma, J.; Chan, T. H. *Tetrahedron Lett.* **1998**, 39, 2499. For a related Wurtz-type reaction in organic solvent, see: Kasatkin, A. N.; Tsyppyshev, O. Y.; Romanova, T. Y.; Tolstikov, G. A. *Organomet. Chem. USSR* **1989**, 1, 830.

(11) 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.

Table 2. Alkylation of Aldehydes Mediated Mn–Cu

entry	substrates	product/yield(%) ^a	entry	substrates	product/yield(%) ^a
1	(1a)	3a/83	9	(1i)	3i/59
2	(1b)	3b/72	10	(1j)	3j/54 ^b
3	(1c)	3c/74	11	(1k)	3k/0
4	(1d)	3d/62	12	(1l)	3l/42
5	(1e)	3e/81 ^b	13	(1m)	3m/78
6	(1f)	3f/68 ^b	14	(1n)	3n/74
7	(1g)	3g/51 ^b	15	(1o)	3o/65
8	(1h)	3h/66 ^b	16	(1p)	3p/63 ^b

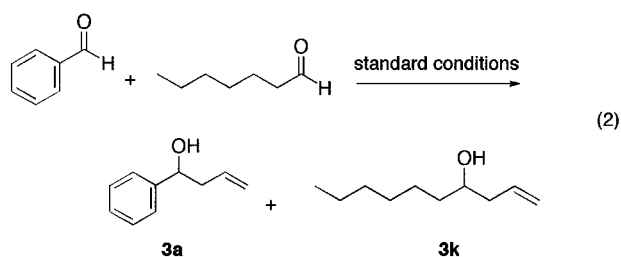
Reaction conditions: allyl chloride/Mn/Cu (3 : 3 : 0.1), overnight at room temperature in water. a: isolated yield; b: in H₂O-THF (4:1).

Table 3. Alkylation of Benzaldehyde by Various Methods

entry	method	3a:3k ^a	yield (%) ^b
1	allyl chloride/Mn/Cu (1:3:0.1), H ₂ O	100:0	58
2	allyl bromide/Zn (1:2), 0.1 N HCl(aq)	50:50	67
3	allyl bromide/In (1:1.2), 0.1 N HCl(aq)	50:50	59
4	allyl bromide/Sn (1:2), 0.1 N HCl(aq)	50:50	71
5	allylmagnesium bromide (2 equiv), Et ₂ O	50:50	96

^a Ratios were determined by ¹H NMR. ^b Total isolated yields without being optimized.

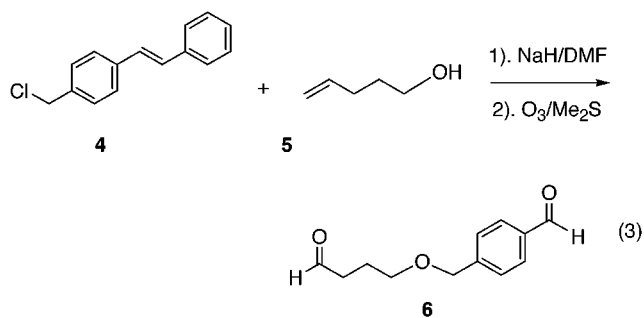
To test this hypothesis, competitive studies were carried out between aliphatic and aromatic aldehydes with different methods (eq 2) (Table 3). By using the



present combination, a single alkylation product was generated when a mixture of heptanal 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 alkylation products of both aldehydes. A 1:1 mixture of products was also generated when the alkylation was

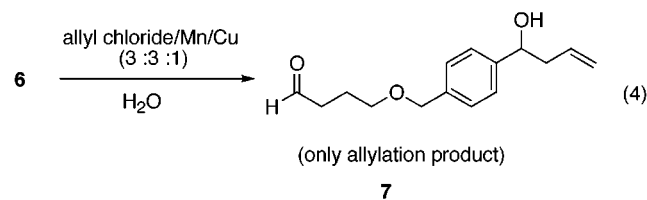
performed with allylmagnesium bromide¹² in ether. Rather than accelerating the reaction, the addition of a water-soluble quaternary ammonium salt (tetraethylammonium chloride, 0.1 equiv) depressed the reaction.

