

ORGANOMANGANESE (II) REAGENTS XVI¹: COPPER-CATALYZED 1,4-ADDITION OF ORGANOMANGANESE CHLORIDES TO CONJUGATED ENONES

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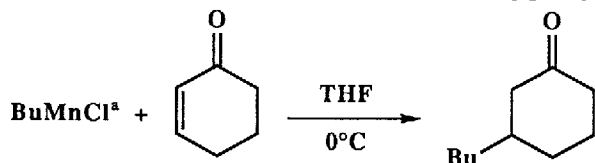
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Abstract : Copper-catalyzed conjugate addition of organomanganese chlorides to conjugated enones in THF, at 0°C, leads to the 1,4 addition products in high yields. The scope of the reaction is very large and the results are generally better than those obtained from organomagnesium compounds in the presence of a copper salt as well as from organocopper or cuprate reagents. Furthermore organomanganese chlorides are indisputably cheaper and more stable than the latter.

In a recent report, we have shown that symmetrical organomanganese reagents R₂Mn and organomanganates R₃MnM (M= MgX, Li) are able to add in a 1,4 fashion to cyclohexenone or to promote its β-reductive dimerization whereas organomanganese halides RMnX lead to a mixture of products resulting from the 1,2 and 1,4-additions and the β-reductive dimerization. These results cannot be extended to other α,β-ethylenic ketones which predominantly give an intractable mixture of heavy products or do not react².

Nevertheless, the propensity of organomanganese reagents to give a conjugate addition to α,β-unsaturated carbonyl derivatives has been used successfully in the case of the alkylidene malonic esters since excellent yields of conjugate addition adducts have been obtained¹.

In this letter we now report that the course of the reaction of organomanganese halides RMnX with conjugated enones is dramatically influenced by the presence of a catalytic amount of copper chloride. Thus, in THF, the copper-catalyzed reaction of butyl manganese chloride with cyclohexenone quantitatively affords the 3-butyl cyclohexanone whereas in the absence of copper salt, this latter is formed in very poor yield.



a) Prepared from BuLi or BuMgCl

No catalyst : 0 to 10%
5% CuCl : 95%
0.1% CuCl : 93%

It is interesting to note that excellent yields of 3-butyl cyclohexanone were obtained at 0°C from equimolar amounts of butyl manganese chloride and cyclohexenone. In addition, 0.1% cuprous chloride is sufficient to catalyze the

conjugate addition reaction efficiently and the butyl manganese chloride could be indifferently prepared from butyllithium or butylmagnesium halide.

As shown in Table I and II, the scope of this reaction is very broad. Thus, high yields of 1,4-addition products were obtained from a vast array of cyclic or acyclic conjugated enones (Table I). Even the β,β -bisubstituted α,β -ethylenic ketones, which are well known to undergo the conjugate addition of an organocopper or an organocuprate reagent with difficulty, react easily and cleanly under our conditions (*entries 7 to 11*).

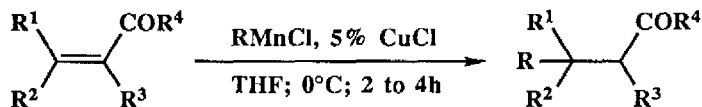
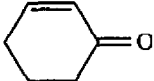
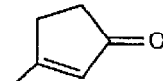
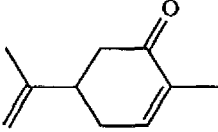
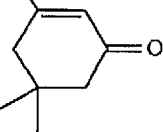
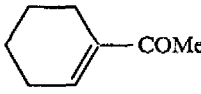
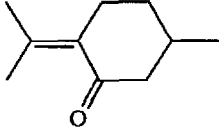
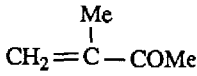
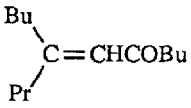


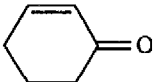
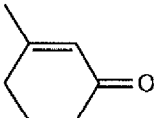
Table I. Copper-Catalyzed Conjugate Addition of Organomanganese Chlorides^a RMnCl to Various α,β -ethylenic ketones in THF at 0°C.

