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ORGANOMANGANESE (II) REAGENTS XV [1]. CONJUGATE ADDITION OF ORGANOMANGANESE REAGENTS TO ALKYLIDENEMALONIC ESTERS AND RELATED COMPOUNDS

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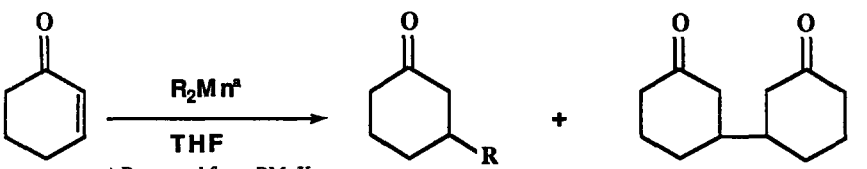
Abstract : *Organomanganese reagents react with alkylidenemalonic esters or related compounds to give the conjugate addition products in good yields. Several examples illustrate the scope and the efficiency of this reaction*

Lately, we have reported that organomanganese reagents react with cyclohexenone to give the 1,4 addition or the β-reductive dimerization products[2].

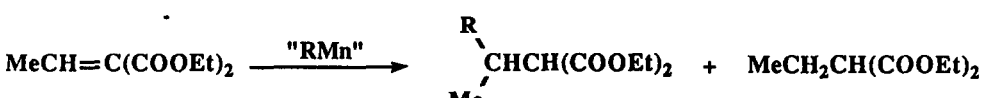


a) Prepared from RMgX

R =			
	Bu; 20°C	29%	68%
	Bu; -30°C	70%	25%
	Me; 20°C	72%	5%
	i-Pr; 20°C	3%	84%

Unfortunately, the synthetic interest of these reactions is quite limited since, with most conjugated enones, they generally proceed in very poor yields (< *30 %*). Nevertheless, the study reported hereafter demonstrates that the ability of organomanganese reagents to add to α,β-unsaturated carbonyl systems in a 1,4 manner can be used advantageously in the case of the alkylidenemalonic esters.

The results summarized in Table I (*entries 1 to 18)* show that a β-monosubstituted alkylidenemalonic ester such as ethyl ethylidenemalonate **1** rapidly reacts with one equivalent of butyl manganese iodide (*in ether*) or chloride (*in THF*) to give the conjugate addition product **2** in good yields (*80-87 %, entries 2, 4 and 5*).



1 **2** **3**

The reaction must be performed at -35°C since a higher temperature favours the side formation of polyaddition products whereas a lower temperature does not improve the yield (*entries 1 to 3*). In THF, dibutylmanganese as well as lithium or magnesium tributylmanganates have been also used successfully (*80-82 %, entries 6,7 and 8*). It should be noted that lithium tributylmanganate gave a better yield in THF than in ether (*entries 8 and 9*). As a rule, all, whether one, two or three, butyl groups bonded to manganese participate in the reaction.

Table I. Addition of Organomanganese Reagents to $MeCH{=}C(COOEt)_2$.

Entry	"RMn" [a]	RLi or RMgCl [b]	Reaction Conditions	Isolated Yield (%)[c] 2 (*1,4-addition*)	3 (*reduction*)
1	BuMnCl	Mg	THF, 10°C [d]	67	8
2	BuMnCl	Mg	THF, -30°C [d]	87	6
3	BuMnCl	Mg	THF, -60°C [d]	75	1
4	BuMnCl	Li	THF, -30°C [d]	82	4
5	BuMnI	Li	Ether, -30°C [d]	83	11
6	Bu_2Mn *(0.52 eq.)*	Mg	THF, -30°C [d]	82	8
7	$Bu_3MnMgCl$ *(0.35 eq.)*	Mg	" "	82	12
8	Bu_3MnLi *(0.35 eq.)*	Li	" "	80	7
9	Bu_3MnLi *(0.35 eq.)*	Li	Ether, -30°C [d]	65	3
10	MeMnCl	Mg	THF, 20°C [e]	89	0
11	i-PrMnCl	Mg	THF, -30°C [d]	70	11
12	t-BuMnCl	Mg	" "	10	40
13	$Me_2C{=}CHMnCl$	Li	THF, 20°C [e]	86	0
14	$BuC{\equiv}CMnCl$	Mg	" "	72	0
15	$BuC{\equiv}CMnCl$	Li	" "	27	0
16	$BuC{\equiv}CMnI$	Li	Ether, 20°C [e]	61	0
17	PhMnCl	Mg	THF, 20°C [e]	85	0
18	$CH_2{=}CHCH_2MnCl$	Mg	" "	91	0

