Benzylic Manganese Halides, Sulfonates, and Phosphates: Preparation, Coupling Reactions, and Applications in Organic Synthesis

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The use of highly active manganese, prepared by the Rieke method, for the direct preparation of benzylic manganese reagents was investigated. The oxidative addition of the highly active manganese (Mn*) to benzylic halides was easily completed under mild conditions. More importantly, benzylic manganese sulfonates and phosphates were prepared by direct oxidative addition of Mn* to the carbon−oxygen bonds of benzylic sulfonates and phosphates. The resulting benzylic manganese reagents were found to undergo cross-coupling reactions with a variety of electrophiles. The majority of these reactions were carried out in the absence of any transition metal catalyst under mild conditions. This approach also provided a facile synthetic route to the preparation of resorcinolic lipids.

Introduction

Benzylic organometal reagents play an important role in organic synthesis, especially in homologation of organometallics. Despite their significance, however, few synthetic methods for the preparation of benzylic metal reagents have been accomplished by either direct or indirect methods using an appropriate metal and a benzyl derivative.

Most benzylic lithium reagents have been prepared via bond cleavage reactions[1] and/or transmetalation reactions.[2] Unfortunately, these methods are often accompanied by the formation of complex mixtures and homocoupling products even at low temperature.[1] Similar problems are frequently observed in the preparation of benzylic Grignard reagents. The magnesium anthracene complex has been extensively used to alleviate these problems.[3]

In some cases, direct synthetic methods utilizing the oxidative addition of a metal to the corresponding benzyl halides have provided an efficient procedure for the preparation of benzylic metal reagents including activated zinc[4] and cadmium.[5] However, a copper catalyst was needed to complete the cross-coupling reaction of benzylic zinc halides with electrophiles. Recently, an interesting new synthetic procedure for benzylic zinc reagent has been reported using triorganozincate and 4-iodobenzyl mesylate.[6] This system appears very useful for the preparation of 4-alkyl substituted benzylic zinc reagents.

We now describe an alternative synthetic route for the direct formation of nonfunctionalized and functionalized benzylic manganese halides from the oxidative addition reaction of highly active manganese to benzylic halides.[7] And, more significantly, benzylic manganese sulfonates and phosphates were prepared by the reaction of Mn* (manganese prepared by the Rieke method) with the corresponding benzylic sulfonates and phosphates. The resulting benzylic manganese reagents were found to undergo a variety of cross-coupling reactions. This approach has yielded an alternative synthetic route for the preparation of resorcinols isolated from many plants.

Limitations found in the preparation of benzylic manganese reagents as well as in the coupling reactions are also discussed.

Results and Discussion

Preparation and Coupling Reactions of Benzylic Manganese Halides. Treatment of the highly active manganese (Mn*) with benzyl halides (bromide and chloride) gave high yields of the corresponding benzylic manganese halides. The resulting benzylic manganese halides reacted readily with an appropriate electrophile to give the corresponding cross-coupled product. Significantly, most of these coupling reactions were carried out

(1) (a) Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem.* **1979**, *44*, 713. (b) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481. (c) Parham, W. E.; Jones, L. D.; Sayed, Y. A. *J. Org. Chem.* **1976**, *41*, 1184. (d) Gilman, H.; McNinch, H. A. *J. Org. Chem.* **1961**, *26*, 3723.

(2) (a) Clarembeau, M.; Krief, A. *Tetrahedron Lett.* **1985**, *26*, 1093. (b) Seyferth, D.; Suzuki, R.; Murphy, C. J.; Sabet, C. R. *J. Organomet. Chem.* **1964**, 431. (c) Gilman, H.; Rosenberg, S. D. *J. Org. Chem.* **1959**, *24*, 3.

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(4) (a) Betzemeier, B.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2623. (b) Rottländer, M.; Knochel, P. *Synlett* **1997**, 1084. (c) Klement, I.; Lennick, K.; Tucker, C. E.; Knochel, P. *Tetrahedron Lett.* **1993**, *34*, 4623. (d) Chia, W.- L.; Shiao, M.-J. *Tetrahedron Lett.* **1991**, *32*, 2033. (e) Shing, T.-L.; Chia, W.- L.; Shiao, M.-J. Chau, T.-Y. *Synthesis* **1991**, 849. (f) Chen, H. G.; Hoechstetter, C.; Knochel, P. *Tetrahedron Lett.* **1989**, *30*, 4795. (g) Berk, S. C.; Knochel, P.; Yeh, M. C. P. *J. Org. Chem.* **1988**, *53*, 5789.

(5) Burkhardt, E. R.; Rieke, R. D. *J. Org. Chem.* **1985**, *50*, 416.

(6) Harada, T.; Kaneko, T.; Fujiwara, T.; Oku, A. *J. Org. Chem.* **1997**, *62*, 8966.

(7) (a) An attempt to prepare benzylic manganese reagent has been carried out using manganese powder, resulting in the formation of homocoupling product (89%). Hiyama, T.; Sawahata, M.; Obayashi, M. *Chem. Lett.* **1983**, 1237. (b) Use of manganese for the preparation of allylic manganese reagent. Hiyama, T.; Obayashi, M.; Nakamura, A. *Organometallics* **1982**, *1*, 1249.

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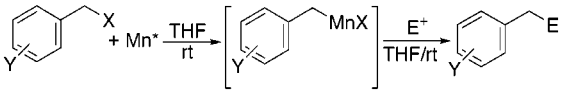
Scheme 1. Preparation and Coupling Reaction of Benzylic Manganese Halides



X = Br, Cl
Y = H, Br, Cl, F, OMe, CF_3, CH_3CO_2

without a transition metal catalyst. The environmental advantages of carrying out these reactions without a transition metal present are significant.

The oxidative addition of Mn* prepared from manganese bromide and chloride to benzyl halides was completed at room temperature in 20 min in THF (Scheme 1). During the oxidative addition reaction, small amounts (3−9%) of homocoupling product of benzyl halide were observed. This problem was alleviated by using manganese[8] prepared from manganese iodide. Trace amounts (less than 1%) of homocoupling products were formed in these cases.

