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Preparation of Allyl-, Alkenyl- and of Functionalized Arylmanganese Reagents by Oxidative Insertion of Manganese-Graphite into Organic Halides

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Abstract: Reduction of $MnBr_2{\cdot}nLiBr$ (n = 1,2) with 2 C_8K in THF affords highly active Mn-graphite, which readily inserts into allyl-, alkenyl-, (substituted) aryl- and heteroaryl halides. The functionalized organomanganese compounds thus obtained may be efficiently trapped with different electrophiles such as aldehydes, anhydrides and acid chlorides, or can be cross-coupled with alkenyl halides in the presence of catalytic amounts of $Fe(acac)_3$.

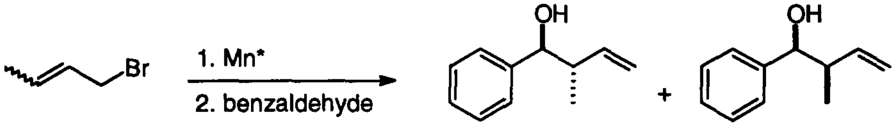
Organomanganese reagents are usually prepared by transmetallation of *e. g.* organolithium- or organomagnesium compounds with Mn(2+)-salts and turned out to be valuable nucleophiles for selective C-C-bond formations.[1,2] However, the need for reactive RLi (RMgX) precursors largely precludes the formation of *functionalized* organomanganese species by such a metathetic route. As they are perfectly feasible in view of the tolerance of the C-Mn bond towards an array of functional groups, the preparation of RMnX by oxidative insertion of Mn(0) into substituted organic halides is tempting. Metallic manganese exhibits an appropriate reduction potential but its reactivity is corrumpated by the resistant oxide coating of its surface.[3,4] Thus, commercial Mn powder, when activated with iodine or by Lewis acids such as $ZnCl_2$, inserts only into the most reactive substrates such as allylic halides or α-bromoesters at elevated temperatures,[5,6] while ultrasonication results in exclusive Wurtz coupling of such compounds.[7] Reports on the use of more appropriately activated Mn* samples are scarce: an ill-defined species was obtained upon reduction of $MnCl_2$ with $LiAlH_4$, which affords homoallylic alcohols from allylic halides and carbonyl compounds;[8] only recently, Rieke-Mn has been described which holds the promise of a broader scope, although only reactions with simple alkyl bromides and with 3-bromothiophene have been disclosed so far.[9]

$$2\,K + 16\,C \xrightarrow{150°C, 10\ min,\ Ar} 2\,C_8K \xrightarrow[THF,\ -20°C,\ 60\ min]{MnBr_2{\cdot}nLiBr} \text{Mn-graphite} + n\,LiBr + 2\,KBr \quad (1)$$

In the following we report some preliminary results on the preparation and use of highly activated Mn-graphite which properly adds to a wide range of allyl-, alkenyl-, and differently substituted aryl halides at ambient temperature. This reagent is obtained upon reduction of the well soluble *ate*-complex $MnBr_2{\cdot}nLiBr$ (n = 1,2)[10] with the potassium-graphite intercalation compound C_8K in THF at -20°C (Eq. 1).[11-13] Other manganese salts gave inferior results, mainly due to their low solubility and/or to concomitant cleavage of the ethereal solvent used.

Mn-graphite promotes stereodivergent reactions of crotyl bromide with aldehydes as shown in Table 1 (entries 1,2). Although this outcome reflects the behavior of many other crotyl metal species,[14] it is surprising in the light of the results of *Hiyama* who reported just the reversed selectivity in a reaction of (*E*)-crotyl bromide promoted by Mn* obtained from $MnCl_2$ and $LiAlH_4$ (Table 1, entry 3).[8]

Table 1. Mn*-induced reactions of (*Z*)- and (*E*)-crotyl bromide with benzaldehyde.



Entry	Substrate	Reagent	Yield (%)	*threo*:*erythro*
1	(*Z*)-crotyl bromide	Mn-graphite	65%	41 : 59
2	(*E*)-crotyl bromide	Mn-graphite	72%	64 : 36
3	(*E*)-crotyl bromide	$MnCl_2 + LiAlH_4$	78%	35 : 65[8]

Mn-graphite (1.5-3 eq.) also reacts smoothly with different alkenyl-, aryl- and heteroaryl halides tolerating several functional groups in the starting materials. Even 4-chlorobenzonitrile is metallated (Table 3, entry 5), although a slightly higher amount of the reagent (5 eq.) is necessary in this case in order to achieve complete conversion. Our results are summarized in Tables 2 and 3. The nucleophiles obtained show the regular reactivity pattern of RMnX species and can be trapped *i.a.* with differently substituted aldehydes, acid chlorides or anhydrides. Of interest is the efficient O→C silatropic rearrangement observed upon metallation of 2,4-bis-(trimethylsilyloxy)-5-iodopyrimidine which leads to 5-trimethylsilyluracil[15] in 75% isolated yield (Table 3, entry 8). Finally it should be noted that the cross-coupling of *o*-FC_6H_4MnBr with (*E*)-1-iodo-1-hexene catalyzed by $Fe(acac)_3$ (3 mol%) worked nicely (Table 3, entry 10). This methodology which was recently pioneered by *Cahiez* et al.[2a] may well evolve into an attractive alternative to the established Pd- or Ni-catalyzed C-C-bond formations between C(sp^2)-centers. Further work on this and related projects is currently in progress.

