Manganese-catalyzed Phenylation of Acetylenic Compounds with a Phenyl Grignard Reagent

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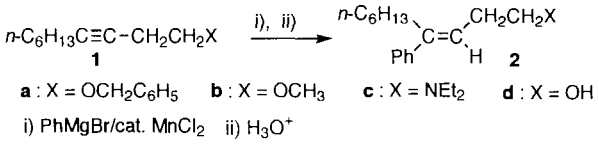
Treatment of homopropargylic alcohol derivatives or phenylacetylene compounds with phenylmagnesium bromide in the presence of a catalytic amount of manganese(II) chloride afforded phenylated products in good yields with high regio- and stereoselectivities.

The synthesis of stereospecifically substituted alkenes is a major challenge in organic synthesis. Among the many methods now available for such syntheses, carbometallation of alkynes by organometallic reagents is widely studied.[1] There are many reports on allylmetallation and alkylmetallation reactions. In contrast, few examples are known about phenylmetallation[2] of acetylenic compounds.

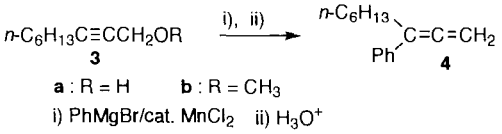
Recently, we have reported that allylmagnesium bromide added to homopropargylic alcohol derivatives in the presence of a manganese catalyst with high regio- and stereoselectivities.[3] On further exploration of the carbomanganation, it was found that phenylmagnesium bromide added not only to homopropargylic alcohol and homopropargylic amine derivatives but also to phenylacetylenic compounds.

Phenylmagnesium bromide (1.0 M tetrahydrofuran solution, 1 M = 1 mol dm^{-3}, 3.0 mL, 3.0 mmol) was added to a suspension of manganese(II) chloride (12 mg, 0.1 mmol) in toluene (10 mL) containing benzyl ether of 3-decyn-1-ol (**1a**, 244 mg, 1.0 mmol) at 25 °C under argon atmosphere. The reaction mixture was heated to 100 °C and immediately it turned to a clear solution. After being stirred for 7 h at 100 °C, the resulting mixture was poured into water. Extraction with ethyl acetate (3 x 20 mL) followed by silica-gel column purification provided a benzyl ether of (*E*)-4-phenyl-3-decen-1-ol **2a** (229 mg) in 71% yield. Methyl ether **1b** or diethylamine **1c** gave the corresponding adduct **2b** or **2c** in 74% or 59% yield, respectively. The reaction of 3-decyn-1-ol (**1d**) with PhMgBr under $MnCl_2$ catalysis provided **2d** and its (*Z*) stereoisomer in 85:15 ratio in 50% combined yield (Scheme 1).



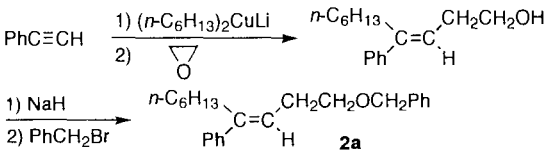
Scheme 1.

The reaction was clearly hetero atom-assisted and heavily dependent on the nature of the hetero atom substituents of the substrates. The presence of a benzyl ether, methyl ether, or diethylamino moiety was essential for the successful reaction. No phenylation product was detected in the reaction of 6-dodecyne with PhMgBr in the presence of a catalytic amount of $MnCl_2$. *N*-(3-Decynyl)-*N*-methylaniline and 3-decynyl phenyl sulfide also provided no phenylation products under the same reaction conditions. 2-Nonyn-1-ol (**3a**) provided 3-phenyl-1,2-nonadiene (**4**) in 70% yield upon treatment with 4 molar amounts of PhMgBr at 100 °C for 12 h in the presence of $MnCl_2$ catalyst. The use of a methyl ether of 2-nonyn-1-ol (**3b**) resulted in formation of **4** in only 25% yield along with an unidentified complex mixture (Scheme 2).



Scheme 2.

The reaction proceeded with high regio- and stereoselectivities except **1d**. The *cis* addition of a phenyl group and manganese metal to the triple bond is ascertained by the comparison of **2a** with a sample generated according to the reported procedure[4] (Scheme 3).



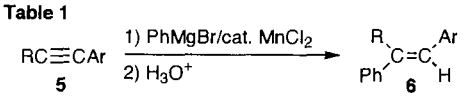
Scheme 3.

Phenylacetylene derivatives[5] proved to react with phenylmagnesium bromide in the presence of a catalytic amount of $MnCl_2$ to give the corresponding adducts in good yields as well as homopropargylic alcohol derivatives. The representative results are shown in Table 1. The following features deserve comment. (1) Other manganese salts such as Mn(acac)$_3$ and $(MeC_5H_4)Mn(CO)_3$ were equally effective for the phenylmetallation reaction. For instance, treatment of **5c** with PhMgBr in the presence of Mn(acac)$_3$ or $(MeC_5H_4)Mn(CO)_3$ afforded **6c** in 90% or 85% yield, respectively. (2) Phenylacetylene itself was not a good substrate for the phenylation reaction. (*E*)-1,2-Diphenylethene was obtained in only 20% yield along with an unidentified complex mixture. (3) Phenylacetylenic derivatives (**5c** and **5d**) having a dimethylamino or a methoxy group in the ortho position facilitated the reaction and the yields of the phenylation products increased dramatically. In contrast, a methoxy group on the para position deactivated the reaction and *p*-methoxyphenylacetylene **5f** provided the phenylated product **6f** in only 38% yield in addition to the starting material **5f** (52%) after stirring the reaction mixture at 100 °C for 12 h. *m*-Methoxyphenylacetylene **5e** gave the phenylated product **6e** in moderate yield (63%). Thus, the coordination of methoxy and dimethylamino groups to manganese could play a critical role in the rate acceleration.[8] (4) The reaction proceeded with high regio- and stereoselectivities. A phenyl group added to the carbon bearing an alkyl moiety and magnesium attached to the other carbon having an aryl moiety. The *cis*-addition products