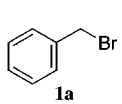
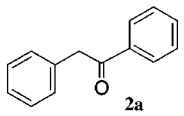
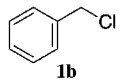
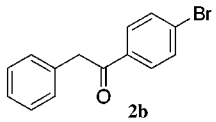
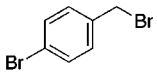
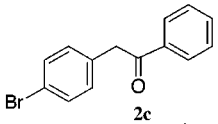
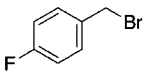
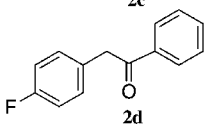
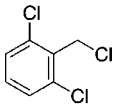
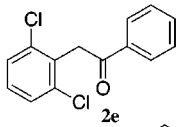
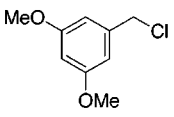
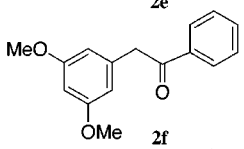
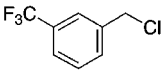
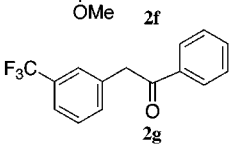
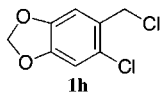
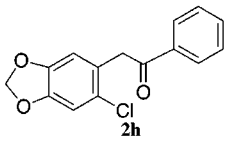
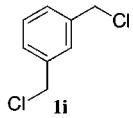
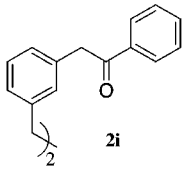
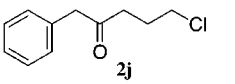
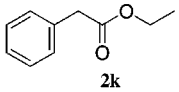
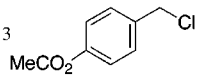
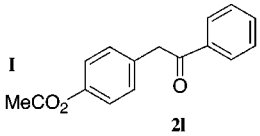
The benzylic manganese halides were reacted with acid chlorides to obtain the cross-coupling products. The cross-coupling reactions with acid chlorides were carried out at room temperature and were completed in 30 min in THF. It is worthy to note that the cross-coupling reaction was performed in the absence of any transition metal catalyst (except entry 13, Table 1). An excess of acid chloride was employed in these reactions to avoid the further reaction of the remaining benzylic manganese halides with the ketone formed. Both aryl (**I**, **II**) and alkyl (**III**, **IV**) acid chlorides gave excellent yields (Table 1). As shown in Table 1, some functionalized benzylic manganese halides (entries 4−9 and 13, Table 1) have been obtained as well as nonfunctionalized ones (entries 1 and 2, Table 1). From these results, it can be inferred that the present conditions tolerate a wide range of functional groups attached to the benzyl halides. Of special interest is entry 8 in Table 1. Preparing organometallics with molecules containing a trifluoromethyl group can be problematic. However, **1g** was readily converted to the corresponding organomanganese reagent, and subsequent cross-coupling proceeded in excellent yield. The oxidative addition will tolerate an electron-withdrawing group such as a carbomethoxy group (entry 13, Table 1). In contrast to the rest of the entries in Table 1, the manganese derivative of **1j** does not undergo cross-coupling in the absence of a catalyst. However, in the presence of a catalytic amount of CuI, product **2l** readily forms. The reason for this is not clear but may be the reduced nucleophilicity caused by the carbomethoxy group. Interestingly, treatment of Mn* with α,α′-dichloro-*m*-xylene (**1i**) and the consecutive coupling reaction with benzoyl chloride gave a symmetrical biaryl compound **2i** in 79% yield (entry 10, Table 1).

The benzylic manganese halides were found to add to several other electrophiles including aldehydes, ketones, and di-*tert*-butylazodicarboxylate (DBAD). The results are summarized in Table 2. Addition to aldehydes (entries 1−4 and 7, Table 2) gave the corresponding secondary alcohols in good yields (78−93%).

The reaction tolerated halides or a nitrile group (entry 3, Table 2) in the aldehyde but not a nitro group (Scheme 3). The addition to an alkyl ketone yielded the corre-

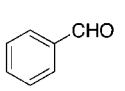
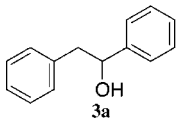
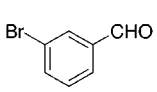
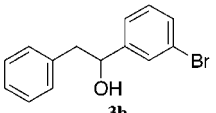
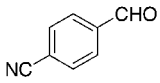
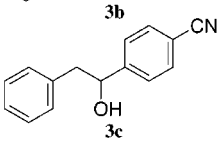
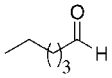
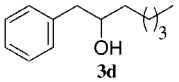
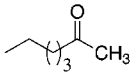
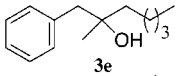
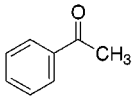
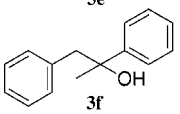
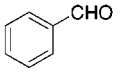
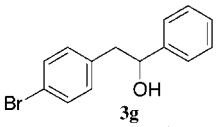
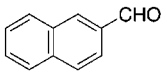
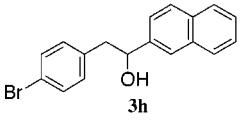
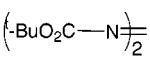
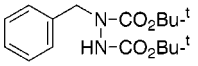
(8) Different reactivity of Mn* depending on manganese halide. Kim, S.-H.; Rieke, R. D. *Synth. Commun.* **1998**, *28*, 1065.

Table 1. Coupling Reaction with Acid Chloride[a]

Entry	Halide	Electrophile[b]	Product[c]	Yield(%)[d]
1	 **1a**	**I**	 **2a**	82
2	 **1b**	**I**	**2a**	91
3	**1b**	**II**	 **2b**	85
4	 **1c**	**I**	 **2c**	84
5	 **1d**	**I**	 **2d**	74
6	 **1e**	**I**	 **2e**	75
7	 **1f**	**I**	 **2f**	86
8	 **1g**	**I**	 **2g**	71
9	 **1h**	**I**	 **2h**	89
10	 **1i**	**I**	 **2i**	79
11	**1a**	**III**	 **2j**	78
12	**1b**	**IV**	 **2k**	69
13	 **1j**	**I**	 **2l**	75[e]

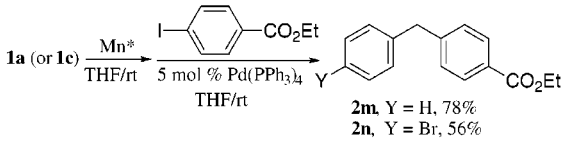
[a] Oxidative addition reaction and coupling reaction were carried out at room temperature in THF. [b] Electrophile: **I** = benzoyl chloride, **II** = *p*-bromobenzoyl chloride, **III** = 4-chlorobutyryl chloride, **IV** = ethyl chloroformate. [c] All products were fully characterized by ^{1}H NMR, ^{13}C NMR, and HRMS (or EIMS). [d] Isolated yield (based on benzyl halides). [e] An amount of 5 mol % CuI was used as a catalyst.

Table 2. Cross-Coupling Reaction of Benzylic Manganese Bromide[a]

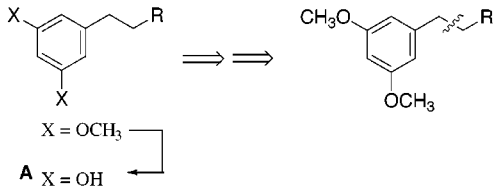
Entry	Halide	Electrophile	Product	Yield(%)[b]
1	**1a**		 **3a**	93
2	**1a**		 **3b**	95
3	**1a**		 **3c**	87
4	**1a**		 **3d**	78
5	**1a**		 **3e**	72
6	**1a**		 **3f**	46
7	**1c**		 **3g**	80
8	**1c**		 **3h**	89
9	**1a**		 **3i**	80

[a] Oxidative addition reaction and coupling reaction were carried out at room temperature in THF. [b] Isolated yields (based on electrophile).

Scheme 2. Palladium-Catalyzed Coupling Reaction



Scheme 3



sponding tertiary alcohol **3e** in good yield (entry 5, Table 2). Coupling with acetophenone was successful; however, the yield was low (entry 6, Table 2). DBAD was also employed as an electrophile, and the corresponding coupling product **3i** was obtained in excellent yield (80%). Once again, it should be noted that the coupling reactions described above have been readily accomplished in the absence of any catalyst under mild conditions.

In 1997, Knochel et al. reported the palladium-catalyzed cross-coupling of benzylic zinc bromide in the presence of the perfluorinated phosphane.[4a] Benzylic manganese halides were also found to undergo palladium-catalyzed cross-coupling reactions with aryl iodides. As shown in Scheme 2, the corresponding coupling compounds **2m** and **2n** were achieved in moderate to good yields (56% and 78%, respectively) using 5 mol % palladium catalyst [$Pd(PPh_3)_4$] in THF at room temperature.

Preparation and Coupling Reactions of Benzylic Manganese Sulfonates and Phosphates. In 1992, Yus et al. reported that allylic and benzylic mesylates reacted with lithium naphthalenide to give the corresponding organolithium reagents giving cross-coupling products upon treatment with electrophiles.[9]

Considering the exceptional reactivity of our active manganese, we attempted the oxidative addition to a variety of carbon−oxygen bonds. Our first approach employed benzyl sulfonates. This was expanded to functionalized and nonfunctionalized benzylic mesylates.