An intramolecular discrimination study has also been carried out on a compound bearing both aromatic and aliphatic carbonyl groups. Reaction of 4-(chloromethyl)-stilbene (**4**) with 4-pentenol (**5**) and sodium hydride in DMF in the presence of a catalytic amount of 18-crown-6 generated, after ozonolysis of the intermediate, the dialdehyde **6** (eq 3). Alkylation of this dialdehyde under

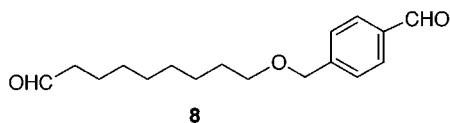


the standard conditions mediated by manganese and copper resulted in 45% of the alkylation product **7** (eq 4). A complete chemoselectivity was observed in which the alkylation occurs exclusively on the aromatic carbonyl. However, under the identical reaction conditions, no

(12) Wakefield, B. J. *Organomagnesium Methods in Organic Chemistry*; Academic Press: New York, 1995.



reaction was observed in compound **8** which involves a



long aliphatic chain. The addition of a cosolvent such as THF did not improve the reaction. It is not clear what inhibits the proceeding of the reaction. The uses of terminally substituted allyl halides, e.g. 1-chloro-2-butene, 3-methyl-1-chloro-2-butene, cinnamyl chloride, and ethyl 4-bromocrotonate, for the reaction were all successful yet generating mixtures of regio- and diastereoisomers, which somewhat limits the present method.

The encouraging results obtained from the allylation reaction led us to investigate other carbon–carbon bond formations mediated by manganese under aqueous conditions. The pinacol-coupling reaction is another fundamental reaction in organic chemistry.¹³ Traditionally, pinacol coupling was effected by using active metals such as sodium,¹⁴ lithium,¹⁵ or magnesium¹⁶ under anhydrous conditions. Other reagents used for such a reaction include the Zn–Cu couple,¹⁷ chromium or vanadium,¹⁸ SmI₂,¹⁹ Ce–I₂,²⁰ Yb,²¹ and Bu₃SnH,²² as well as TiCl₃-based reducing agents (the McMurry pinacol coupling).²³ Recently, Clerici and Porta extensively studied the aqueous pinacol coupling reactions mediated by Ti(III).²⁴ Aromatic ketones and aldehydes were coupled by TiCl₃ in aqueous solution under alkaline or acetic conditions.^{25,26} Very recently, Schwartz reported a diastereoselective pinacol coupling with a sterically hindered (cyclopentadiene)titanium complex.²⁷ Other metals such as Zn–Cu have been also found to promote this reaction under ultrasonic radiation in aqueous acetone.²⁸ When

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(14) Nelsen, S. F.; Kapp, D. C. *J. Am. Chem. Soc.* **1986**, *108*, 1265.

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(19) Namy, J. L.; Souppé, J.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765.

(20) Imamoto, T.; Kusumoto, T.; Hatanaka, Y.; Yokoyama, M. *Tetrahedron Lett.* **1982**, *23*, 1353.

(21) Hou, Z.; Takamine, K.; Fujiwara, Y.; Taniguchi, H. *Chem. Lett.* **1987**, 2061.

(22) Hays, D. S.; Fu, G. C. *J. Am. Chem. Soc.* **1995**, *117*, 7283.

(23) For reviews, see: Fürstner, A.; Bogdanović, B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2443. McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513. Kahn, B. E.; Rieke, R. D. *Chem. Rev.* **1988**, *88*, 733.

(24) Clerici, A.; Porta, O. *Tetrahedron Lett.* **1982**, *23*, 3517.