Table 2. Mn-graphite induced reactions of alkenyl iodides.

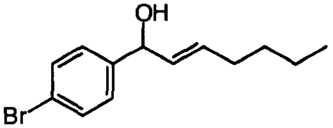
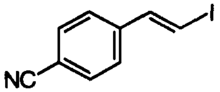
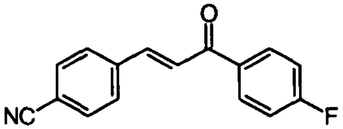
Entry	RX	Electrophile	Product	Yield (%)
1	(*E*)-1-iodo-1-hexene	p-BrC_6H_4CHO		62
2		p-FC_6H_4COCl		61

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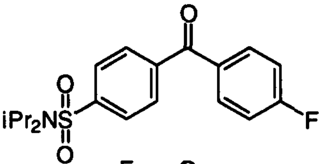
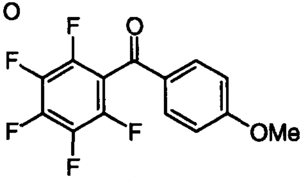
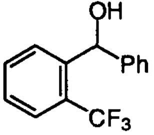
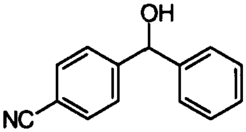
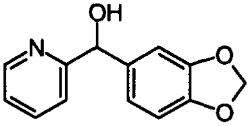
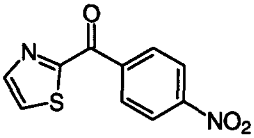
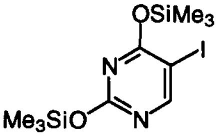
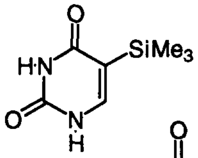
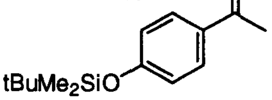
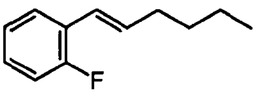
Table 3. Mn-graphite induced reactions of aryl halides[16]

Entry	RX	Electrophile	Product	Yield (%)
1	4-Br$C_6H_4SO_2N$-iPr$_2$	p-FC_6H_4COCl		64
2	F_5C_6Br	p-$MeOC_6H_4COCl$		69
3	2-(CF_3)C_6H_4Br	PhCHO		75
4	4-NC-C_6H_4Br	PhCHO		65
5	4-NC-C_6H_4Cl	PhCHO		68 [a]
6	2-bromopyridine	2,3-(methylenedioxy)-benzaldehyde		70
7	2-bromothiazole	p-$NO_2C_6H_4COCl$		60
8				75
9	4-(tBuMe_2SiO)C_6H_4Br	Ac_2O		66
10	2-F-C_6H_4Br	(*E*)-1-iodo-1-hexene		67 [b]

[a] with 5 equiv. of Mn-graphite; [b] in the presence of Fe(acac)$_3$ (3 mol%) as catalyst using THF rather than THF/NMP as the solvent as described in ref. 2a.

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16. *Representative Procedure*: A precooled yellow solution (-15°C) of $MnBr_2$ (645 mg, 3 mmol) and LiBr (261 mg, 3 mmol) in THF (15 mL) was added to a suspension of C_8K (810 mg, 6 mmol)[11] in THF (10 mL) at -20°C. After stirring for 1h at that temperature, F_5C_6Br (0.25 mL, 2 mmol) was added and the mixture stirred at ambient temperature for 1h. The graphite was allowed to settle and the supernatant solution separated via canula. After cooling to -78°C, 4-methoxybenzoyl chloride (341 mg, 2 mmol) was added and the reaction slowly warmed to room temperature overnight. Addition of HCl (0.5M, 80 mL), followed by a standard extractive work-up and flash chromatography (hexane/EtOAc 10/1) afforded 2,3,4,5,6-penta-fluoro-4'-methoxybenzophenone as colorless crystals (417 mg, 69%). mp = 78-80°C; MS: *m/z* (rel.%): 302 (58, $[M^+]$), 135 (100). ^1H NMR ($CDCl_3$): δ 7.81 (d, 2H), 6.97 (d, 2H), 3.89 (s, 3H); ^{19}F NMR ($CDCl_3$): δ -140.1 (vt, J = 7), -152.0 (t, J = 19), -160.8 (dt, J = 7, 19).

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