One of the reasons for choosing benzyl mesylates is that these mesylates can be easily prepared from the corresponding alcohols using standard literature procedures.[10] Simply stirring the mixture of an alcohol and methane sulfonyl chloride in methylene chloride at room temperature in the presence of triethylamine followed by a simple workup procedure yielded the mesylates in over 90% isolated yields. By use of this method, a variety of functionalized benzyl mesylates could be easily prepared, and the resulting mesylates were used for the preparation of functionalized benzylic manganese reagents. This provides another synthetic route to benzylic metal chemistry.

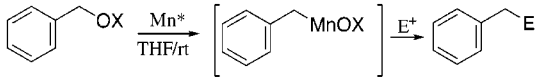
As described before, few synthetic methods for the direct preparation of benzylic metal reagents have been reported. Most of these benzylic metal compounds contain a halide atom. Interestingly, by use of this new protocol for the direct formation of nonfunctionalized as well as functionalized benzylic manganese mesylates, halide-free benzylic manganese reagents can be prepared. More importantly, this study demonstrates that highly active manganese readily undergoes oxidative addition to carbon−oxygen bonds of benzyl mesylates. Also, the subsequent cross-coupling reactions with a variety of electrophiles can be readily carried out.

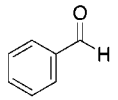
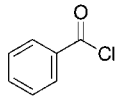
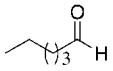
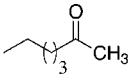
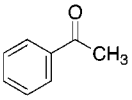
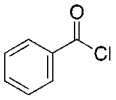
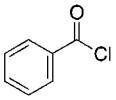
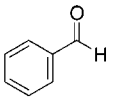
Table 3 represents the preparation and coupling reaction of benzylic manganese sulfonates. The oxidative addition of highly active manganese prepared from manganese iodide to the carbon−oxygen bond of benzyl mesylate was easily completed at room temperature in 30 min. According to gas chromatography analysis, a very small amount (less than 8%) of homocoupled product, bibenzyl, was formed during the reaction. The resulting benzylic manganese mesylates were cross-coupled with several electrophiles. The coupling reactions were carried out under mild conditions in the absence of any transition metal catalyst, and the results are summarized in Table 3. At this time, we do not understand why the manganese bromides give better yields than the manganese sulfonates or phophates.

(9) (a) Guijarro, D.; Mancheño, B.; Yus, M. *Tetrahedron* **1992**, *48*, 4593. (b) A review. Yus, M. *Chem. Soc. Rev.* **1996**, 155 and references therein.

(10) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.

Table 3. Preparation of Benzylic Manganese Sulfonates and Phosphates and Their Coupling Reactions



Entry	X[a]	Electrophile	Product	Yield(%)[b]
1	CH_3SO_2 **1k**		**3a**	72
2	**1k**		**2a**	63[c]
3	**1k**		**3d**	50
4	**1k**		**3e**	27
5	**1k**		**3f**	36
6	*p*-$CH_3C_6H_4SO_2$ **1l**		**2a**	74[c]
7	$P(O)(OEt)_2$ **1m**[d]		**2a**	52[c]
8	**1m**[d]		**3a**	73

[a] Oxidative addition was carried out at room temperature in 20 min unless otherwise mentioned. [b] Isolated yields (based on electrophile unless otherwise mentioned). [c] Excess benzoyl chloride was used (yield was based on mesylate). [d] For the preparation, see ref 9b. Oxidative addition was completed at room temperature overnight.

The coupling reaction of nonfunctionalized benzylic manganese mesylate **1k** with aldehydes (entries 1 and 3, Table 3) gave the corresponding secondary alcohols in good isolated yields (72% and 50% of **3a** and **3d**, respectively). Ketone (**2a**) was also obtained in good yield (63%) from the coupling of **1k** with an acid chloride (entry 2, Table 3). Lower yields were observed from the reactions with ketones (entries 4 and 5, Table 3). Overall, the isolated yields obtained from using benzyl mesylates were lower than those from using benzyl halides. Similar results were obtained using benzyl tosylate and phosphate. Once again, the oxidative addition of Mn* to the C−O bond of benzyl tosylate was completed at room temperature in 30 min, and then the resulting benzylic manganese tosylate coupled with benzoyl chloride to give rise to the ketone, **2a**, in 74% isolated yield. To expand this approach, a mixed phosphate, benzyl diethylphosphate, was treated with Mn* under the same conditions used for benzyl sulfonates. A trace amount of homocoupling product was observed on GC analysis. However, in this case, a longer reaction time was required to complete the oxidative addition. According to TLC analysis, the oxidative addition of Mn* to the C−O bond of the phosphate was completed after being stirred at room-temperature overnight. The subsequent coupling reactions with benzoyl chloride and benzaldehyde giving the corresponding products, **2a** and **3a**, were carried out at room temperature in THF in the absence of a catalyst.

With the preliminary results from the nonfunctionalized benzylic mesylate in hand, functionalized benzylic mesylates containing a halogen atom were investigated. The functionalized benzylic mesylates (**1n**−**s**) were easily prepared by the procedure used for benzyl mesylate **1k**. The oxidative addition was monitored by gas chromatography. Small amounts (less than 8%) of both homocoupled product and toluene (less than 2% in the cases of **1n**, **1o**, **1q**, and **1r**) were indicated by GC. The small amount of reductive cleavage of halogens on the aryl ring proves that the reaction conditions will tolerate the presence of halogen atoms. Table 4 contains the cross-coupling reactions using the functionalized benzylic manganese mesylates.

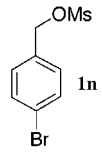
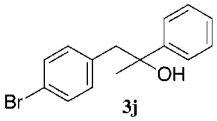
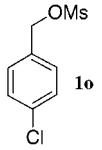
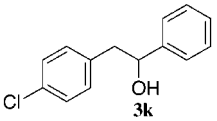
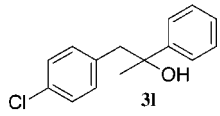
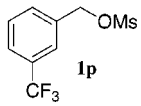
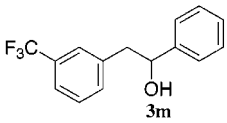
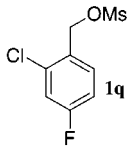
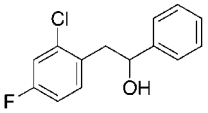
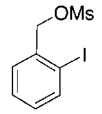
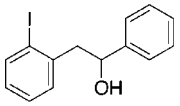
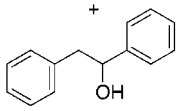
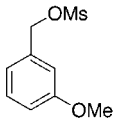
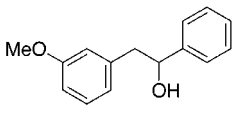
4-Bromobenzyl manganese mesylate **1l** also reacted with acid chlorides, aldehydes, and ketones to yield the corresponding ketone, secondary alcohol, and tertiary alcohol (**2c**, **3g**, and **3j**, respectively) in good to excellent isolated yields. Reaction of 4-chlorobenzyl manganese mesylate **1o** with an aldehyde and ketone also yielded **3k** and **3l** in 95% and 92% of the products, respectively (entries 4 and 5, Table 4). As mentioned earlier, it is of interest that mesylate **1p** containing a trifluoromethyl group has been successfully employed for the preparation of benzylic manganese mesylate, and the subsequent coupling reaction proceeded in good yield (89%). Entry 7 in Table 4 represents the use of dihalogenated benzyl mesylate under the present conditions. Interestingly, reaction of 2-iodobenzyl mesylate **1r** with benzaldehyde afforded two different products, **3o** (36%) and **3a** (12%), respectively. Probably the relatively low yield (36%) is due to the steric hindrance of the iodide atom in the 2-position of the benzyl mesylate. And it can be easily rationalized that the formation of **3a** results from another oxidative addition of an excess Mn* to carbon−iodine bond in the benzylic manganese mesylate.