(25) Clerici, A.; Porta, O. *J. Org. Chem.* **1982**, *47*, 2852. Gansauer, A. *Chem. Commun.* **1997**, 457–458.

(26) Clerici, A.; Porta, O.; Riva, M. *Tetrahedron Lett.* **1981**, *22*, 1043 and references cited therein. Very recently, activated manganese was used for pinacol coupling; see: Rieke, R. D.; Kim, S. H. *J. Org. Chem.* **1998**, *63*, 5235.

(27) Barden, M. C.; Schwartz, J. *J. Am. Chem. Soc.* **1996**, *118*, 5484.

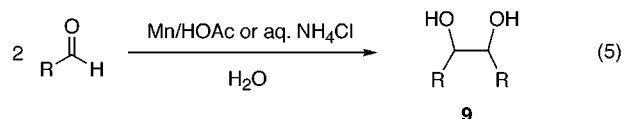
(28) Delair, P.; Luche, J. L. *J. Chem. Soc., Chem. Commun.* **1989**, 398.

Table 4. Pinacol Coupling Mediated by Manganese/HOAc in Aqueous Medium

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

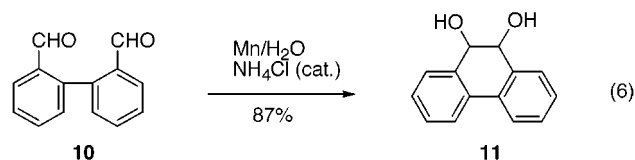
The reactions were carried out with carbonyl compound (1 mmol), manganese (2.5 mmol) and acetic acid (0.1 mmol) in water (3 mL) at r.t. for 16 hrs. a: isolated yields; b: measured by ¹H NMR.

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 5) were coupled



similarly to give the corresponding diols **9** (Table 4). 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. The pinacol coupling was found equally successful with

manganese powder in aqueous ammonium chloride solution, instead of using a catalytic amount of acetic acid. Similarly, only aromatic aldehydes react under these conditions (Table 5). However, only reduction was observed when benzaldehyde was substituted by either a cyano or a dimethylamino group (entries 9 and 10). An intramolecular pinacol coupling occurred as well as the intermolecular reaction (eq 6). Interestingly, only one diastereomer (*trans*) was observed in this reaction. The assignment of the stereochemistry was based on the literature method.²⁹



In conclusion, we found manganese to be highly effective for mediating both aqueous medium carbonyl allylations in the presence of a catalytic amount of copper reagent and pinacol-coupling reactions when combined with either a catalytic amount of acetic acid or in aqueous NH_4Cl . In aqueous media, this metal offers a higher reactivity (compared with previously reported ones) and a complete chemoselectivity toward aromatic aldehydes in allylation of carbonyl compounds and in pinacol coupling. We are presently exploring this new reactivity and selectivity in synthetic applications.

Experimental Section

Air-sensitive reactions were generally conducted under a positive pressure of dry N_2 within glassware which had been flame-dried under a stream of dry N_2 . Anhydrous solvents and reaction mixtures were transferred by oven-dried syringe or cannula. Manganese (325 mesh) and copper (200 mesh) powders were purchased from Aldrich and were used directly as received. Flash chromatography employed E. Merck silica gel (Kiesegel 60, 230–400 mesh) purchased from Scientific Adsorbents. Mass spectra and elemental analysis were obtained at the Center of Instrumental Facility of Tulane University and at the Biomedical Mass Spectrometry Unit of McGill University. Water was deionized before use.

General Procedure for Allylation of the Aldehyde. To a 25 mL flask was added benzaldehyde (106 mg, 1 mmol), allyl chloride (230 mg, 3 mmol), and water (2 mL). Then manganese (165 mg, 3 mmol) and copper (6.4 mg, 0.1 mmol) (premixed) were added to the reaction mixture. The flask was stoppered and stirred vigorously at room temperature for 8 h followed by quenching with 1 N HCl and extracted with diethyl ether. The ethereal solution was washed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The crude product was purified through flash column chromatography on silica gel (hexanes–ethyl acetate) to give the desired product (123 mg, 83%).