a) Unless otherwise stated, 1.05 eq. of organomanganese reagent was used. b) Organomanganese reagents were prepared from RLi or RMgX (in ether, X= Br; in THF, X= Cl). c) All products have been isolated by distillation. d) 2h. e) Addition of $MeCH{=}C(COOEt)_2$ at 0°C then 20°C, 1h.

A large range of organomanganese reagents can be employed. Thus, good yields of 1,4 adducts **2** have been obtained from alkyl, alkenyl, aryl or even alkynyl and allyl manganese chlorides (*entries 2, 10 to 15, 17 and 18*). The sole limitation was encountered with the bulky alkyl manganese halides which contain β-eliminable hydrogen atoms. Indeed, the steric hindrance then favours the reduction of the ethyl ethylidenemalonate **1** into **3** (*β-hydrogen transfer*) and, therefore, the yields of the expected 1,4 adduct **2** decrease (*e.g. compare the yield for R= nBu, iPr and tBu; entries 2, 11 and 12*). Organomanganese halides issued from organomagnesium and organolithium compounds gaves similar results with the exception of alkynyl manganese chlorides in THF. In fact these ones must be prepared from the corresponding alkynyl magnesium compounds to give good yield of conjugate addition products **2** (*entries 14 and 15*).

We have also investigated the reaction of organomanganese reagents with ethyl isopropylidene malonate **4**, a β,β-bisubstituted alkylidenemalonic ester (*Table II*).

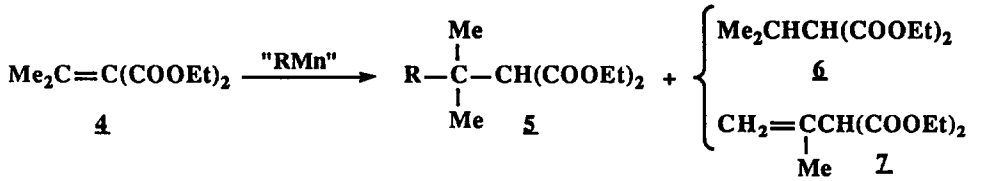


Table II. Addition of Organomanganese Reagents to $Me_2C{=}C(COOEt)_2$.

Entry	"RMn" [a]	RLi or RMgCl [b]	Reaction Conditions	Isolated Yield (%)[c] 5 (*1,4-addition*)	6	7	4
19	BuMnCl	Mg	THF, -30°C [e]	54	10	8	23
20	BuMnCl *(1.5 eq.)*	Mg	" "	74	17	5	1
21	BuMnCl	Mg	THF, -30 to 20°C [f]	74	20	4	0
22	BuMnCl *(1.5 eq.)*	Li	THF, -30°C [e]	4	0	19	74
23	BuMnI	Li	Ether, -30 to 20°C [f]	63	25	9	0
24	BuMnI	Mg	Ether, -30°C [g]	65	26	3	0
25	Bu_2Mn *(0.52 eq.)*	Mg	THF, -30°C [e]	63	24	11	0
26	Bu_3MnLi *(0.35 eq.)*	Li	Ether, -30 to 20°C [f]	53	12	30	0
27	Bu_3MnLi *(0.35 eq.)*	Li	THF, -30°C [e]	5	24	55	9
28	$Bu_3MnMgCl$ *(0.35 eq.)*	Mg	" "	57	26	9	0
29	MeMnCl	Mg	THF, 20°C [h]	82	0	10	0
30	PrCH=CHMnCl	Mg	THF, 0°C [i]	46 [j]	0	50	0
31	PhMnCl	Mg	THF, 20°C [h]	87	0	12	0
32	BuC≡CMnCl	Mg	" "	9	0	62	24

a) Unless otherwise stated, 1.05 eq. of organomanganese reagent was used. b) Organomanganese reagents were prepared from RLi or RMgX (in ether, X= Br; in THF, X= Cl). c) All products have been isolated by distillation. d) Unreacted starting product e) About 8h. f) -30°C, 3h then 20°C, 2h. g) -30°C, 2h. h) Addition of $Me_2C{=}C(COOEt)_2$ at 0°C then 20°C, 2h. i) 1h. j) The yield has been improved in the presence of CuCl (see below).