6b–6h were obtained exclusively except in the case of the reaction of **5a**, in which contamination by a *trans*-addition product was observed. Treatment of **5a** with PhMgBr gave a small amount of (*Z*)-1,2-diphenyl-1-octene in addition to (*E*)-isomer **6a** (*Z*:*E* = 1:10).[9]

Table 1. Phenylation of phenylacetylenic compounds[a]

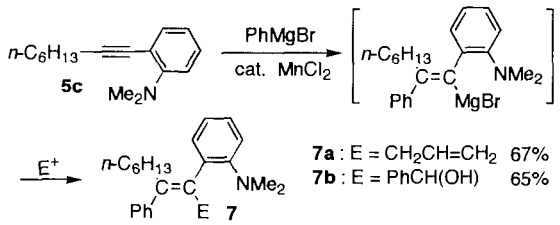
Table 1



Entry	Substrate **5**		Reaction time/h	Product **6** yield/%[b]
	R	Ar		
1 **5a**	*n*-C_6H_{13}	Ph	8	**6a** 66
2 **5b**	Ph	Ph	4	**6b** 60
3 **5c**	*n*-C_6H_{13}	*o*-$Me_2NC_6H_4$	3	**6c**[c] 94
4 **5d**	*n*-C_6H_{13}	*o*-$MeOC_6H_4$	12	**6d**[d] 80
5 **5e**	*n*-C_6H_{13}	*m*-$MeOC_6H_4$	12	**6e** 63
6 **5f**	*n*-C_6H_{13}	*p*-$MeOC_6H_4$	12	**6f** 38[e]
7 **5g**	*n*-C_6H_{13}	*o*-FC_6H_4	12	**6g** 47[f]
8 **5h**	*n*-C_6H_{13}	*p*-FC_6H_4	12	**6h** 71
9 **5i**	*n*-C_6H_{13}	*p*-$CH_3C_6H_4$	12	**6i** 63
10 **5j**	*n*-C_6H_{13}	*p*-$CF_3C_6H_4$	12	**6j** 0[g]

[a]The reaction was performed at 100 °C in toluene. Manganese(II) chloride (0.1 mmol), PhMgBr (3.0 mmol), and acetylenic compound (1.0 mmol) were employed. [b]Isolated yield based on the starting acetylene. [c]See reference 6. [d]See reference 7. [e]Starting material (52%) was recovered. [f]Starting material (17%) was recovered. [g]Starting material (95%) was recovered.

The intermediary alkenylmagnesium compounds have been trapped by various electrophiles. For instance, an addition of allyl bromide to a $MnCl_2$–catalyzed reaction mixture of **5c** and phenylmagnesium bromide gave the allylated product **7a** in 67% yield. The use of benzaldehyde instead of allyl bromide provided the corresponding adduct **7b** in 65% yield (Scheme 4).



Scheme 4.

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6 **6c**: IR (neat) 2922, 2852, 2776, 1595, 1487, 1451, 1318, 1192, 1157, 1144, 1097, 1049, 948, 758, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (t, *J* = 6.6 Hz, 3H), 1.14–1.34 (m, 6H), 1.34–1.47 (m, 2H), 2.73 (t, *J* = 7.8 Hz, 2H), 2.74 (s, 6H), 6.73 (s, 1H), 7.00 (d, *J* = 7.8 Hz, 2H), 7.20–7.39 (m, 5H), 7.49 (d, *J* = 6.9 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 13.89, 22.48, 28.41, 29.41, 30.15, 31.47, 43.93, 117.27, 121.13, 126.67, 126.86, 127.50, 127.58, 128.33, 130.25, 131.58, 140.86, 143.25, 152.68. Found: C, 86.08; H, 9.69%. Calcd for $C_{22}H_{29}N$: C, 85.94; H, 9.51%.

7 **6d**: IR (neat) 3020, 2924, 2852, 1598, 1487, 1459, 1289, 1244, 1176, 1109, 1029, 750, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (t, *J* = 6.9 Hz, 3H), 1.16–1.33 (m, 6H), 1.33–1.45 (m, 2H), 2.65 (t, *J* = 7.5 Hz, 2H), 3.82 (s, 3H), 6.75 (s, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 7.24–7.40 (m, 5H), 7.48 (d, *J* = 6.9 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 13.90, 22.49, 28.63, 29.25, 30.11, 31.45, 55.36, 110.49, 120.15, 123.79, 126.81, 127.01, 127.47, 128.12, 128.30, 129.75, 142.96, 143.12, 157.65. Found: C, 85.38; H, 8.96%. Calcd for $C_{21}H_{26}O$: C, 85.66; H, 8.90%.

8 Although the precise mechanism to account for the results of entries 1–10 remains unclear, we assume that the electronic effect of substituents on benzene ring should play an important role.

9 The reaction of **5c** with other Grignard reagent such as *p*-methoxyphenylmagnesium bromide or 1-naphthylmagnesium bromide provided the corresponding adduct in 50% or 25% yield, respectively along with the recovered starting material (35% or 63%). The use of 2-thienylmagnesium bromide resulted in complete recovery of **5c**.