Applications and Limitations. As described above, the benzylic manganese reagents have been found to undergo reaction with aldehydes and acid chlorides under mild conditions. Interestingly, this approach can be easily applied to the preparation of resorcinolic lipid precursors. As presented below, resorcinolic lipids of the general type A are mainly isolated from many plants. In general, 5-*n*-alkylresorcinols have shown a variety of biological activities including antimicrobial, antiparasitic, cytotoxic activity, growth regulator, and DNA cleaving properties.[12] As shown in Scheme 3, the key step in this synthesis is the C−C bond formation. The C−C bond can be obtained by the reaction of an arylmetallic reagent with alkyl substrates (or vice versa) followed by the reduction of functional groups to give rise to the alkyl chains.

To this end, a few synthetic methods have been reported for the preparation of 5-*n*-alkylresorcinols. These methods include the use of 3,5-dimethoxybenzaldehyde,[13] 3,5-dimethoxybenzylic alcohol,[14] and 3,5-dimethoxyphenol.[15] Until recently, because of the dif-

(11) Recent example of homocoupling product. Goswami, S.; Mahapatra, A. K. T*etrahedron Lett*. **1998**, *39*, 1981.
(12) Kozubek, A.; Tyman, J. H. *Chem. Rev*. **1999**, *99*, 1.
(13) Fürstner, A.; Seidel, G. *J. Org. Chem*. **1997**, *62*, 2332.
(14) Alonso, E.; Ramón, D.; Yus, M. *J. Org. Chem*. **1997**, *62*, 417.

Table 4. Preparation and Coupling Reaction of Functionalized Benzylic Manganese Mesylates

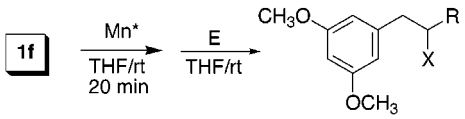
Entry	Mesylates[a]	Electrophile[b]	Product	Yield[c]
1	 **1n**	I[d]	**2c**	50[e]
2	**1n**	II	**3g**	90
3	**1n**	III	 **3j**	80
4	 **1o**	II	 **3k**	95
5	**1o**	III	 **3l**	92
6	 **1p**	II	 **3m**	89
7	 **1q**	II	 **3n**	92
8	 **1r**[f]	II	 **3o** +  **3a**	36[g] 12[g]
9	 **1s**	II	 **3p**	92

[a] Oxidative addition was carried out at room temperature unless otherwise noted. [b] Electrophile: **I** = benzoyl chloride, **II** = benzaldehyde, **III** = acetophenone. [c] Isolated yield (based on electrophile unless otherwise mentioned). [d] Excess benzoyl chloride was used. [e] Yield was based on mesylate. [f] Oxidative addition was carried out at 0 °C. [g] Obtained as a mixture (characterized by NMR and GC−MS).

ficulty of the preparation of benzylic metal reagents,[16] only one resorcinol, olivetol, has been prepared using 3,5-dimethoxybenzylic magnesium chloride.[17]

As already reported, the benzylic manganese halides were easily prepared from highly active manganese and the corresponding benzylic halides. We can apply this approach to the preparation of 5-*n*-alkylresorcinols and/or their precursors.

Scheme 4



Entry	X	R	Yield (%)
1	OH	*n*-$C_{11}H_{23}$ **4a**	80[a]
2	OH	*n*-$C_{13}H_{27}$ **4b**	83[a]
3	O	*n*-$C_{13}H_{27}$ **4c**	82[b]
4	O	*n*-$C_{15}H_{31}$ **4d**	89[b]

[a] Based on aldehyde [b] Based on **1f**

First, cross-coupling reactions of 3,5-dimethoxybenzylic manganese chloride with alkyl aldehydes and acid chlorides were carried out to give the corresponding coupling products (**4a**−**d**), respectively. The reactions were carried out at room temperature for 2 h to yield the corresponding cross-coupling products (**4a**,**b**) in excellent isolated yields in the absence of any catalyst. The ketones (**4c**−**d**) were also readily obtained from the reaction with acid chlorides, and the resulting products can also be used for the preparation of lipid derivatives. All of the compounds listed in Scheme 4 can be used as intermediates for the preparation of 5-*n*-alkylresorcinols.[18]

Along with the 5-*n*-alkylresorcinolic lipids, bibenzyl derivatives are among the most frequently isolated lipids from plants. Since these bibenzyl compounds have two carbons between two aromatic rings, this type of bond construction can be easily achieved by the reaction of benzylic manganese reagent with the corresponding aryl aldehydes or acid chlorides. Further reactions, dehydration and/or reduction, with the resulting coupling products can afford the bibenzylic lipids.

As described in Scheme 5, simple coupling reactions of **1f** with aryl aldehydes yielded the coupling products in excellent isolated yields under mild conditions. It should be noted that this approach provides a more facile route than using benzyloxytrimethylsilane[14] in terms of the yield. Once again, the coupling reaction was carried out in the absence of any catalyst.

As described above, the highly active manganese was employed to provide a variety of benzylic manganese reagents. It is also observed that the reaction system tolerates some functional groups during the preparation and coupling reactions of benzylic manganese reagents. Despite the convenience of this system, some limitations were also found in some cases. As shown in Table 5, treatment of Mn* with 3- and 4-cyanobenzyl bromides gave exclusively homocoupling product[11] in high yield under the same conditions used before. To obtain the corresponding benzylic manganese bromide, different

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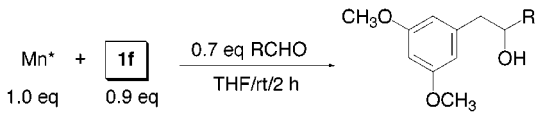
Scheme 5



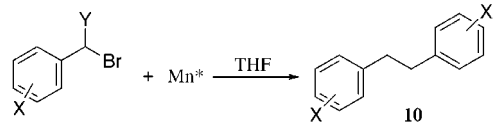
5- 9

Entry	R	Yield (%)[a]		Lipid[b]
1	C_6H_5	89	**5**	*Pinosilvine*[14,19a] *Dihydopinosilvine*[14,19a]
2	*m*-$CH_3OC_6H_4$	93	**6**	*Batatasin III dimethyl ether*[19b]
3	*p*-$CH_3OC_6H_4$	91	**7**	*Resveratrol*[14]
4	*m,p*-$(CH_3O)_2C_6H_3$	91	**8**	*Piceatannol*[14] *Combretastatin B-4 tetramethyl ether*[14]
5	*m*-(CH_3O),*p*-$(BzO)C_6H_3$	95	**9**	*Aloifol*[19c]

[a] Isolated yield based on aldehyde

[b] Can be prepared using **5 -9**, respectively

Table 5. Formation of Homocoupling Product



10

Entry	X	Y	temp/time	Product	Yield (%)[a]
1	3-CN	H	rt/20 min	**10a**	90
2	4-CN	H	rt/20 min	**10b**	82
3	4-CN	H	-78 °C ~ -30 °C/6 h	**10b**	83
4	H	Me	rt/20 min	**10c**	85

[a] Isolated yield.

conditions such as low temperatures (−78 and 0 °C) and use of cosolvent (THF/ether) were also employed but were not successful. The same result, formation of homocoupling product **10c**, was obtained in high yield from the reaction of 1-bromoethylbenzene (entry 4, Table 5).

To examine the oxidative addition of Mn* to different types of benzyl substrates, diethyl benzylphosphonate, benzyl methyl sulfide, benzyl phenyl sulfide, benzyl benzoate, benzyl phenyl ether, 4-methoxybenzyl chloride, 4-methoxybenzyl *p*-toluenesulfonate, and benzyloxy trimethylsilane were also treated with Mn*. Unfortunately, according to TLC and/or gas chromatography analyses, no oxidative addition occurred with these substrates.

