Salt Effects on the Reactivity and the Stability of Organomanganese Reagents[1]

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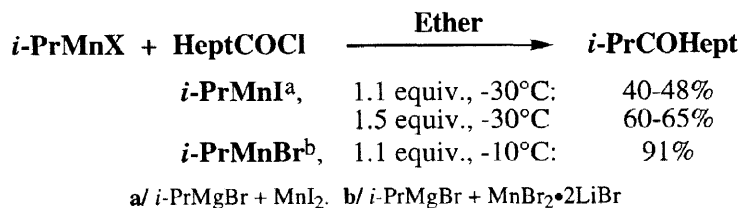13 Boulevard de l'Hautil, F-95092 Cergy-Pontoise, France.

Abstract: The reactivity and the stability of organomanganese reagents prepared from the ate complexes $MnX_2 \cdot 2LiBr$ (X= Br,I) and $MnCl_2 \cdot R_4NX$ (X= Br, Cl) were studied. The preparation and the use for synthetic applications of stable *sec-* and *tert-* alkylmanganese bromides in ether as well as the acylation of RMnCl by R'COOCOOEt in THF were successfully achieved for the first time.
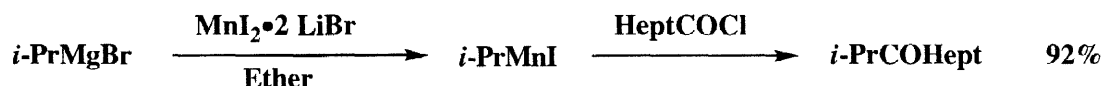© 1998 Elsevier Science Ltd. All rights reserved.

Organomanganese reagents are generally prepared by transmetallation from the corresponding organolithium or magnesium compounds in ether or in THF.[2] The choice of the solvent is sometimes determinant for synthetic applications. For instances, the Cu-catalyzed 1,4 addition to enones or related compounds only takes place in THF[3] whereas the 1,2 addition to ketones gives higher yields in ether (in THF a partial deprotonation of the ketone occurs).[4] According to these considerations, it is important to be able to prepare efficiently organomanganese halides in both solvents. In THF, organomanganese chlorides are easily obtained from the ate complex $MnCl_2 \cdot 2LiCl$.[2a] This is very interesting for large scale applications since manganese chloride is a cheap starting material, moreover, organomanganese chlorides prepared in this way are generally stable between 0°C and room temperature. In ether, the first preparations of organomanganese halides have been achieved by using manganese iodide which is the only manganese halide soluble enough in this solvent to react efficiently with organolithium or magnesium compounds. Later, we have described a more convenient and economic route to prepare organomanganese halides in ether from the soluble ate complex $MnBr_2 \cdot 2LiBr$.[5] This one is readily obtained by stirring a mixture of anhydrous manganese bromide (commercially available) with two equivalents of lithium bromide in suspension in ether at room temperature until obtention of a clear colourless solution.

Until now, the use of *sec-* and *tert-*alkylmanganese reagents prepared in ether seemed limited. Thus, we had shown that *sec-* and *tert-*alkylmanganese iodides prepared in this solvent from the corresponding organomagnesium compounds[6] are poor reagents for preparative organic chemistry since they are too unstable (β-elimination).[7] Recently, we have discovered that *sec-* and *tert-*alkylmanganese bromides prepared from the complex $MnBr_2 \cdot 2LiBr$ are much more stable and can be used efficiently for synthetic applications.

i-PrMnX + HeptCOCl	Ether	*i*-PrCOHept
i-PrMnI[a],	1.1 equiv., -30°C:	40-48%
	1.5 equiv., -30°C	60-65%
i-PrMnBr[b],	1.1 equiv., -10°C:	91%

a/ *i*-PrMgBr + MnI₂.   b/ *i*-PrMgBr + MnBr₂•2LiBr

As shown above, *iso*-propylmanganese iodide prepared from *iso*-propylmagnesium bromide and manganese iodide reacts with heptanoyl chloride at -30°C to lead to the expected ketone in only 40 to 48% yield. Even by using an excess of organometallic the yield remains moderate (60-65%). On the other hand, from the more stable *iso*-propylmanganese bromide (1.1 equiv.) prepared from $MnBr_2 \cdot 2LiBr$ the ketone was obtained in excellent yield at -10°C. A similar stabilizing effect was observed when *iso*-propylmanganese iodide was prepared from the complex $MnI_2 \cdot 2LiBr$ instead of MnI_2.