1-(4-(Hydroxymethyl)phenyl)-3-buten-1-ol (3h). The reaction of 4-(hydroxymethyl)benzaldehyde (136 mg, 1 mmol) with allyl chloride (230 mg, 3 mmol), manganese (165 mg, 3 mmol), and copper (6.4 mg, 0.1 mmol) by the general allylation procedure followed by column chromatography on silica gel (eluent: 2:1 hexane/ethyl acetate) generated 1-(4-(hydroxymethyl)phenyl)-3-buten-1-ol (117 mg, 66% yield). IR (CDCl_3): 1695, 1641, 1421, 1209, 1041, 1010, 918, 821, 551 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.33 (s, 4H), 5.73–5.85 (m, 1H), 5.10–5.18 (m, 2H), 4.72 (t, $J = 8.4$ Hz, 1H), 4.64 (s, 2H), 2.44–2.54 (m, 2H), 2.22 (br, 1H), 1.97 (br, 1H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 143.3, 140.2, 134.3, 127.1,

Table 5. Pinacol Coupling of Aldehydes Mediated by Mn in Aqueous NH_4Cl

entry	substrates	product (9)	yield (%) ^a	threo: erythro ^b
1		9a	65	39 : 61
2		9b	81	52 : 48
3		9d	69	65 : 35
4		9e	64	33 : 67
5		9f	81	50 : 50
6		9c	52	51 : 49
7		9j	58	46 : 54
8		9k	74	70 : 30
9		reduced		
10		reduced		
11		no reaction		

The reactions were carried out with carbonyl compound (1 mmol), manganese (3 mmol) and NH_4Cl (3 mmol) in 3 ml of H_2O -THF (4 : 1) at r.t. for 16 hrs. a: isolated yields; b: ratios were measured by ^1H NMR.

126, 118.4, 73.1, 65, 43.8. HRMS: calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$ (M^+), m/e 178.0994; found, m/e 178.0995.

1-(2,6-Dichlorophenyl)-3-buten-1-ol (3f). The reaction of 2,6-dichlorobenzaldehyde (175 mg, 1 mmol) with allyl chloride (230 mg, 3 mmol), manganese (165 mg, 3 mmol), and copper (6.4 mg, 0.1 mmol) by the general allylation procedure followed by column chromatography on silica gel (eluent: 10:1 hexane/ethyl acetate) generated 1-(2,6-dichlorophenyl)-3-buten-1-ol (148 mg, 68% yield). IR (CDCl_3): 3587, 3401, 1641, 1590, 1573, 1446, 1184, 1099, 1015, 930, 778 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.28 (d, $J = 8.2$ Hz, 2H), 7.13 (t, $J = 8.2$ Hz, 1H), 5.76–5.89 (m, 1H), 5.48 (t, $J = 3.9$ Hz, 1H), 5.04–5.18 (m, 2H), 2.95 (br, 1H), 2.79–2.89 (m, 1H), 2.62–2.72 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 137.2, 134.2, 133.8, 129.4, 128.9, 118.1, 71.4, 40.0. Anal. Calcd for $\text{C}_{10}\text{H}_{10}\text{Cl}_2\text{O}_2$: C, 55.33; H, 4.64. Found: C, 55.21; H, 4.70.

1-(3-Fluorophenyl)-3-buten-1-ol (3o). IR (film): 3365, 1610, 1585, 1235 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.29 (m, 1H), 7.08 (m, 2H), 6.95 (m, 1H), 5.78 (m, 1H), 5.16 (m, 2H), 4.72 (t, $J = 7$ Hz, 1H), 2.48 (m, 2H), 2.12 (br, 1H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 164.15, 161.71, 146.51,

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129.85, 121.38, 118.91, 114.32, 112.63, 72.54, 43.80. Anal. Calcd for $C_{10}H_{11}FO$: C, 72.27; H, 6.67. Found: C, 72.53; H, 6.09.