Entry	α -Enone	R	Isolated Yield ^b (%)	Entry	α -Enone	R	Isolated Yield ^b (%)
1		Bu	95	7		Bu	90
2		Bu	98	8		Bu	95
3		Bu	86 ^c	9		Bu	88 ^e
4	CH ₂ =CHCOMe	Hept	90 ^d	10	Me ₂ C=CHCOMe	Bu	94
5		Hept	89	11		Bu	90
6	PentCH=CHCOMe	Bu	90				

a) Unless otherwise stated, 1.05 eq. of RMnCl was used. Organomanganese reagents RMnCl were prepared from RLi or RMgX (X = Cl, Br, I). b) 1,4-addition products were isolated by distillation. c) 1.5 eq. of BuMnCl was used. With 1.05 eq. of BuMnCl the yield drops to 77%. d) The reaction was performed in the presence of 1.2 eq. of Me₃SiCl to trap the enolate resulting from the 1,4-addition in order to prevent its addition to the starting methyl vinylketone (*Michael addition or aldol condensation*). A mixture THF/AcOEt 50:50 was used as solvent. e) A mixture THF/AcOEt 50:50 was used as solvent (a 82% yield was obtained in THF alone).

The results summarized in Table II point out that our procedure allows the 1,4-transfer of a large variety of R groups since methyl, alkyl, alkenyl or aryl manganese chlorides have been used successfully.

Table II. Copper-Catalyzed Conjugate Addition of Various Organomanganese Chlorides^a RMnCl to α,β -ethylenic ketones in THF at 0°C

Entry	α -Enone	R	Isolated Yield ^b (%)	Entry	α -Enone	R	Isolated Yield ^b (%)
12		Bu	95	18		Bu	95
13	"	Ph	94	19	"	Me	90
14	"	Me ₂ C=CH	92	20	"	Ph	89
15	"	Me	90	21	"	PrCH=CH	94
16	"	i-Pr	81				
17	"	t-Bu	78 ^c				

a) Unless otherwise stated, 1.05 eq. of RMnCl was used. Organomanganese reagents RMnCl were prepared from RLi or RMgX (X = Cl, Br, I). b) 1,4-addition products were isolated by distillation. c) The reaction was performed at -30°C in the presence of 1.2 eq. of Me₃SiCl (without Me₃SiCl : 51%).

The copper-catalyzed reaction of organomanganese chloride described above gives better yields than the classical copper-catalyzed reaction of organomagnesium compounds (Table III, entries 22 and 23). This is interesting since these organomanganese reagents are easily prepared from organomagnesium compounds in very mild conditions by addition of manganese chloride, a very cheap material³. Moreover they can be also prepared from organolithium compounds and they are used in THF.

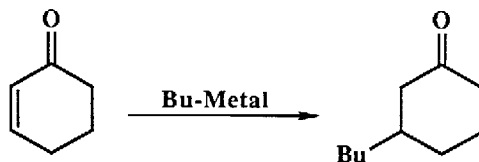


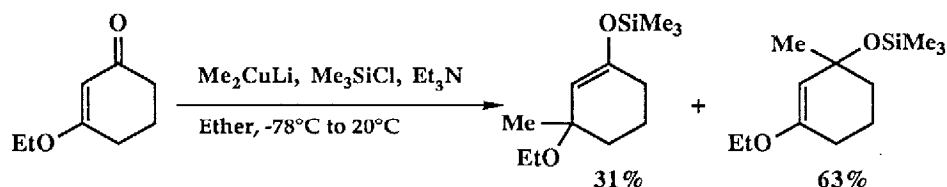
Table III. Conjugate Addition of Various Bu-metal Compounds to Cyclohexenone.

