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ORGANOMANGANESE (II) REAGENTS XX[1]: MANGANESE MEDIATED BARBIER AND REFORMATSKY LIKE REACTIONS AN EFFICIENT ROUTE TO HOMOALLYLIC ALCOHOLS AND β-ACETOXYESTERS

Gérard CAHIEZ * and Pierre-Yves CHAVANT

Laboratoire de Chimie des Organoéléments, UA 473, tour 44-45
Université P. et M. Curie, 4 Place Jussieu F-75252 PARIS Cédex 05

Abstract : *Allylic halides and α-bromoesters react with manganese metal in ethyl acetate; THF can also be used as solvent if a catalytic amount of zinc chloride is added to the reaction mixture. When the reaction is performed in the presence of various aldehydes or ketones, excellent yields of 1,2-addition products are obtained in preparative conditions.*

Until now, organomanganese reagents have always been prepared from organolithium or organomagnesium compounds[2] according to a metal-metal exchange reaction:

$$\mathrm{RMgX \;\; or \;\; RLi \;\; + \; MnX_2 \;\; \xrightarrow[X=Cl,\ Br,\ I]{\text{Ether or THF}} \;\; RMnX}$$

In the course of our studies on the chemistry of organomanganese reagents, we have tried to prepare these ones directly from manganese metal and organic halides.

$$\mathrm{RX + Mn \longrightarrow RMnX}$$

We report now our first positive results on the reaction of some reactive organic halides such as allylic halides and α-bromoesters with manganese metal.

To prevent side reactions (*i. a. Würtz coupling reaction*), all the experiments presented herein have been performed in the presence of a carbonyl compound (*Barbier and Reformatsky reactions*) in order to trap the expected organomanganese reagent. Moreover, for practical considerations, these experiments have been carried out with a commercial coarse-ground manganese[3], which is easily available and cheap. We have first shown, in the case of the reaction of allyl bromide with manganese, that the choice of the solvent is decisive. Indeed, among usual organic solvents, only ethyl acetate allows to perform the reaction. Some preparative examples are given in Table I :

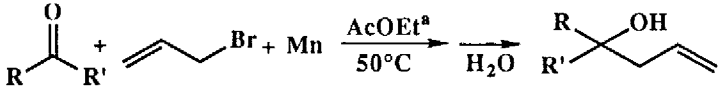
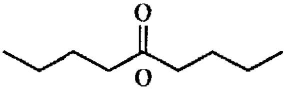
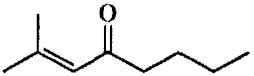
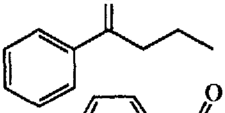
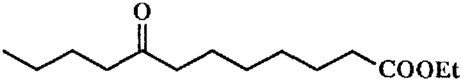
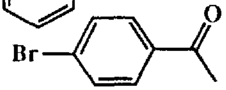
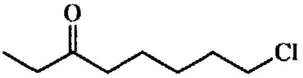
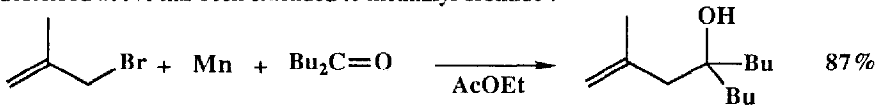


Table I[a]

RCOR'	yield[b]	RCOR'	yield[b]
	86%		75%
	91%		87%
	85%		79%

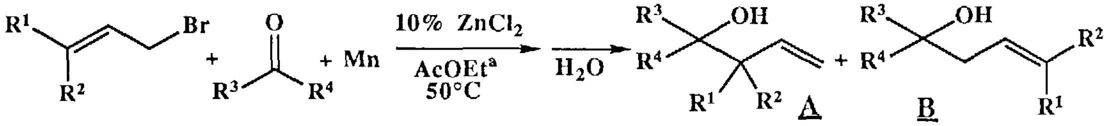
a) for a general procedure see note 4. b) isolated yield.

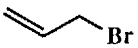
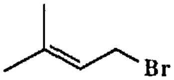
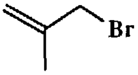
The reaction described above has been extended to methallyl bromide :



Unfortunately, with aldehydes and methyl ketones, as well as with other allylic bromides (*e. g. crotyl bromide*), the yields of homoallylic alcohol are low. However, the addition of a catalytic amount of $ZnCl_2$ (*or* $CdCl_2$ *or* $HgCl_2$) to the reaction mixture dramatically improves the results (Table II).

Table II

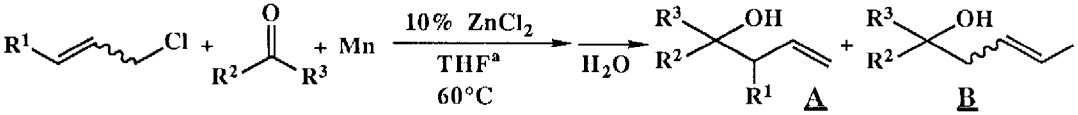


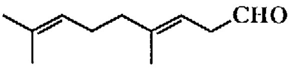
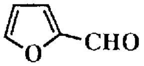
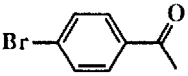
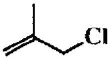
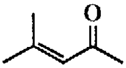
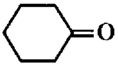
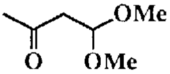
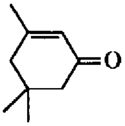
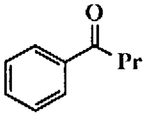
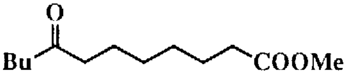
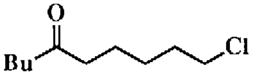
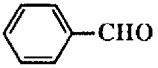
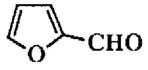
allylic halide	carbonyl compound	yield[b]	allylic halide	carbonyl compound	yield[b] (A/B ratio)
	n-HexCHO	85%[d]		BuCOBu	87%[e] (>99/1)
"	t-BuCHO	87%[d]	"	HeptCOMe	80%[e] (>99/1)
"	PhCHO	82%[d]	"	n-HexCHO	84%[d, e] (100/0)
"	HeptCOMe	86%		n-HexCHO	79%[d] (100/0)
	n-HexCHO	83%[d]	"	BuCOBu	77% (80/20)