$$i\text{-PrMgBr} \xrightarrow[\text{Ether}]{\text{MnI}_2 \cdot 2 \text{ LiBr}} i\text{-PrMnI} \xrightarrow{\text{HeptCOCl}} i\text{-PrCOHept} \quad 92\%$$

This beneficial influence of lithium bromide on the stability of *sec*- and *tert*-alkylmanganese halides prepared in ether is general and allows us to prepare various *sec*- or *tert*-alkylketones in excellent yields (for a general procedure see ref. 8).

$$\text{RMgBr} \xrightarrow[\text{Ether, -10°C}]{\text{MnBr}_2 \cdot 2 \text{ LiBr}} \text{RMnBr} \xrightarrow{\text{R'COCl}} \text{RCOR'}$$

R	*tert*-Bu	*tert*-Pent	*i*-Pr	*sec*-Bu	*c*-Pent	*c*-Hex
R'	Hept	Hept	Ph	Bu	Bu	Bu
Yield (%)[a]	92	91	85	90	80	92

a/ Yield of distillated product.

The 1,2 addition of *iso*-propylmanganese bromide to heptanal also proceeded in good yields.

$$i\text{-PrMgBr} \xrightarrow[\text{Ether, -10°C}]{\text{MnBr}_2 \cdot 2 \text{ LiBr}} i\text{-PrMnBr} \xrightarrow[\text{-10°C to rt}]{\text{HexCHO}} \begin{array}{c} \text{Hex} \\ \diagdown \\ \diagup \end{array}\text{CHOH} \quad 83\%$$
(with i-Pr group)

In the course of our study on the chemistry of organomanganese reagents, we have also examined the influence of various salts on their reactivity. Thus, we have found that it is possible to form an ate complex by stirring a mixture of anhydrous manganese bromide with one equivalent of anhydrous Bu_4NBr in ether for 4h. During the formation of the complex the reaction mixture became thick. Further addition of butylmagnesium bromide at 0°C, then stirring at 10°C for 1h, led to a suspension of butylmanganese bromide. We have observed that the reactivity of this reagent is modified by the presence of Bu_4NBr. Indeed, it reacted with acyl chlorides to give the expected ketones but 5 to 10% of tertiary alcohols resulting from the 1,2 addition to the ketone were always obtained as side product. It was surprising since, under similar conditions the formation of tertiary alcohols is never observed in the absence of Bu_4NBr.[9, 2]
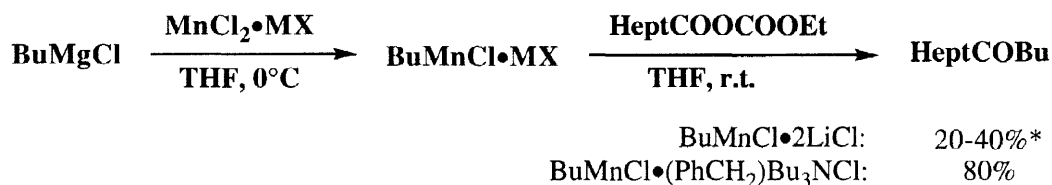
This difference of reactivity is confirmed by the following comparison. Previously, we had reported that, the reaction of butylmanganese iodide in excess (2.2 equiv.) with pentanoyl chloride leads at first to 4-nonanone which undergoes a 1,2 addition only very slowly under the reaction conditions.[9] Now, we show that with an organomanganese iodide prepared from $MnI_2 \cdot Bu_4NBr$ the 1,2 addition takes place much more rapidly.

$$2.2 \text{ BuMgBr} \xrightarrow[\text{Ether, -10°C}]{\text{MnX}_2{}^{a,\,b}} 2.2 \text{ BuMnI} \xrightarrow{\text{BuCOCl}} \text{BuCOBu} + \text{Bu}_3\text{COH}$$