Preparation of 4-(4-Oxo-1-butanoxymethyl)benzaldehyde (6). To a suspension of sodium hydride (120 mg, 60% in mineral oil, 3 mmol) in DMF (80 mL) was added 4-penten-1-ol (250 mg, 2.9 mmol). The mixture was stirred at room temperature for 30 min under nitrogen followed by the addition of 4-(chloromethyl)stilbene (448 mg, 2 mmol), and the stirring was continued overnight. The reaction was quenched with saturated aqueous ammonium chloride and extracted with ether. The organic phase was washed with water and brine, dried over magnesium sulfate, and concentrated. The product (4-penten-1-yl 4-vinylbenzyl ether) was obtained by column chromatography on silica gel (eluent: 10:1 hexane/ethyl acetate). Polymerization of this compound was observed within days on standing at room temperature. IR (CDCl₃): 1641, 1629, 1570, 1512, 1448, 1406, 1361, 1103, 989, 908, 825, 551 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.42 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 6.66–6.75 (m, 1H), 5.78–5.89 (m, 1H), 5.77 (d, *J* = 18 Hz, 1H), 5.25 (d, *J* = 12 Hz, 1H), 4.91–5.08 (m, 2H), 4.51 (s, 2H), 3.49 (t, *J* = 7.2 Hz, 2H), 2.12–2.22 (m, 2H), 1.68–1.78 (m, 2H). ¹³C NMR (100 MHz, CDCl₃, ppm): δ 138.3, 138.2, 136.9, 136.6, 127.9, 126.2, 114.8, 113.7, 72.6, 69.7, 30.4, 29.0.

The above compound (910 mg, 3.3 mmol) was dissolved in methylene chloride (20 mL). The solution was ozonized at –78 °C until the appearance of a bluish color solution. Dimethyl sulfide (500 mg, 8.1 mmol) was added, and the mixture was allowed to warm to room temperature slowly. The stirring was continued for another 2 h. The solvent was removed in vacuo, and the crude material was subjected to column chromatography on silica gel (eluent: 2:1 hexane/ethyl acetate) to give the title compound (556 mg, yield 82%). IR (CDCl₃): 2741, 1726, 1607, 1582, 1396, 1362, 1311, 1209, 1176, 1184 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, ppm): δ 9.98 (s, 1H), 9.78 (s, 1H), 7.85 (d, *J* = 8 Hz, 2H), 7.47 (d, *J* = 8 Hz, 2H), 4.55 (s, 2H), 3.53 (t, *J* = 7.3 Hz, 2H), 2.58 (t, *J* = 7.3 Hz, 2H), 1.93–2.02 (m, 2H). ¹³C NMR (100 MHz, CDCl₃, ppm): δ 202.2, 192, 145.4, 135.7, 129.9, 127.6, 72.2, 69.7, 40.9, 22.5. HRMS: calcd for $C_{12}H_{15}O_3$ (M + H⁺), *m/e* 207.1021; found, *m/e* 207.1021.