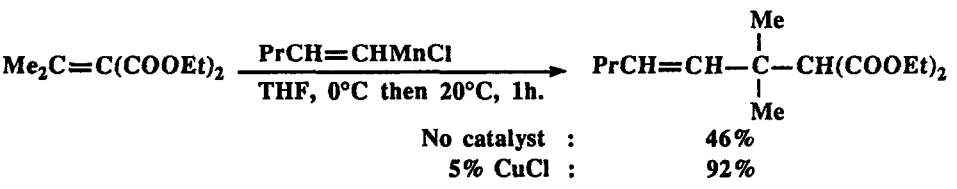
With substrate (**4**) the 1,4 addition rate is clearly slowed down owing to the presence of two methyl groups in the β-position. As a result, butyl manganese halides in ether or in THF gave moderate yields of the conjugate addition product **5** since the reduction of alkylidenemalonic ester **4** into **6** competes seriously (*10-26%, entries 19 to 24*).Besides, the ethyl isopropylidenemalonate **4** cannot be entirely consumed, in THF at -30°C, with a stoichiometric amount of butyl manganese chloride (*cf. entry 19*) since this latter partially decomposes on account of too long a reaction time (*about 8 h*). Fortunately, this problem was overcome by carrying out the reaction for

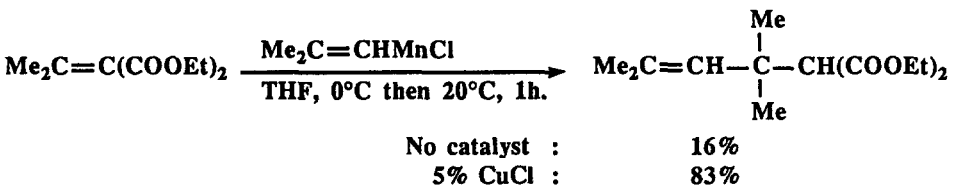
3 hours at -30°C then 2 hours at 20°C, and a satisfactory yield of the 1,4 adduct **5** was finally obtained (*74% from 1 equivalent of BuMnCl, entry 21*).

In ether, the presence of lithium or magnesium salts in the reaction mixture seems indifferent (*entries 23 and 24*). On the contrary, in THF, the nature of the salts formed during the preparation of butyl manganese halides (*BuLi + MnX_2 → BuMnX + LiX or BuMgX + MnX_2 → BuMnX + MgX_2*) profoundly influences the outcome of the reaction[3] e.g. 74% of **5** from BuMnCl;$MgCl_2$ and only 4% from BuMnCl;LiCl (*entries 21 and 22*). Such an influence was observed whatsoever the nature of the R group in RMnCl (*and not only with RC≡CMnCl as for 2*). Therefore, in THF, all the organomanganese chloride compounds must be prepared from the corresponding organomagnesium derivatives (*or from RLi + MgX_2*) to add to β,β-disubtituted alkylidenemalonic esters in good yields.

Dibutylmanganese and lithium or magnesium tributylmanganate also led to the 1,4 adduct **5** (*53-63%, entries 25 to 28*) though the enolization or the reduction of **4** occur more substantially. As above, the presence of magnesium salts is needful to perform the reaction in THF (*e.g. 5% of 5 from Bu_3MnLi in THF against 57% from $Bu_3MnMgCl$, entries 27 and 28*).

Generally speaking, the conjugate addition of alkyl and aryl manganese chlorides to ethyl isopropylidenemalonate **4** proceeds in good yields (*74-87%, entries 21, 29 and 31*). With the less reactive alkenyl manganese halides the yields of 1,4 adducts are moderate (*i.e. 46 %, entry 30*). However, in the presence of copper chloride, they become excellent (for a comparison with copper-catalyzed alkenylmagnesium reagents, see hereinafter).