As shown in previous tables containing cross-coupling products, a number of different types of electrophiles were used to complete the cross-coupling reaction of benzylic manganese reagents prepared via direct oxidative addition of Mn* to the corresponding benzylic halides, sulfonates, and phosphates. Obviously, functional group tolerance is a big advantage of this system. In some cases, however, no coupling product was obtained from the coupling reactions with the following substrates: *p*-nitrobenzaldehyde, epoxide, ester, and alkyl cyanide.

In summary, a facile route to benzylic manganese reagents has been developed. The starting benzylic halide can contain a wide variety of substituents, and more importantly, benzyl alcohols can be used to make benzylic manganese reagents via benzyl sulfonates and phosphates. The subsequent cross-coupling reactions of the resulting benzylic manganese reagents proceed with good to excellent yields with several electrophiles in the absence of any catalyst. And also, it has been found that this approach can be used for the preparation of resorcinolic lipid derivatives.

Experimental Section

1. General Methods. ^{1}H NMR (300 MHz) spectra were recorded in $CDCl_3$ solution. All chemical shifts are reported in parts per million (δ). Fully decouopled ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ solution. The center peak of $CDCl_3$ (77.0 ppm) was used as the internal reference. Mass spectra were performed at the Nebraska Center for Mass Spectrometry at the University of Nebraska-Lincoln.

All manipulations were carried out under an atmosphere of argon on a dual manifold vacuum/argon system. The Linde prepurified grade argon was further purified by passage over a BASF R3-11 catalyst column at 150 °C, a phosphorus pentoxide column, and a column of granular potassium hydroxide. Lithium wire was purchased from Aldrich, and then it was cut into small pieces before use. Lithium, naphthalene, and metal halides were weighed out and charged into reaction flasks under argon in a Vacuum Atmospheres Company drybox. Tetrahydrofuran was distilled immediately before use from Na/K alloy under an atmosphere of argon.

Gas chromatographic analyses were done on a Hewlett-Packard 5890A chromatograph using a stainless steel column (12 ft × 1/8 in.) packed with GP 10% SP 2100 on 100/120 Supelcoport. Analytical thin-layer chromatography was performed using Merck 5735 indicating plates precoated with silica gel 60 F254 (layer thickness 0.2 mm). The product spots were visualized with phosphomolybdic acid reagent, 20 wt % solution in ethyl alcohol. Preparative thin-layer chromatographic separations were obtained using Analtech silica gel GF (layer thickness 2 mm) preparative plates. Liquid chromatographic purification was performed by flash column chromatography using glass columns packed with Merck silica gel 60 (230−400 mesh). Compounds obtained from column chromatography for isolated yields were found to be 99%−100% pure by gas chromatography.

2. Preparation of Highly Active Manganese (Mn*). To the mixture of lithium (20 mmol), naphthalene (2 mmol), and manganese iodide (10 mmol) was added via syringe freshly distilled THF (10 mL) at room temperature. The resulting mixture was then stirred at room temperature for 30 min. A black slurry was obtained and ready for use. (Note: The number of millimoles of Mn* cited in this paper refers to the theoretical amount possible based on the original amount of anhydrous manganese halide.) No attempt was made to determine whether the Mn*, either wet as a slurry or predried, was pyrophoric. However, it should be treated as if it is pyrophoric and kept under argon at all times.

3. Typical Preparation of Benzylic Manganese Halides and Their Coupling Reactions with Benzoyl Chlorides To Give Ketones (2a−l). Benzyl halide (9 mmol) was added via syringe to a slurry of highly active manganese (10 mmol) being stirred in THF (15 mL) at room temperature. The slurry was stirred at room temperature for 20 min. The reaction was monitored by gas chromatography. After the completion of the oxidative addition, the mixture was cooled to 0 °C. 1,2-Dibromoethane was added to the mixture at this temperature to react with the excess Mn*, and the mixture was stirred for 5 min. The resulting mixture was transferred via cannula to the benzoyl chloride solution in THF at room temperature. After being stirred for 30 min, the mixture was quenched with 3 M HCl solution and extracted with diethyl ether. The combined organic layers were washed with $NaHCO_3$, $Na_2S_2O_3$, and brine, dried over anhydrous $MgSO_4$, and concentrated using a rotary evaporator. Flash column chromatography (ethyl acetate/hexanes) afforded the corresponding ketones.

Benzyl Phenyl Ketone (2a). White solid; mp 55−56 °C. ^{1}H NMR ($CDCl_3$): δ 8.05−7.28 (m, 10H), 4.31 (s, 2H). ^{13}C NMR: δ 197.55, 136.54, 134.48, 133.10, 129.41, 128.60, 128.58, 126.83, 45.43.

Benzyl 4-Bromophenyl Ketone (2b). White solid; mp 112−113 °C. ^{1}H NMR ($CDCl_3$): δ 8.02−7.24 (m, 9H), 4.26 (s, 2H). ^{13}C NMR: δ 196.54, 135.20, 134.09, 132.35, 131.92, 130.10, 129.33, 128.74, 128.33, 127.00, 45.47. EIMS *m/z* (relative intensity): 275 (M^+, 3).

4-Bromobenzyl Phenyl Ketone (2c). White solid; mp 147−148 °C. ^{1}H NMR ($CDCl_3$): δ 8.02−7.13 (m, 9H), 4.25 (s, 2H). ^{13}C NMR: δ 196.92, 136.30, 133.39, 133.32, 131.66, 131.22, 128.68, 128.44, 120.89, 44.67. EIMS *m/z* (relative intensity): 275 (M^+, 2).

4-Fluorobenzyl Phenyl Ketone (2d). White solid; mp 108−110 °C. ^{1}H NMR ($CDCl_3$): δ 8.02−7.00 (m, 9H), 4.26 (s, 2H). ^{13}C NMR: δ 197.29, 162.84, 160.88, 136.46, 132.21, 131.02, 130.96, 130.15, 130.12, 128.64, 128.45, 115.52, 115.34, 44.41. HRMS calcd for $C_{14}H_{11}FO$ 214.0794, found 214.0787.

2,6-Dichlorobenzyl Phenyl Ketone (2e). White solid; mp 79−80 °C. ^{1}H NMR ($CDCl_3$): δ 8.11−7.20 (m, 8H), 4.72 (s, 2H). ^{13}C NMR: δ 194.54, 136.11, 133.36, 132.13, 128.76, 128.69, 128.15, 127.92, 41.32. EIMS *m/z* (relative intensity): 265 (M^+, 1).

3,5-Dimethoxybenzyl Phenyl Ketone (2f). White solid; mp 60−61 °C. ^{1}H NMR ($CDCl_3$): δ 8.03−6.35 (m, 8H), 4.22 (s, 2H), 3.77 (s, 6H). ^{13}C NMR: δ 197.39, 160.90, 146.68, 136.67, 136.51, 133.15, 128.60, 107.46, 98.89, 55.25, 45.79. HRMS calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1100.

Phenyl 3-Trifluoromethylbenzyl Ketone (2g). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 8.05−7.45 (m, 9H), 4.37 (s, 2H). ^{13}C NMR: δ 196.56, 136.27, 135.33, 133.44, 133.09, 128.92, 128.72, 128.37, 126.38, 126.33, 123.83, 123.77, 123.73, 44.77. EIMS *m/z* (relative intensity): 264 (M^+, 1).

6-Chloropiperonyl Phenyl Ketone (2h). Pale-yellow solid; mp 124−125 °C. ^{1}H NMR ($CDCl_3$): δ 8.06−6.72 (m, 7H), 5.96 (s, 2H), 4.34 (s, 2H). ^{13}C NMR: δ 196.44, 147.39, 146.74, 136.49, 133.25, 128.63, 128.27, 125.97, 125.74, 110.86, 109.80, 101.72, 42.92. HRMS calcd for $C_{15}H_{11}ClO_3$ 274.0397, found 274.0401.