4-(4-(3-buten-1-ol-1-yl)benzoxymethyl)butyraldehyde (7). The reaction of 4-(4-oxo-1-butanoxymethyl)benzaldehyde (103 mg, 0.5 mmol) with allyl chloride (116 mg, 1.5 mmol), manganese (82.5 mg, 1.5 mmol), and copper (3.2 mg, 0.05 mmol) by the general allylation procedure followed by column chromatography on silica gel (eluent: 5:1 hexane/ethyl acetate) generated 4-(4-(3-buten-1-ol-1-yl)benzoxymethyl)butyraldehyde (56 mg, 45% yield). IR (CDCl₃): 2800, 1722, 1641, 1417, 1359, 1097, 916, 823, 540 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, ppm): δ 9.77 (t, *J* = 1.2 Hz, 1H), 7.35–7.25 (m, 4H), 5.81–5.72 (m, 1H), 5.21–5.08 (m, 2H), 4.75–4.70 (m, 1H), 4.47 (s, 2H), 3.50 (t, *J* = 6 Hz, 2H), 2.61–2.41 (m, 4H), 1.98–1.89 (m, 2H), 1.72 (br, 1H). ¹³C NMR (100 MHz, CDCl₃, ppm): δ 202.4, 143.3, 137.5, 134.4, 127.8, 125.9, 118.5, 73, 72.7, 69.2, 43.9, 41, 22.5. HRMS: calcd for $C_{15}H_{20}O_3$ (M + H⁺ – H₂O), *m/e* 231.1385; found, *m/e* 231.1386.

Preparation of 4-(9-Oxo-1-nonanoxymethyl)benzaldehyde (8). To a suspension of sodium hydride (62 mg, 60% in mineral oil, 1.5 mmol) in DMF (10 mL) was added *Z*-octadecen-1-ol (322 mg, 1.2 mmol). The mixture was stirred at room temperature for 15 min under nitrogen followed by the addition of 4-(chloromethyl)stilbene (224 mg, 1 mmol), and the stirring was continued for 4 h. The reaction was quenched with saturated aqueous ammonium chloride and extracted with ether. The organic phase was washed with water and brine, dried over magnesium sulfate, and concentrated.

The above crude compound (300 mg, 0.65 mmol) was dissolved in methylene chloride (10 mL). The solution was ozonized at –78 °C until the appearance of a bluish color solution. Dimethyl sulfide (200 mg, 3.3 mmol) was added, and the mixture was warmed to room temperature slowly. The stirring was continued for another 2 h. The solvent was removed in vacuo, and the crude material was subjected to column chromatography on silica gel (eluent: 2:1 hexane/ethyl

acetate) to give the title compound (140 mg, yield 78%). IR (CDCl₃): 1725, 1685, 1110 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, ppm): δ 10.01 (s, 1H), 9.78 (s, 1H), 7.86 (d, *J* = 8 Hz, 2H), 7.51 (d, *J* = 8 Hz, 2H), 4.55 (s, 2H), 3.50 (t, *J* = 7.3 Hz, 2H), 2.48 (t, *J* = 7.3 Hz, 2H), 1.40–1.80 (m, 12H). ¹³C NMR (100 MHz, CDCl₃, ppm): δ 195.1, 191.1, 164.9, 139.5, 130.5, 130.4, 129.6, 69.4, 44.8, 29.3, 29.1, 29.0, 28.6, 25.9, 22.2. Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 71.77; H, 8.31.

General Procedure for Pinacol Coupling Reaction by Manganese–Acetic Acid. 1,2-Dichlorobenzaldehyde (175 mg, 1 mmol) and manganese (138 mg, 2.5 mmol) were mixed with water (3 mL), and then acetic acid (6 μL, 0.1 mmol) was added. The reaction was left at room temperature for 16 h. The reaction mixture was neutralized by adding hydrochloric acid (1 M, 10 mL) and was extracted with ether (10 mL × 2). The combined ether layer was washed twice with water (10 mL) and dried over anhydrous MgSO₄. The solvent was removed, and the residue was purified by a flash column (on silica gel with ethyl acetate in hexane (10%) to give the diol (150 mg, 0.43 mmol, 85%) as a mixture of threo and erythro isomers (48:52). The ratio of threo and erythro isomers was measured by ¹H NMR.³⁰