a) for a general procedure see note. 4. b) isolated yield. c) a mixture of primary and secondary crotyl bromide (87/13) was used. d) obtained as acetate, since under our conditions, the secondary homoallylic alcoholate reacts with the solvent. e) diastereoisomeric mixture.

The addition of a catalytic amount of $ZnCl_2$ also allows to perform the reaction in THF. Furthermore, under these conditions, it should be emphasized that allylic chlorides can be used successfully. This is evidenced in Table III:

Table III :

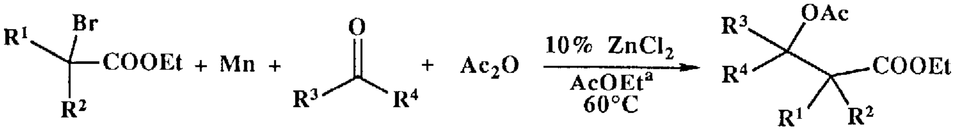


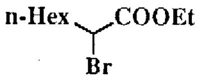
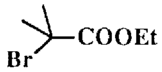
allylic halide	carbonyl compound	yield[b]	allylic halide	carbonyl compound	yield[b] (A/B ratio)
	PentCOPent	88%			80%
"	HeptCOMe	91%	"		94%
"		76%			70%
"		81%	"		95%
"		94%	 [c]		89%[d] (74/26)
"		66%	"	PentCOPent	98%[d] (96/4)
"		93%	"	HeptCOMe	85%[d] (98/2)
"		90%	"	HexCHO	88%[d] (100/0)
"	HexCHO	85%	"		88%[d] (91/9)

a) for a general procedure see note 4. b) isolated yield. c) a mixture of primary and secondary crotyl chlorides (70/30) was used d) diastereoisomeric mixture.

Finally, our procedure has been extended to α-bromoesters ; the reaction have to be performed in the presence of a stoichiometric amount of acetic anhydride, in order to trap the alcoholate resulting from the 1,2-addition reaction[5] :

Table IV :



α-halo-ester	carbonyl compound	yield[b]	α-halo-ester	carbonyl compound	yield[b,c]
BrCH$_2$COOEt	n-HexCHO	80%		n-HexCHO	80%
"	PhCHO	89%	"	PhCHO	86%
"	HeptCOMe	86%	"	t-BuCHO	60%
	n-HexCHO	81%	"	HeptCOMe	35%

a) for general procedure see note 4. b) isolated yield. c) diastereoisomeric mixtures.

In conclusion, we have shown that manganese metal, without any special preparation, easily reacts with a reactive organic halide (allylic halides and α-halogenoesters) in the presence of a carbonyl compound under conditions of real preparative interest. The scope of the reaction is very broad, thus, a vast array of homoallylic alcohols and β-hydroxy-esters are easily prepared in excellent yields. Lastly, the high chemoselective conversion of numerous functional ketones (keto-esters, keto-acetals, ω-chloro-ketones) into the corresponding functional alcohols should be pointed out[6].

Acknowledgements : We thank the C.N.R.S. (U. A. 473) and Elf Aquitaine (Groupement de Recherches de Lacq, France) for their financial support.

References and notes :

1. For part XIX see : G. Cahiez and B. Laboue, Tetrahedron Lett., preceding letter.
2. G. Cahiez and M. Alami, Tetrahedron, 1989, 45, 4163.
3. Manganese Gran., 99,8%, Fluka was used. Commercial micronized manganese powders must be avoided, since they contain large amounts of oxides ; with such a material, the reaction requires a large excess of manganese (7 eq.) and allylic halide (6 eq.). Moreover, the manganese has to be activated by addition of one equivalent of iodine. These conditions do not present any preparative value : T. Hiyama, M. Sawahata, M. Obayashi, Chem. Lett., **1983**, 1237.
4. A typical experimental procedure is as follows : in a round-bottomed flask equipped with an efficient mechanical stirring, under N$_2$ atmosphere, are introduced 75 mmoles (4.13g) of manganese powder and (if necessary) 5 mmoles of dry ZnCl$_2$ (0.68g, 0.1 eq.with regard to the carbonyl compound). To ensure the startup of the reaction, 1 ml of the solvent (ethyl acetate or THF) and a few drops of allyl bromide are introduced, and the mixture is stirred at 60°C for 30 min. Then, a solution of the carbonyl compound (50 mmoles), the allylic halide (70 mmoles) or the α-bromo-ester (55 mmoles) and eventually acetic anhydride (if necessary, 55 mmoles), in an appropriate amount of solvent to obtain 50 ml of solution, are added dropwise, at 60°C, over a period of 3 to 4 h (mechanical pump). The stirring is continued for 15 min. then the reaction mixture is quenched at 0°C with 50 ml of HCl 1N. After the usual work-up, the alcohol is isolated by distillation.
5. In the absence of acetic anhydride, the yields are lower, since retroaddition occurs.
6. French Patents (Elf-Aquitaine) n° 87 18352 and 87 18353, 30 December 1987, G. Cahiez, P. Y. Chavant and P. Tozzolino.

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