1,2-Di-(3′-benzylmethylphenyl)ethane (2i). White solid; mp 131−132 °C. ^{1}H NMR ($CDCl_3$): δ 8.03−7.04 (m, 18H), 4.25 (s, 4H), 2.88 (s, 4H). ^{13}C NMR: δ 197.71, 142.10, 136.62, 134.48, 133.10, 129.58, 128.60, 127.03, 45.46, 37.71. HRMS calcd for $C_{30}H_{26}O_2$ 418.1933, found 418.1928.

5-Chloro-1-phenyl-2-pentanone (2j). Pale-brown oil. ^{1}H NMR ($CDCl_3$): δ 7.33−7.17(m, 5H), 3.69(s, 2H), 3.51(t, J = 6.60 Hz, 2H), 2.64(t, J = 6.60 Hz, 2H), 2.08 (q, J = 6.60 Hz, 4H). ^{13}C NMR: δ 206.80, 133.86, 129.17, 128.52, 126.84, 49.92, 44.13, 43.88, 27.39. EIMS *m/z* (relative intensity): 196 (M^+, 9).

Ethyl Phenylacetate (2k). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.39−7.24 (m, 5H), 4.22 (q, J = 7.15 Hz, 2H), 3.67 (s, 2H), 1.31 (t, J = 7.15 Hz, 3H). ^{13}C NMR: δ 171.42, 134.08, 129.11, 128.42, 126.90, 60.67, 41.29, 14.05. EIMS *m/z* (relative intensity): 164 (M^+, 17).

4-Carbomethoxybenzyl Phenyl Ketone (2l). White solid; mp 93−94 °C. ^{1}H NMR ($CDCl_3$): δ 8.03−7.05 (m, 9H), 4.28 (s, 2H), 2.29 (s, 3H). ^{13}C NMR: δ 197.26, 169.39, 149.53, 136.42, 133.22, 131.98, 130.43, 128.63, 128.57, 121.66, 44.61, 21.05. CIMS *m/z* (relative intensity): 255 (M^++1, 100).

4. Alcohols from the Reactions of Benzylic Manganese Halides with Aldehydes and Ketones (3a−i). Benzyl halide (9 mmol) was added via syringe to a slurry of highly active manganese (10 mmol) being stirred in THF (15 mL) at room temperature. The slurry was stirred at room temperature for 20 min. The reaction was monitored by gas chromatography. After the completion of the oxidative addition, the mixture was cooled to 0 °C. 1,2-Dibromoethane was added to the mixture at this temperature, and the mixture was stirred for 5 min. To the resulting mixture was added aldehyde (or ketone) at room temperature. After being stirred for 1 h, the mixture was quenched with 3 M HCl solution and extracted with diethyl ether. The combined organic layers were washed with $NaHCO_3$, $Na_2S_2O_3$, and brine, dried over anhydrous $MgSO_4$, and concentrated using a rotary evaporator. Flash column chromatography (ethyl acetate/hexanes) afforded the corresponding alcohols.

1,2-Diphenylethanol (3a). Pale-yellow solid; mp 64−65 °C. ^{1}H NMR ($CDCl_3$): δ 7.39−7.21 (m, 10H), 4.92, 4.91 (dd, J = 5.10, 5.10 Hz, 1H), 3.06−3.02 (m, 2H), 2.04 (s, 1H). ^{13}C NMR: δ 143.76, 137.99, 129.46, 128.43, 128.34, 127.54, 126.54, 125.85, 75.26, 46.01. EIMS *m/z* (relative intensity): 198 (M^+, 1).

1-(3′-Bromophenyl)-2-phenylethan-1-ol (3b). Pale-brown oil. ^{1}H NMR ($CDCl_3$): δ 7.55−7.19 (m, 9H), 4.87, 4.84 (dd, J = 4.80, 4.80 Hz, 1H), 3.06−2.90 (m, 2H), 2.07 (s, 1H). ^{13}C NMR: δ 146.04, 137.42, 130.55, 129.90, 129.45, 128.95, 128.56, 126.77, 124.49, 122.49, 74.52, 46.01. HRMS calcd for $C_{14}H_{13}OBr$ 276.0150; found 276.0150 (M^+), 258.0051 ($M^+ - H_2O$).

1-(4′-Cyanophenyl)-2-phenylethan-1-ol (3c). White solid; mp 66−67 °C. ^{1}H NMR ($CDCl_3$): δ 7.61−7.13 (m, 9H), 4.94, 4.92 (dd, J = 5.48, 5.25 Hz, 1H), 2.98 (m, 2H), 2.43 (s, 1H). ^{13}C NMR: δ 148.98, 136.81, 132.02, 129.39, 128.52, 126.81, 126.49, 118.75, 110.92, 74.35, 45.83. HRMS calcd for $C_{15}H_{13}NO$ 223.0997, found 205.0889 ($M^+ - H_2O$). EIMS *m/z* (relative intensity): 223 (M^+, 1).

1-Phenylheptan-2-ol (3d). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.35−7.22 (m, 5H), 3.82 (m, 1H), 2.87−2.62 (m, 2H), 1.60 (s, 1H), 1.54−1.33 (m, 8H), 1.92 (t, J = 6.60 Hz, 3H). ^{13}C NMR: δ 138.65, 129.38, 128.47, 126.35, 72.63, 44.00, 36.73, 31.82, 25.39, 22.59, 14.00. EIMS *m/z* (relative intensity): 192 (M^+, 1).

2-Methyl-1-phenylheptan-2-ol (3e). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.35−7.22 (m, 5H), 2.77 (dd, J = 33.62, 6.91 Hz, 2H), 1.47−1.29 (m, 10H), 1.16 (s, 3H), 0.93 (t, J = 7.16 Hz, 3H). ^{13}C NMR: δ 137.60, 130.51, 128.11, 126.35, 72.48, 47.92, 41.80, 32.36, 26.45, 23.67, 22.65, 14.03. HRMS calcd for $C_{14}H_{22}O$ 206.1671; found 191.1434 ($M^+ - CH_3$), 188.1563 ($M^+ - H_2O$). EIMS *m/z* (relative intensity): 191 ($M^+ - CH_3$, 4).

2,3-Diphenylpropan-2-ol (3f). Pale-yellow solid; mp 49−50 °C. ^{1}H NMR ($CDCl_3$): δ 7.45−7.02 (m, 10H), 3.10 (dd, J = 20.27, 46.73 Hz, 2H), 1.92 (s, 1H), 1.60 (s, 3H). ^{13}C NMR: δ 147.51, 136.70, 130.57, 128.01, 126.61, 124.94, 74.39, 50.45, 29.32. EIMS *m/z* (relative intensity): 195 ($M^+ - OH$, 1).

2-(4′-Bromophenyl)-1-phenylethan-1-ol (3g). Pale-yellow solid; mp 39−40 °C. ^{1}H NMR ($CDCl_3$): δ 7.43−7.03 (m, 9H), 4.85 (t, J = 6.67 Hz, 1H), 2.98 (d, J = 6.44 Hz, 2H), 2.04 (s, 1H). ^{13}C NMR: δ 143.46, 136.96, 131.38, 131.22, 128.43, 127.73, 125.84, 120.41, 75.10, 45.15. EIMS *m/z* (relative intensity): 277 (M^+, 1).

2-(4′-Bromophenyl)-1-(2′-naphthyl)ethan-1-ol (3h). White solid; mp 96−97 °C. ^{1}H NMR ($CDCl_3$): δ 7.88−7.04 (m, 11H), 5.00 (t, J = 6.44 Hz, 1H), 3.05 (d, J = 6.44 Hz, 2H), 2.18 (d, J = 8.58 Hz, 1H). ^{13}C NMR: δ 140.83, 136.89, 133.15, 132.96, 131.41, 131.24, 128.24, 127.94, 127.66, 126.19, 125.93, 124.62, 123.92, 120.44, 75.19, 45.03. EIMS *m/z* (relative intensity): 327 (M^+, 1).