General Procedure for Pinacol Coupling Reaction by Manganese–Ammonium Chloride. To a mixture of benzaldehyde (106 mg, 1 mmol) in 3 mL of H₂O–THF (4:1) at room temperature was added ammonium chloride (161 mg, 3 mmol) and manganese powder (165 mg, 3 mmol) in one portion. The reaction mixture was stoppered and stirred vigorously at room temperature for 16 h. The reaction was then stopped by the addition of 1 N HCl. The mixture was extracted with ether. The combined organic phase was washed with brine, dried over magnesium sulfate, and concentrated. The corresponding allylation product, as a mixture of threo and erythro isomers (39:61) (70 mg, yield 65%), was isolated by flash column chromatography on silica gel eluting with hexane/ethyl acetate (10:1).

1,2-Bis(2,3-dichlorophenyl)-1,2-ethanediol (9f). The compound is prepared from 2,3-dichlorobenzaldehyde by the above general pinacol coupling procedure. IR (CDCl₃): 1035, 1058, 1216, 3153 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, ppm): δ 1.70 (s, 1H), 5.36 (s, 1H), 2.85 (s, 1H), 5.64 (s, 1H), 7.05–7.70 (m, 3H). ¹³C NMR (100 MHz, CDCl₃, ppm): δ 72.30, 72.97, 126.25, 126.59, 126.70, 129.12, 129.41, 130.65, 130.79, 131.76, 132.47, 137.77, 138.94. HRMS: calcd for $C_{14}H_9Cl_4O$ (M + H⁺ – H₂O), *m/e* 332.9407; found, *m/e* 332.9406.

1,2-Bis(*p*-(trifluoromethyl)phenyl)-1,2-ethanediol (9g). The compound is prepared from *p*-(trifluoromethyl)benzaldehyde by the general pinacol coupling procedure. IR (CDCl₃): 1041, 1215, 3154 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, ppm): δ 2.45 (s, 1H), 4.96 (s, 1H), 7.45–7.65 (m, 4H); 2.98 (s, 1H), 4.99 (s, 1H), 7.45–7.65 (m, 4H). ¹³C NMR (100 MHz, CDCl₃, ppm): δ 72.30, 72.97, 126.25, 126.59, 126.70, 129.12, 129.41, 130.65, 130.79, 131.76, 77.16, 78.35, 124.58, 126.66, 126.71, 129.46, 130.10, 142.37, 142.53. HRMS: calcd for $C_{16}H_{11}F_6O$ (M + H⁺ – H₂O), *m/e* 333.0714; found, *m/e* 332.0713.

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buten-1-ol, 156091-01-9; 1-(3-bromophenyl)-3-buten-1-ol, 114095-73-7; 4-(hydroxymethyl)benzaldehyde, 52010-97-6; 1,2-bis(4-methoxyphenyl)-1,2-ethanediol, 4464-76-0; 1,2-bis(4-bromophenyl)-1,2-ethanediol, 126082-5-50-6; 1,2-diphenyl-1,2-ethanediol, 492-70-6; 1,2-bis(4-chlorophenyl)-1,2-ethanediol, 38152-44-2; 1,2-bis(3,4-dichlorophenyl)-1,2-ethanediol, 34848-44-7; 1,2-bis(p-tolyl)-1,2-ethanediol, 24133-59-3; 1,2-bis(o-tolyl)-1,2-ethanediol, 64158-25-4; 1,2-bis(p-phenylphenyl)-1,2-ethanediol,

116204-40-1; 1,2-bis(1-naphthenyl)-1,2-ethanediol, 116204-39-8; 1-phenyl-1,5-hexadien-3-ol, 13891-95-7; 4-fluoro- α -2-propenylbenzenemethanol, 136185-86-9; 2-fluoro- α -2-propenylbenzenemethanol, 144486-11-3; 4-(1-hydroxy-3-butenyl)benzotrile, 71787-53-6; 1,1'-biphenyl-2,2'-dicarboaldehyde, 1210-05-5; 9,10-dihydro-9,10-phenanthrenediol, 25061-77-2.

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