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ORGANOMANGANESE (II) REAGENTS XIX[1]. ACYLATION OF ORGANOMANGANESE CHLORIDES BY CARBOXYLIC ACID CHLORIDES IN THF: A CLEAR IMPROVEMENT IN THE FIELD OF THE PREPARATION OF KETONES FROM ORGANOMANGANESE COMPOUNDS.

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Abstract : *Organomanganese chloride reagents react with carboxylic acid chlorides, in THF, to give the corresponding ketones in excellent yields. The reaction is of broad scope, it is very interesting from practical and economical point of view since organomanganese chlorides (in THF) are the most stable and cheap organomanganese reagents. With methyl, aryl, alkenyl and s- or t-alkylmanganese chlorides, the acylation is advantageously performed in the presence of a catalytic amount of copper chloride. This new procedure allows to prepare methyl, aryl and alkenylketones as well as s- or t-alkylketones in good yields.*

The acylation of organomanganese iodides by carboxylic acid chlorides, in ether, allows to prepare a large array of ketones in excellent yields[2, 3]. The high preparative value of this reaction is noticeable especially for the synthesis of functional ketones[2, 3]. Recently, we have shown that, in ether, organomanganese bromide reagents can be prepared and acylated in high yields as their iodides counterparts[2]. This is an interesting improvement, the major advantage being that organomanganese bromides are less expensive. We have also attempted to use organomanganese chlorides, which must be prepared in THF, since they are clearly cheaper than their bromides and iodides analogous. Moreover, organomanganese reagents are more stable in THF than in ether. Unfortunately, until now, only carboxylic acid anhydrides had been successfully employed as acylating reagents in THF[3].

$$\text{HeptMnCl} + (\text{EtCO})_2\text{O} \xrightarrow[0^\circ\text{C to } 20^\circ\text{C, 2h}]{\text{THF}} \text{HeptCOEt} \qquad 85\%$$

$$\text{C}_5\text{H}_{11}\text{C}\equiv\text{CMnCl} + (\text{CF}_3\text{CO}_2)\text{O} \xrightarrow[20^\circ\text{C, 4h}]{\text{THF}} \text{C}_5\text{H}_{11}\text{C}\equiv\text{CCOCF}_3 \qquad 84\%$$

We now report that organomanganese chlorides can be also acylated by carboxylic acid chlorides in THF. Good results were obtained by using organomanganese reagents prepared indifferently from organolithium or organomagnesium compounds:

$$\text{MnCl}_2\text{; 2 LiCl} \xrightarrow[\text{or BuLi}]{\text{BuMgCl}} \text{BuMnCl}^4 \xrightarrow{\text{PhCOCl}} \text{BuCOPh}$$

from BuMgCl : 90%
from BuLi : 88%

As shown in Table I, this reaction led to various saturated, ethylenic, aromatic and acetylenic ketones in good yields[4].

$$\mathrm{RMgCl} + \text{"}\mathrm{MnCl_2;\ 2\ LiCl}\text{"} \xrightarrow{\mathrm{THF}} \mathrm{RMnCl}^{4} \xrightarrow[\text{-10°C to 20°C, 1h to 2h}]{\mathrm{R'COCl}} \mathrm{RCOR'}$$

Table I. Preparation of Ketones from Organomanganese Chlorides and Carboxylic Acid Chlorides in THF.

Entry	R	R'	Yield of Ketone (%)[a]
1	Hept	Bu	95
2	Hept	i-Pr	90
3	Hept	t-Bu	81
4	Bu	Ph	90
5	Hept	$Me_2C{=}CH$	83
6	$PentC{\equiv}C$	Et	75
7	Ph	Hept	75
8	$Me_2C{=}CH$	Hept	80
9	i-Pr	Hept	69
10	t-Bu	Hept	0
11	Me	Hept	40

a) All products were isolated by distillation.

Linear and α-branched aliphatic carboxylic acid chlorides (*entries 1 to 3*) as well as the less reactive conjugated aromatic and ethylenic acid chlorides (*entries 4 and 5*) lead to the corresponding ketones in excellent yields. Concerning the nature of the organomanganese reagents, alkyl, aryl, alkenyl and alkynylmanganese chlorides are easily acylated (*75% to 95%, entries 1 to 8*).

Allylic ketones can also be prepared successfully from allylic manganese chlorides:

$$\mathrm{Me_2C{=}CHCH_2MnCl} + \mathrm{HeptCOCl} \xrightarrow[\text{-10°C to 20°C}]{\mathrm{THF}} \mathrm{Me_2C{=}CHCH_2COHept} \qquad 89\%$$

It is the first time that an allylic manganese halide has been acylated in good yield by a carboxylic acid chloride.

In comparison with these results, methylmanganese chloride affords the expected ketones in lower yields (*40%, entry 11*). Furthermore, the course of the reaction is considerably affected when a s- or t-alkylmanganese reagent is used (*entries 9 and 10*), thus, no ketone was obtained from t-butylmanganese chloride (*entry 10*).

Most of these limitations disappear when the acylation is carried out in the presence of a catalytic amount of copper chloride. Thus, the yields of ketones clearly increased in the case of the s-alkylmanganese chlorides:

$$\mathrm{i\text{-}PrMnCl} + \mathrm{HeptCOCl} \xrightarrow[\text{-30°C to 20°C}]{\mathrm{THF}} \mathrm{i\text{-}PrCOHept}$$

No CuCl, 1.5h : 69%

1% CuCl, 30min. : 93%

With the t-alkylmanganese chlorides, the improvement is more spectacular since t-butylheptylketone was produced in 96% yield instead of 0% (Table II, *entries 12 and 14*).

$$\text{t-BuMnCl} + \text{HeptCOCl} \xrightarrow[\text{30 min. to 1.5h}]{\text{THF}} \text{t-BuCOHept}$$

Table II. Influence of a catalytic amount of copper chloride on the acylation of t-BuMnCl by HeptCOCl in THF.