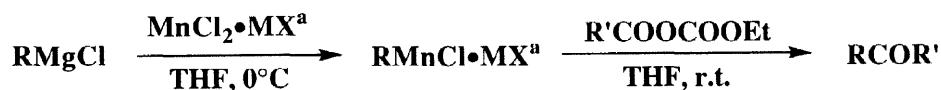| Reaction time (hr)	Without Bu₄NBr[a] Yield (%)[c] of		In the presence of Bu₄NBr[b] Yield (%)[c] of	
	BuCOBu	Bu₃COH	BuCOBu	Bu₃COH
0.2	81	0	5	95
0.5	99	0	2	98
36	22	63		

a/ BuMnI prepared from MnI₂. b/ BuMnI prepared from MnI₂•Bu₄NBr. c/ GC yield.

We have thought that such a modification of the reactivity could be useful in the case of the acylation of organomanganese chlorides by mixed anhydrides RCOOCOOEt in THF. Effectively, this reaction is slow and leads to poor yields of ketone since the main product is the ethyl ester RCOOEt resulting probably from the decomposition of the mixed anhydride.[10] Thus, it was tempting to try to favor the formation of the ketone by increasing the acylation rate. At first, we have tried to prepare an ate complex by mixing manganese chloride with (PhCH₂)Bu₃NCl (1:1) in THF at room temperature. This attempt was successful and a clear yellow solution was rapidly obtained. Butylmanganese chloride was then easily prepared by adding butylmagnesium chloride at 0°C, the transmetallation reaction occured quickly. As expected, the organomanganese reagent thus formed in the presence of (PhCH₂)Bu₃NCl reacted more rapidly with mixed anhydride HeptCOOCOOEt than butylmanganese chloride prepared from MnCl₂•2LiCl and gave a higher yield of 5-dodecanone.

$$\text{BuMgCl} \xrightarrow[\text{THF, 0°C}]{\text{MnCl}_2\text{•MX}} \text{BuMnCl•MX} \xrightarrow[\text{THF, r.t.}]{\text{HeptCOOCOOEt}} \text{HeptCOBu}$$

BuMnCl•2LiCl: 20-40%*
BuMnCl•(PhCH₂)Bu₃NCl: 80%

* The reaction led to irreproducible yields of ketone. HeptCOOEt is the main product.

Various ketones have been prepared in satisfactory yields from aliphatic, ethylenic and aromatic mixed anhydrides (for a general procedure see ref. 11). From a practical point of view, it should be noted that these acylating reagents[12] are interesting since they are prepared under very mild conditions and can be used very advantageously in place of the corresponding carboxylic acid chlorides which are tedious to prepare and to store when the corresponding carboxylic acid is acid-sensitive (racemisation...).

$$\text{RMgCl} \xrightarrow[\text{THF, 0°C}]{\text{MnCl}_2\text{•MX}^a} \text{RMnCl•MX}^a \xrightarrow[\text{THF, r.t.}]{\text{R'COOCOOEt}} \text{RCOR'}$$

R	Ph	Hept	Bu	i-Pr	Hept
R'	Hept	i-Pr	Ph	Ph	Me₂C=CH
Yield (%)	68	78	85	79	83

a/ MX= (PhCH₂)Bu₃NCl ou Bu₄NBr. b/ Yield of distillated product.

The influence of (PhCH$_2$)Bu$_3$NCl on the reactivity of organomanganese halides could be due to the complexation of the manganese atom by the chlorine anion. A similar influence has already been described in the case of the 1,2 addition of organozincs and Grignards reagents.[13]

In conclusion, we shown for the first time that the nature of the salts present in the reaction mixture has a strong influence on the reactivity and on the stability of organomanganese halides. Thus, it is now possible to use sec- and tert-alkylmanganese halides in ether and to acylate organomanganese chlorides with mixed anhydrides RCOOCOOEt in good yields. This new method to modify the reactivity of organomanganese reagents would allow to enlarge their scope of application in preparative organic chemistry.

References and notes.

1. Organomanganese Reagents Part XXXVI. Part XXXV: Riguet, E.; Alami, M.; Cahiez, G. Tetrahedron Lett. **1997**, 38, 4397-4400.