***N*-Benzylhydrozoinodicarboxylic Acid Di-*tert*-butyl Ester (3i).** Pale-yellow solid; mp 102−104 °C. ^{1}H NMR ($CDCl_3$): δ 7.33−7.27 (m, 5H), 6.25 (br s, 1H), 4.64 (s, 2H), 1.49, 1.45 (ss, 18H). ^{13}C NMR: δ 159.30, 128.68, 128.60, 128.46, 127.48, 81.17, 28.20, 28.12.

5. Pd-Catalyzed Coupling Reaction of Benzylic Manganese Halides (2m−n). Benzylic manganese halides were prepared as before. After being stirred, the mixture was cooled to 0 °C and 1,2-dibromoethane was syringed neat at this temperature. The resulting mixture was added via cannula to a mixture of ethyl 4-iodobenzoate and 5 mol % of $Pd(PPh_3)_4$ catalyst in THF at room temperature. The mixture was stirred at room temperature for 2 h. An aqueous solution of 3 M HCl (10 mL) was added, and then the mixture was extracted with diethyl ether (2 × 20 mL). The combined organic layers were washed sequentially with saturated $NaHCO_3$ (2 × 20 mL), saturated $Na_2S_2O_3$ (2 × 20 mL), and saturated NaCl (2 × 20 mL) and then dried over $MgSO_4$. Removal of solvents and flash

chromatography (ethyl acetate/hexanes) afforded **2m** in 56% isolated yield.

Ethyl 4-Benzylbenzoate (2m). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 8.05−7.20 (m, 9H), 4.41 (q, J = 7.15 Hz, 2H), 4.06 (s, 2H), 1.42 (t, J = 7.15 Hz, 3H). ^{13}C NMR: δ 166.42, 146.27, 140.06, 129.68, 128.82, 128.79, 128.49, 128.34, 126.25, 60.68, 41.77, 14.22. HRMS calcd for $C_{16}H_{16}O_2$ 240.1150 found 240.1151.

Ethyl 4-(4′Bromobenzyl)benzoate (2n). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 8.00−7.03 (m, 8H), 4.37 (q, J = 7.15 Hz, 2H), 3.98 (s, 2H), 1.39 (t, J = 7.15 Hz, 3H). ^{13}C NMR: δ 166.39, 145.56, 139.10, 131.60, 130.58, 129.99, 129.81, 129.00, 128.78, 128.63, 120.19, 60.80, 41.18, 14.27. EIMS *m/z* (relative intensity): 319 (M^+, 34).

6. Typical Procedure for the Cross-Coupling Reactions of Benzyl Manganese Sulfonates. Benzyl mesylate[10] (9 mmol) was added via syringe to a slurry of active manganese (10 mmol) being stirred in THF (10 mL) at room temperature. The resulting mixture was stirred at room temperature for 20 min. The reaction was monitored by gas chromatography. After the completion of the oxidative addition, the mixture was cooled to 0 °C. 1,2-Dibromoethane was added to the mixture at this temperature, and the mixture was stirred for 5 min. Benzoyl chloride was added to the resulting mixture at room temperature. After being stirred for 30 min, the mixture was quenched with 3 M HCl solution and extracted with diethyl ether. The combined organic layers were washed with $NaHCO_3$, $Na_2S_2O_3$, and brine, dried over anhydrous $MgSO_4$, and concentrated using a rotary evaporator. Flash column chromatography (ethyl acetate/hexanes) afforded the corresponding ketones.

3-(4′-Bromophenyl)-2-phenylpropan-2-ol (3j). Pale-brown oil. ^{1}H NMR ($CDCl_3$): δ 7.41−6.85 (m, 9H), 3.04 (q, J = 13.50 Hz, 2H), 1.59 (s, 3H). ^{13}C NMR: δ 147.00, 135.77, 132.20, 130.90, 128.04, 126.74, 124.88, 120.56, 74.33, 49.78, 29.18.

2-(4′-Chlorophenyl)-1-phenylethan-1-ol (3k). Pale-yellow solid; mp 55−56 °C. ^{1}H NMR ($CDCl_3$): δ 7.36−7.08 (m, 9H), 4.84 (t, J = 6.60 Hz, 1H), 2.99 (d, J = 6.90 Hz, 2H), 2.14 (d, J = 4.20 Hz, 1H). ^{13}C NMR: δ 143.45, 136.41, 132.26, 130.80, 128.39, 127.67, 125.81, 75.13, 45.03.

3-(4′-Chlorophenyl)-2-phenylpropan-2-ol (3l). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.41−6.90 (m, 9H), 3.05 (q, J = 13.50 Hz, 2H), 1.89 (br s, 1H), 1.58 (s, 3H). ^{13}C NMR: δ 147.04, 135.24, 132.42, 131.81, 128.05, 127.98, 126.76, 124.89, 74.40, 49.74, 29.23. HRFAB calcd for $C_{15}H_{15}ClO$ 246.0811, found $(M + Li)^+$ 253.0969.

2-(3′-Trifluoromethylphenyl)-1-phenylethan-1-ol (3m). Pale-yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.52−7.31 (m, 9H), 4.89, 4.87 (dd, J = 5.96, 5.72 Hz, 1H), 3.08 (m, 2H), 2.14 (s, 1H). ^{13}C NMR: δ 143.36, 139.00, 132.94, 128.62, 128.44, 127.80, 126.19 (q), 125.80, 123.27 (q), 75.05, 45.41. HRFAB calcd for $C_{15}H_{13}F_3O$ 266.0918, found $(M + Li)^+$ 273.1076.

2-(2′-Chloro-4′-fluorophenyl)-1-phenylethan-1-ol (3n). Pale-yellow solid; mp 64−66 °C. ^{1}H NMR ($CDCl_3$): δ 7.36−6.86 (m, 8H), 4.96, 4.93 (dd, J = 5.25, 5.01 Hz, 1H), 3.18−3.03 (m, 2H), 2.39 (br s, 1H). ^{13}C NMR: δ 162.87, 159.58, 143.62, 134.66, 134.53, 132.81, 132.69, 131.81, 131.76, 128.36, 127.64, 125.64, 116.76, 116.44, 113.83, 113.56, 73.30, 42.68. HRFAB calcd for $C_{14}H_{12}ClFO$ 250.0561, found $(M + Li)^+$ 257.0729.

2-(3′-Methoxyphenyl)-1-phenylethan-1-ol (3p). ^{1}H NMR ($CDCl_3$): δ 7.39−6.75 (m, 8H), 4.91, 4.88 (dd, J = 5.48, 5.45 Hz, 1H), 3.78 (s, 3H), 3.03, 3.00 (dd, J = 3.10, 5.96 Hz, 2H), 2.24 (s, 1H). ^{13}C NMR: δ 159.50, 143.70, 139.52, 129.33, 128.27, 127.45, 125.81, 121.72, 114.95, 111.98, 75.06, 54.99, 45.98.

7. Typical Procedure for the Coupling Reaction of 1f with Aldehydes and Acid Chlorides (4a−4d, 5−9). Benzylic manganese reagent was prepared as before. To the resulting benzylic manganese reagent was added the aldehyde (or acid chloride) at room temperature. After being stirred for 1 h, the mixture was quenched with 3 M HCl solution and extracted with diethyl ether. The combined organic layers were washed with $NaHCO_3$, $Na_2S_2O_3$, and brine, dried over anhydrous $MgSO_4$, and concentrated using a rotary evaporator. Flash column chromatography (ethyl acetate/hexanes) afforded the corresponding coupling product.

