Tetrahedron Letters, Vol.27, No.5, pp 569-572, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

ORGANOMANGANESE (II) REAGENTS XI[1].

A Study of their Reactions with Cyclic Conjugated Enones : Conjugate Addition and Reductive Dimerization

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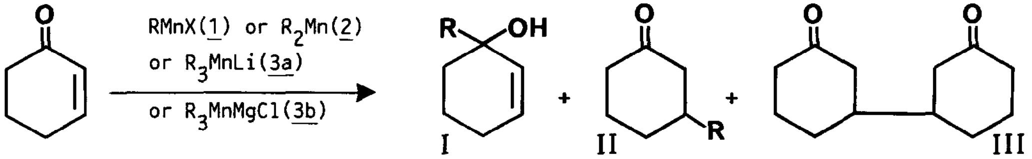
Summary : The reaction of organomanganese reagents such as RMnX, R_2Mn, R_3MnLi and R_3MnMgX with cyclohexenone has been studied. Two major pathways have been observed : conjugate addition and β reductive dimerization. Similar results have been obtained with organomagnesium compounds in presence of a catalytic amount of manganous salts.

Our continuing interest in the chemistry of organomanganese (II) reagents[1-3,5] led us to investigate their reactions with various conjugated unsaturated carbonyl derivatives. As part of this work we now report some results about the reaction of cyclic conjugated enones with organomanganese reagents such as RMnX, R_2Mn, R_3MnLi and R_3MnMgX.
With cyclohexenone, this reaction gave three products in variable amounts (Table I) depending on the solvent and the nature of the organomanganese reagent[4].



As shown in Table I, the best results have been obtained in THF from symmetrical organomanganese reagents 2 and manganates 3a and 3b. With these reagents, only two major competing pathways have been observed : 1-4 addition and β reductive dimerization. Thus the bicyclic diketone III which results from the β reductive dimerization of cyclohexenone was produced in good yields (74 to 83%) when butyl or isopropyl manganates (3a or 3b ; entries 23, 24 and 25) as well as diisopropyl manganese (entry 14) were used. On the other hand, satisfactory yields of 3-substituted ketones II were mostly obtained by conjugate addition of the symmetrical organomanganese reagents 2. However, it should be noted that the reagents 2 led to better yields of 1-4 addition product in the presence of a mixture of lithium and magnesium salts (62-72%, entries 9, 12 and 16) than in the presence of only one of these two salts (30-40%, entries 8, 11, 13 and 15). This is unexpected since such a discrepancy due to the nature of the salts generated or introduced during the preparation of manganese reagents (transmetallation) has never been observed until now.

TABLE I - REACTION OF ORGANOMANGANESE REAGENTS 1,2,3a and 3b WITH CYCLOHEXENONE [a]

Ent.	R	Solvent	Starting^{b} organometallic	Isolated Yield(%)^{c}		
				I	II	III
	1 : RMnX^{b}					
1	Me	Ether	Li	34	7	25
2	Me	THF	Li	-	-	-
3	Bu	Ether	Li	20	18	27
4	Bu	Ether	MgBr	3	26	35
5	Bu	THF	Li	10	10	-
6	Bu	THF	MgCl	-	-	-
7	i-Pr	THF	MgCl	4	23	33
	2 : R_2Mn^{b}					
8	Me	THF	Li		40	-
9	Me	THF	MgCl		72	5
10	Bu	Ether^{d}	Li	10	20	38
11	Bu	THF	Li		30	50
12	Bu	THF	MgCl^{e}		70	25
13	Bu	THF	MgCl(no LiCl)^{f}		36	39
14	i-Pr	THF	MgCl		4	83
15	Ph	THF	Li		30	30
16	Ph	THF	MgCl		62	21
17	$Me_2C=CH$	THF	MgBr		30	
18	PrC≡C	THF	MgCl	-^{g,h}		
	3a : R_3MnLi ; 3b : $R_3MnMgCl^{b}$					
19	Me	Ether	Li		20	15
20	Me	THF	Li		31	23
21	Me	THF	MgCl		42	21
22	Bu	Ether	Li		14	31
23	Bu	THF	Li		18	74
24	Bu	THF	MgCl		20	74
25	i-Pr	THF	MgCl		13	74
26	Ph	Ether	Li		63	-
27	Ph	THF	Li		31	31
28	Ph	THF	MgCl		45	16

a/ Ratio organomanganese reagent/cyclohexanone : 1/1. Cyclohexanone was added at -30°C then the reaction mixture was allowed to warm to room temperature within 45min. and stirred for 1 to 2h. Generally these reactions were over in less than 1h after addition of cyclohexenone

b/ Organomanganese reagents were prepared from RLi or RMgX and MnX_2 (see also note f) according to references 2 and 5 (except that the transmetallation was performed at -30°C when R= i-Pr). *The formulae of the reagents 1,2 and 3 are attributed in respect of the* ratio of the reactants. However, an equilibrium between several organomanganese species cannot be discarded.