Entry	Bu-Metal	Reaction Conditions	Isolated Yield (%) ^a
22	BuMnCl	1% CuCl; THF, 0°C, 30 min.	95
23	BuMgCl	5% CuCl; THF, 0°C	54 ^b
24	BuCu	2.2 eq. Bu ₃ P; ether, -78°C to -40°C	82 ^c
25	Bu ₂ Cu(CN)Li ₂	Ether, -78°C, 5h	86 ^d

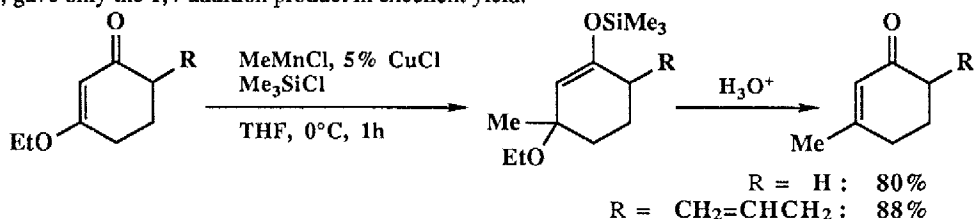
a) For butyl copper and cuprate reagents we have tried to select the best yields corresponding to isolated product from the numerous results reported in the literature. b) 7% CuI, ether, 0°C : 47% ; 2 eq. BuMgBr, 10% CuBr-Me₂S, ether, 0°C: 65%. c) Ref. 4. d) only one of the two Bu groups is transferred, ref. 5.

The comparison of our results with those obtained with organocopper or cuprate reagents evidences that the organomanganese reagents, in the presence of 1% copper chloride, afford the 1,4-addition products in better yields in the case of very reactive α -enones such as cyclohexenone (Table III, entries 22, 24 and 25).

With the less reactive α -enones, the difference is often more decided. Thus, the great efficiency of our procedure is well demonstrated by the following example. Indeed, the conjugate addition of organometallic derivatives to 3-ethoxycyclohexenone is a real challenge. So, methyl copper or lithium dimethyl cuprate do not react whereas lithium dimethyl cuprate activated by adding trimethylchlorosilane leads to a mixture of the 1,4 and 1,2-addition products (respectively 31% and 63%), the 1,2 addition product being clearly predominant⁶.



The contrast with our results is very impressive since methyl manganese chloride, in the presence of copper chloride, gave only the 1,4-addition product in excellent yield.



Furthermore, the conjugate addition reaction takes place also in the absence of trimethylchlorosilane (*i.e.*, 68% from an excess of MeMnCl for $R = \text{H}$). However the expected 3-methylcyclohexanone is then always accompanied by the 3,3-dimethyl cyclohexanone resulting from an addition-elimination-addition process (*about 90/10*).

Finally, it is interesting to note that in the presence of a catalytic amount of both manganese and copper chlorides the reaction of an organomagnesium compound with a conjugated enone efficiently leads to the 1,4 addition adduct. Indeed, the yields are clearly better than those obtained in the presence of copper chloride alone (Table IV).

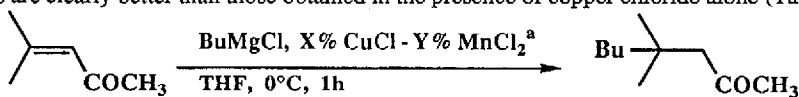


Table IV. Manganese-copper-catalyzed conjugate addition of butylmagnesium chloride to mesityl oxide.

Entry	CuCl (X%)	MnCl ₂ (Y%)	1,4-Addition Product (%) ^b	Entry	CuCl (X%)	MnCl ₂ (Y%)	1,4-Addition Product (%) ^b
26	1	10	88	30	0.2	0	53
27	1	20	89	31	1	0	67
28	1	30	94	32	5	0	82
29	0.1	30	90	33	10	0	63

a) BuMgCl was added, at 0°C , to a mixture of $\text{Me}_2\text{C}=\text{CHCOMe}$, CuCl and MnCl_2 . b) Yield of distilled product.

In conclusion, the use of organomanganese chloride reagents in the presence of copper chloride allows to increase the yields of conjugate addition products generally obtained through the classical organocopper or cuprate reagents as well as from the organomagnesium compounds in the presence of a copper salt. For preparative purposes, further advantages on organocopper or cuprate derivatives should be emphasized:

- the use of low temperatures is avoided since the organomanganese chloride reaction is performed at 0°C
- no stabilizing or solubilizing additives such as HMPA, Bu_3P , Me_2S ...are necessary
- manganese salts are clearly less expensive than copper salts³
- the final work-up is much easier than with organocopper derivatives, especially on a large scale
- the reaction is achieved in THF in place of ether.

References and Note

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