Entry	CuCl (%)	Temperature[a]	Yield of Ketone (%)
12	0	-50°C	0
13	5	-50°C	92
14	1	-50°C	96
15	1	-20°C	82

a) After addition of HeptCOCl at the temperature indicated above, the reaction mixture was allowed to warm to room temperature then stirring was continued for 1.5h (*no CuCl*) or 30 min. (*1 to 5% of CuCl*).

The experiments described above (*Table II*) show that this copper-catalyzed acylation can be performed in the presence of only 1% copper chloride (*entry 14*). Good yields of branched ketones were obtained by adding the carboxylic acid chlorides at -20°C (e.g. *entry 15*); however, it is better to perform the addition at -50°C (e.g. *entries 14 and 15, respectively 96 and 82%*).

It should be emphasized that the afore-mentioned procedure suppresses all the problems previously observed with the s- and t-alkyl manganese iodides prepared in ether[3]. Indeed, these reagents must be used in excess, at low temperature, since they decompose partially:

$$1.5\ \text{i-PrMnI} + \text{HeptCOCl} \xrightarrow[\text{-50°C}]{\text{Ether}} \text{i-PrCOHept} \qquad 65\ \%$$

The copper-catalysis is also efficient with the methylmanganese chloride. So, the corresponding methylketones were prepared in excellent yields:

$$\text{MeMnCl} + \text{HeptCOCl} \xrightarrow[\text{-10°C to 20°C}]{\text{THF}} \text{HeptCOMe}$$

No CuCl, 1.5h : 40%
1% CuCl, 30min. : 91%

This result is interesting, since, in ether, methylmanganese iodide or bromide always give lower yields of ketones than their n-alkyl homologous (*e.g.. 74% instead of 90-95%*). Furthermore, in ether, the presence of copper salts does not allow to improve the yield significantly:

$$\text{MeMnBr} + \text{HeptCOCl} \xrightarrow[\text{-10°C to 20°C, 1.5h}]{\text{Ether}} \text{HeptCOMe}$$

No CuCl : 74%
1% CuCl : 79%

The reaction of aryl and alkenylmanganese chlorides with carboxylic acid chlorides in THF also provided better results in the presence of copper chloride:

$$\mathrm{PhMnCl} + \mathrm{HeptCOCl} \xrightarrow[\text{-10°C to 20°C}]{\text{THF}} \mathrm{PhCOHept}$$

No CuCl, 1.5h : 75%
1% CuCl, 30min. : 92%

$$\mathrm{Me_2CH{=}CHMnCl} + \mathrm{HeptCOCl} \xrightarrow[\text{-10°C to 20°C}]{\text{THF}} \mathrm{Me_2CH{=}CHCOHept}$$

No CuCl, 1.5h : 80%
1% CuCl, 30min. : 87%

It has been previously demonstrated that organomanganese iodides react very chemoselectively, in ether, with many carboxylic acid chlorides containing additional functionalities[3]. Interestingly, organomanganese chlorides behave similarly. Thus, they can be used to prepare, in THF, numerous functional ketones in high yields. For instance :

$$\mathrm{BuMnCl} + \mathrm{ClCO(CH_2)_3COOEt} \xrightarrow[\text{-10°C to 20°C, 1.5h}]{\text{THF}} \mathrm{BuCO(CH_2)_3COOEt} \quad 88\%$$

In this case also, the presence of copper chloride as catalyst sometimes allowed to improve the yields:

$$\mathrm{BuMnCl} + \mathrm{ClCO(CH_2)_5Br} \xrightarrow[\text{-10°C to 20°C}]{\text{THF}} \mathrm{BuCO(CH_2)_5Br}$$

No CuCl, 1.5h : 85%
1% CuCl, 30min. : 92%

In conclusion, we have shown that organomanganese chlorides are efficiently acylated, in THF, by carboxylic acid chlorides. With s- and t-alkylmanganese chlorides as well as with aryl, alkenyl and methylmanganese chlorides, the acylation must be performed in the presence of a catalytic amount of copper chloride. This reaction is of broad scope and gives good to excellent yields of ketones.

It should be pointed out that this new procedure is interesting from both economical and practical point of view. Indeed, organomanganese chlorides are clearly less expensive than their iodide and bromide analogous[4].

It should be also pointed out that organomanganese halides prepared in THF are much more stable than those prepared in ether. This is especially evidenced by the excellent yields of branched ketones obtained in THF from s- and t-alkylmanganese chlorides.

Finally, we had already shown that organomanganese reagents are very often the most suitable organometallic compounds for the preparation of ketones *via* an acylation reaction[3]. The results presented above clearly strengthen their advantages toward, for instance, the very classical organocopper or cuprate reagents. Thus the organomanganese procedure has a larger scope (i.a. *α,β-ethylenic ketones, t-alkyl ketones or various functional ketones such as α-halogenated ketones*) and generally gives the expected ketone in higher yield under milder conditions (e.g. *low temperatures are avoided*). Moreover, organomanganese chlorides are undeniably more stable and less expensive than organocopper or cuprate reagents[4].

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References and Notes.

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