c/ All cyclohexenone was consumed. Beside the products I,II and III only an intractable mixture of heavy products was obtained. A dash means that the yield was lower than 4%.

d/ to avoid some decomposition of Bu_2Mn, the reaction was carried out at -30°C for 3h.

e/ The yield dropped from 70% to 30% when Bu_2Mn (2 $MgCl_2$; 2 LiCl) was prepared from 2 BuLi + ($MnCl_2$) ; 2 $MgCl_2$ instead of 2 BuMgCl + ($MnCl_2$; 2 LiCl). This is quite curious since, at first glance, these two routes lead to the "same" reagent.

f/ In THF, the soluble ate complex "$MnCl_4Li_2$" ($MnCl_2$+2 LiCl) was used to prepare the organomanganese reagents from RMgCl (see references 2 and 5). As an exception, uncomplexed $MnCl_2$ was used for this experiment (entry 13)

g/ Polyunsaturated heavy products were obtained.

h/ In some cases, with the manganates $(RC{\equiv}C)_3MnLi$, the mixture of final products contained as major constituent the 1-2 addition compound (characterized by Carbon-13 NMR ; yield over 50%).

The stability of organomanganese reagents 2, 3a and 3b (or of related intermediates)[6] clearly influences the proportion of 1-4 addition and β reductive dimerization products formed (Table I). Thus the less stable reagents 2 and 3 (R= i-Pr ; entries 14 and 25) primarily gave the β reductive dimerization product III (e.g., i-Pr_2Mn : 83% ; i-$Pr_3MnMgCl$: 74%) whereas the more stable reagents (R= Me,Ph ; entries 9,16,26 and 28) led rather to the 1-4 addition product II (e.g. Me_2Mn : 72% ; Ph_2Mn : 62%).

With the above reagents (R=Me,i-Pr), our investigations (Table II) showed no significant effect of the temperature on the outcome of the reaction between -80°C and 25°C (entries 29 to 32). On the contrary, noticeable variations were observed with the organomanganese reagents having a medium stability. For instance, with dibutyl manganese, the ratio 1-4 addition/ β reductive dimerization is completely inverted between -30°C and 25°C (II/III : 70/25 to 29/68 ; entries 33 and 34).

TABLE II - INFLUENCE OF THE TEMPERATURE ON THE REACTION OF R_2Mn^a WITH CYCLOHEXENONE IN THF

Entry	R	Temperature °C	Yield of II(%)[b] (1-4 addition)	Yield of III(%)[b] (β dimerization)
29	Me	25	66	-[c]
30	Me	-80	50	-[c]
31	i-Pr	25	-[c]	84
32	i-Pr	-90	-[c]	83
33	Bu	25	29	68
34	Bu	-30	70	25

a/ Prepared from RMgCl ; b/ Isolated yields ; c/ Yields below 4%.

The reaction of organomagnesium compounds with cyclohexenone in the presence of a catalytic amount of manganous salts also yielded the conjugate addition and β reductive dimerization products II and III (Table III).

TABLE III - REACTION OF ORGANOMAGNESIUM COMPOUNDS WITH CYCLOHEXENONE IN THE PRESENCE OF A CATALYTIC AMOUNT OF MANGANOUS SALTS[a]

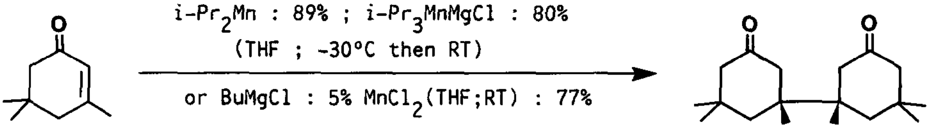
	R	Temp °C	MnX_2	Isolated yield(%) I	II	III
A/ in THF(RMgCl)	Me	25	$MnCl_2$		36	
	Me	-70	"		63	
	Bu	25	$MnCl_2$		47	45
	Bu	-70	"		85	
	i-Pr	25	$MnCl_2$		10	62
	i-Pr	-90	"		45	16[b]
	Ph	-30	$MnCl_2$		47	2
B/ in ether (RMgBr)	Me	-30	$MnBr_2$	30	30	
	Bu	-30	"	8	13	30
	i-Pr	-30	"		64	3