2. For reviews see: (a) Cahiez, G. Butyl Manganese Chloride in Encyclopedia of Reagents for Organic Synthesis, Paquette, L.; Ed., Wiley, Chichester **1995**, 2, 925-928. (b) Cahiez, G. Manganese (II) Chloride in Encyclopedia of Reagents for Organic Synthesis, Paquette, L.; Ed., Wiley, Chichester **1995**, 5, 3227-29. (c) Cahiez, G. Anales de Química **1995**, 91, 561-78.

3. Cahiez, G.; Alami, M. Tetrahedron Lett., **1989**, 30, 3541-44 and 7365-68; **1990**, 31, 7423-24.

4. For instance, see the following example:

$$PrCOPr \xrightarrow[\text{2/ Et(CO)}_2\text{O}]{\text{1/ BuMnCl, THF, r.t.}} Bu(Pr)_2COH + $$

EtCOO

75%

5 to 15%

5. Cahiez, G.; Laboue, B. Tetrahedron Lett., **1989**, 30, 3545-46.

6. sec- and tert-alkylmagnesium halides are always used as starting material since they are easier to prepare than the corresponding organolithiums.

7. Until now, only sec- and tert-RMnCl prepared in THF were stable enough to be used efficiently for synthetic applications. For instance, see Cahiez, G.; Laboue, B. Tetrahedron Lett., **1989**, 30, 7369-72.

8. **Preparation and Acylation of sec- and tert-RMnBr in Ether: Typical Procedure;** A suspension of anhydrous MnBr$_2$ (52 mmoles, 11.2 g) and LiBr (100 mmoles, 8.7 g) in 80 mL of ether was stirred a 20°C until obtention of a clear solution (ca 2h). An ethereal solution of i-PrMgBr (52 mmoles) was then added dropwise at -20°C. After stirring for 30 min at -10°C, HeptCOCl (50 mmoles, 8.15 g) in solution in 10 mL of ether was added. The reaction mixture was stirred for 2h at 20°C then hydrolyzed with a 1N HCl solution (60 mL). After decantation and extraction of the aqueous layer with ether (2x50mL), the combined organic layers were washed with a NaHCO$_3$ aqueous solution (30 mL) dried over MgSO$_4$ and the solvent was removed under vacuo. The ketone i-PrCOHept was isolated by distillation in 91% yield (7.75 g, 101°C/13 torr).

9. Cahiez, G.; Rivas-Enterrios, J.; Granger-Veyron, H. Tetrahedron Lett., **1986**, 27, 4441-44.

10. Friour, G.; Alexakis, A.; Cahiez, G.; Normant, J. Tetrahedron, **1984**, 40, 683-93. For the formation of esters from RCOOCOOEt see: Tarbell, D.S.; Price, J.A. J. Org. Chem. **1957**, 22, 245-50. Domagala, J.M. Tetrahedron Lett. **1980**, 21, 4997-5000 and references therein.

11. **Preparation of RMnCl•(PhCH$_2$)Bu$_3$NCl (or RMnCl•Bu$_4$NBr) in THF; Acylation by R'COOCOOEt : Typical Procedure.** Anhydrous MnCl$_2$ (52 mmoles, 6.6 g), (PhCH$_2$)Bu$_3$NCl (52 mmoles, 20.6 g) and 80 mL of THF were stirred at 20°C until obtention of a solution (ca 2h). A solution of BuMgCl (52 mmoles) in THF then, after 30 min, HeptCOOCOOEt (50 mmoles, 10.91 g) were added dropwise at 0°C. The reaction mixture was stirred fort 2h at 20°C then hydrolyzed with a 1N HCl solution (60 mL). After addition of 50 mL of cyclohexane, decantation and extraction of the aqueous layer with cyclohexane (2x80mL), the combined organic layers were washed with a NaHCO$_3$ aqueous solution (30 mL) dried over MgSO$_4$ and the solvents were removed under vacuo. The ketone BuCOHept was isolated by distillation in 80% yield (7.37 g, 62-63°C/0.3 torr).

12. For the preparation of RCOOCOOEt see: Tarbell, D.S.; Leister, N.A. J. Org. Chem. **1958**, 23, 1149-52 and references therein.

13. Chastrette, M.; Amouroux, R. Bull. Soc. Chim. Fr. **1970**, 4348-53 and Tetrahedron Lett. **1970**, 11, 5165-68.