1-(3,5-Dimethoxyphenyl)-2-hydroxytridecane (4a). ^{1}H NMR ($CDCl_3$): δ 6.37−6.35 (m, 3H), 3.78 (s, 7H), 2.80, 2.75 (dd, J = 3.82 Hz, 3.81 Hz, 1H), 2.58, 2.54 (dd, J = 8.59 Hz, 8.58 Hz, 1H), 1.60 (br s, 1H), 1.52−1.26 (m, 20H), 0.88 (t, J = 5.96 Hz, 3H). ^{13}C NMR: δ 160.89, 140.99, 107.30, 98.38, 72.48, 55.24, 44.36, 36.84, 31.89, 29.64, 29.61, 29.33, 25.75, 22.66, 14.09.

1-(3,5-Dimethoxyphenyl)-2-hydroxypentadecane (4b). ^{1}H NMR ($CDCl_3$): δ 6.38−6.35 (m, 3H), 3.78 (s, 7H), 2.80, 2.75 (dd, J = 4.06 Hz, 4.05 Hz, 1H), 2.59, 2.54 (dd, J = 8.58 Hz, 8.82 Hz, 1H), 1.62 (s, 1H), 1.53−1.26 (m, 24H). 0.89 (t, J = 6.20 Hz, 3H). ^{13}C NMR: δ 160.87, 140.98, 107.28, 98.36, 72.47, 55.21, 44.36, 36.84, 31.89, 29.64, 29.33, 25.74, 22.65, 14.08.

1-(3,5-Dimethoxyphenyl)-pentadecan-2-one (4c). ^{1}H NMR ($CDCl_3$): δ 6.35 (br s, 3H), 3.78 (br s, 6H), 3.60 (s, 2H), 2.44 (t, J = 7.39 Hz, 2H), 1.53 (br s, 2H), 1.25−1.23 (m, 20H), 0.88 (t, J = 6.90 Hz, 3H). ^{13}C NMR: δ 208.46, 160.93, 136.49, 107.28, 98.93, 55.25, 50.42, 41.76, 31.88, 29.59, 29.42, 29.32, 29.05, 23.70, 22.65, 14.06.

1-(3,5-Dimethoxyphenyl)-heptadecan-2-one (4d). ^{1}H NMR ($CDCl_3$): δ 6.35 (br s, 3H), 3.78 (s, 6H), 3.59 (s, 2H), 2.43 (t, J = 7.39 Hz, 2H), 1.59 (br s, 2H), 1.25−1.23 (m, 24H), 0.88 (t, J = 5.72 Hz, 3H). ^{13}C NMR: δ 208.45, 160.91, 136.49, 107.37, 98.93, 55.25, 50.42, 41.76, 31.88, 29.64, 29.61, 29.55, 29.42, 29.32. 29.07, 23.70, 22.65, 14.08.

2-(3,5-Dimethoxyphenyl)-1-phenylethan-1-ol (5). ^{1}H NMR ($CDCl_3$): δ 7.28−7.26 (m, 5H), 6.36 (br s, 3H), 4.91, 4.88 (dd, J = 4.76 Hz, 4.77 Hz, 1H), 3.76 (s, 6H), 3.03−2.88 (m, 2H), 2.09 (br s, 1H). ^{13}C NMR: δ 160.80, 143.70, 140.25, 128.75, 127.57, 125.87, 107.36, 98.67, 75.03, 55.24, 55.21, 46.40.

2-(3,5-Dimethoxyphenyl)-1-(3′-methoxyphenyl)ethan-1-ol (6). ^{1}H NMR ($CDCl_3$): δ 7.29−6.81 (m, 4H), 6.36 (br s, 3H), 4.86, 4.83 (dd, J = 4.77 Hz, 5.01 Hz, 1H), 3.80, 3.75 (ss, 9H), 2.96−2.91 (m, 2H), 2.35 (br s, 1H). ^{13}C NMR: δ 160.62, 159.52, 145.43, 140.22, 129.25, 118.10, 112.99, 111.14, 107.27, 98.52, 74.81, 55.08, 46.20, 3509 (br), 2939, 2836, 1598, 1463, 1262, 1067, 832 cm^{-1}.

2-(3,5-Dimethoxyphenyl)-1-(4′-methoxyphenyl)ethan-1-ol (7). ^{1}H NMR ($CDCl_3$): δ 7.27, 6.88 (dd, J = 11.45 Hz, 8.58 Hz, 4H), 6.35 (br s, 3H), 4.83 (t, J = 7.39 Hz, 1H), 3.80, 3.75 (ss, 9H), 2.94−2.91 (m, 2H), 2.17 (br s, 1H). ^{13}C NMR: δ 160.70, 158.95, 140.41, 135.91, 127.08, 113.66, 107.31, 98.54, 74.62, 55.15, 46.27.

1-(3,4-Dimethoxyphenyl)-2-(3′,5′-dimethoxyphenyl)-ethan-1-ol (8). ^{1}H NMR ($CDCl_3$): δ 6.90−6.80 (m, 3H), 6.34 (br s, 3H), 4.83, 4.81 (dd, J = 5.40 Hz, 5.49 Hz, 1H), 3.86, 3.73 (ss, 12H), 2.94−2.90 (m, 2H), 2.16 (br s, 1H). ^{13}C NMR: δ 160.73, 148.85, 148.31, 140.32, 136.39, 118.04, 110.79, 108.94, 107.73, 98.52, 74.81, 55.82, 55.75, 55.15, 46.33.

1-(4-Benzyloxy-3-methoxyphenyl)-2-(3′,5′-dimethoxyphenyl)ethan-1-ol (9). ^{1}H NMR ($CDCl_3$): δ 7.46−6.78 (m, 8H), 6.35 (br s, 3H), 5.14 (s, 2H), 4.79 (t, J = 6.68 Hz, 1H), 3.86, 3.72 (ss, 9H), 2.92 (d, J = 6.44 Hz, 2H), 2.45 (br s, 1H). ^{13}C NMR: δ 160.49, 149.33, 147.18, 140.25, 136.94, 128.27, 127.57, 127.03, 117.88, 113.50, 109.42, 107.21, 98.33, 74.61, 70.72, 55.69, 54.96, 46.08.

8. Typical Procedure for the Homocoupling Products (10a−c). To a slurry of Mn* was added *m*-cyanobenzyl bromide at room temperature, and the resulting mixture was stirred at this temperature for 20 min. The oxidative addition was monitored by TLC and/or gas chromatography. The mixture was quenched with 3 M HCl solution and extracted with ethyl acetate. The organic layer was washed with saturated Na_2HCO_3 and solutions of NaCl followed by drying over anhydrous $MgSO_4$. Recrystallization with ethanol gave 1,2-di-(*m*-cyanophenyl)ethane in 90% isolated yield.

1,2-Di-(*m*-cyanophenyl)ethane (10a). Pale-brown solid; mp 159−161 °C. ^{1}H NMR ($CDCl_3$): δ 7.53−7.33 (m, 4H), 2.97 (s, 2H). ^{13}C NMR: δ 141.85, 132.97, 131.88, 130.10, 129.23, 118.72, 112.51, 36.77.

1,2-Di-(*p*-cyanophenyl)ethane (10b). Pale-brown solid; mp 200−203 °C. ^{1}H NMR ($CDCl_3$): δ 7.58−7.21 (m, 4H), 3.00 (s, 2H). ^{13}C NMR: δ 146.03, 132.26, 129.20, 118.80, 110.25, 37.15. HRMS calcd for $C_{16}H_{12}N_2$ 232.1000, found 232.1003.

2,3-Diphenylbutane (10c). ^{1}H NMR ($CDCl_3$): δ 7.37−7.23 (m 10H), 2.84−2.80 (m, 2H), 1.06−1.03 (m, 6H). ^{13}C NMR: δ 146.48, 128.27, 127.60, 126.03, 47.23, 21.02.

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for compounds **2a**−**i**, **2m**, **3a**−**h**, **4a**−**d**, **8**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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