a/ Ratio cyclohexenone/organomagnesium reagent : 1/1. Cyclohexenone was added dropwise at the temperature indicated above to a stirred mixture of organomagnesium reagent with 5mol.% manganous salts in ether ($MnBr_2$) or in THF ($MnCl_2$ or a solution of the ate complex $MnCl_4Li_2$ prepared by mixing $MnCl_2$ and 2 LiCl in THF at 25°C). Generally, the reaction was complete in 5min (R=Bu,i-Pr) to 1h (R=Me,Ph) after addition of cyclohexenone.

b/ 9% of enone were recovered.

These results prove the efficiency of the manganese catalysis since 1-2 addition is avoided[7]; however they are not quite similar to those provided by the reaction of manganates as well as symmetrical organomanganese reagents. Therefore, it is not easy to draw a conclusion about the nature of the organomanganese species involved in this catalytic process as effective intermediates.

Finally, all attempts to extend the above reactions to various conjugated enones were disappointing. Thus isophorone was converted into the corresponding β reductive dimerization product in good yields :



but conjugate addition failed (Bu$_2$Mn or Me$_2$Mn in THF : 0% and i-PrMgCl, 5% MnBr$_2$ in ether : 15%). Generally speaking the β dimerization and conjugate addition products were formed in low yields ($<$ 30%) from most of conjugated enones[8] which mainly turned into intractable mixtures of heavy products. Moreover, unreacted enone was sometimes recovered in variable amounts.

In conclusion, the same processes are involved when organomanganese reagents and organomagnesium compounds in presence of a catalytic amount of manganous halides react with conjugated cyclic enones. The β reductive dimerization and conjugate addition are the two main reaction paths which compete to afford isolable products. It must be emphasized that conjugate addition is well known in organometallic chemistry whereas β reductive dimerization has never been performed by means of other organometallic compounds to our knowledge[9].

Further related investigations will be described in due course.

References and notes :

1. Part X : G. Friour, G. Cahiez, J.F. *Normant*, Synthesis 1985, 50.
2. For a general survey : G. Cahiez, L'Actualité Chimique 1984, 9, 24.
   For a survey on the reactions with carbonyl compounds : G. Cahiez, J.F. Normant in Modern Synthetic Methods 1983, R. Scheffold, Ed., J. Wiley and Sons, Inc., Chichester 1983,3,173.
3. For a report on the reaction of organomanganese (II) iodides with saturated carbonyl derivatives see : G. Cahiez, J.F. Normant, Tetrahedron Letters 1977, 3383.
4. Our results are very divergent from those reported in a recent communication : T. Kauffman, M. Bisling, Tetrahedron Letters 1984, 25, 293. We have pointed out this discrepancy to the afore-mentioned authors. They repeated the experiments with cyclohexenone and their results are now similar to our own . We thank Professor Kauffman for this private communication.
5. G. Friour, G. Cahiez, J.F. Normant, Synthesis 1984, 37.
6. An intermediate derived from organomanganese reagents is more likely involved since the reagents 1, 2 and 3 are generally stable in THF at room temperature. The stability of organomanganese species depends, in the first instance, on the number of available β-hydrogen atoms because the hydrogen β-elimination is the major low energy decomposition process for organomanganese derivatives (ref. 2). For a study on the decomposition of dialkyl manganese species see : M. Tamura, J. Kochi, J. Organometal. Chem.1971,29, 111
7. Low yields of 1-2 addition products have sometimes been obtained in ether. It should be noted that, in these cases, the corresponding experiments performed with an equimolecular amount of organomanganese reagents gave similar yields of 1-2 addition products.
8. For instance : 3-methylcyclohexenone, 1-acetylcyclohexene, pulegone, 3-methylcyclopentenone and various acyclic conjugated enones (β mono or bisubstituted).
9. For a general survey on the β reductive dimerization of conjugated enones see : H.G. Thomas, Houben-Weyl, Methoden der Organischen Chemie, 4th Edn 1976, E. Müller, Ed., vol.7/2b George Thieme Verlag, Stuttgart, p. 1870.

(Received in France 26 August 1985)