As expected, the best yields described in Table II have been obtained with organomanganese reagents having no β-eliminable hydrogen atom, i.e. when R= Me, alkenyl, aryl ..., since they cannot reduce **4** into **6** by β-hydrogen transfer or decompose according to a β-hydrogen elimination process (entries 29 to 31). Furthermore, in these cases, the reaction can be performed at room temperature.

The reaction of alkynyl manganese halides with ethyl isopropylidene malonate **4** principally affords the enolization product **7** (*entry 32*) and not the 1,4 adduct as from the ethyl ethylidenemalonate **1**. This result is not surprising since it is well-known that the 1,4 transfer of an alkynyl group to an α,β-unsaturated carbonyl compound is not easy to perform[4]. On the other hand, it is consistent with the afore-mentioned difference of reactivity between β-mono and β,β-bisubstituted alkylidenemalonic esters i.a. **1** and **4**.

As shown in Table III, the present study has been extended with success to various alkylidenemalonic esters (*entries 2, 21 and 33 to 35*) and related compounds (*entries 36 to 38*). These results and those presented in Table I and II illustrate the scope of the reaction.

Table III. Conjugate Addition of BuMnCl [a] to Various Alkylidenemalonic Esters and Related Compounds in THF.

Entry	Starting Compound	Yield [b] of 1,4-Adduct	Entry	Starting Compound	Yield [b] of 1,4-Adduct
2	$MeCH=C(COOEt)_2$	87% [c]			
33	$PrCH=C(COOEt)_2$	83% [c]	36	$PrCH=C(COOEt)(COMe)$	72% [c]
34	$PhCH=C(COOEt)_2$	83% [c]	37	$PrCH=C(COMe)_2$	76% [c]
35	$EtOCH=C(COOEt)_2$	93% [d]	38	$PrCH=C(COOEt)(CN)$	55 [c]
21	$Me_2C=C(COOEt)_2$	74% [e]			

a) In all cases, 1.05 eq. of BuMnCl was used. b) Isolated yield c) -30°C, 1h. d) 0°C, 10 min. ; yield of addition-elimination product **10** (see *infra*). e) -30°C, 3h. then 20°C, 2h.

In order to point out the synthetic interest of the method described above, we have compared the yields of 1,4 addition products obtained from organolithium, organomagnesium and organomanganese compounds

$$MeCH=C(COOEt)_2 \xrightarrow[THF,\ -30°C]{\text{Bu-Metal}} Me(Bu)CHCH(COOEt)_2$$

BuLi :	50%
BuMgCl :	80%
BuMnCl :	87%

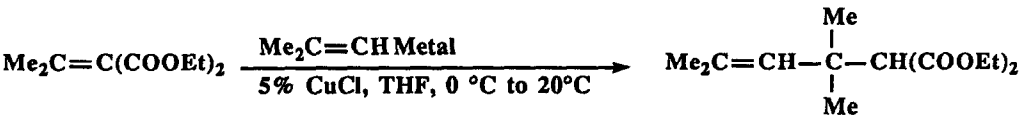
$$Me_2C=C(COOEt)_2 \xrightarrow[-30°C \text{ then } 20°C]{\text{R-Metal, THF}} R-C(Me)_2-CH(COOEt)_2$$

R	Yield from : RLi	RMgCl	RMnCl
Me	-	3%	82%
Ph	-	5%	87%
Bu	0% [a]	62%	74%

a) Quantitative yield of enolization product **7** was obtained.

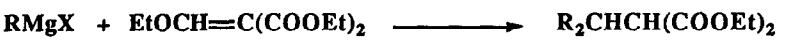
In all instances, the comparison is favourable to organomanganese compounds. Moreover, when the presence of copper salts is necessary to achieve the conjugate addition reaction in good yields with both organomagnesium and

organomanganese reagents, as for the examples depicted below, the organomanganese route is the more efficient one.



$Me_2C=CHLi$: 40%
$Me_2C=CHMgCl$ [5b] : 45%
$Me_2C=CHMnCl$: 83%

It should be noted that the conversion of organolithium or organomagnesium compounds into their organomanganese analogous presents some further advantages. Thus, in some cases, the reaction of the β-alkoxyalkylidenemalonic esters with organomagnesium derivatives was described to lead to the double addition product **8**, whatever the stoichiometry of the reactants[5];



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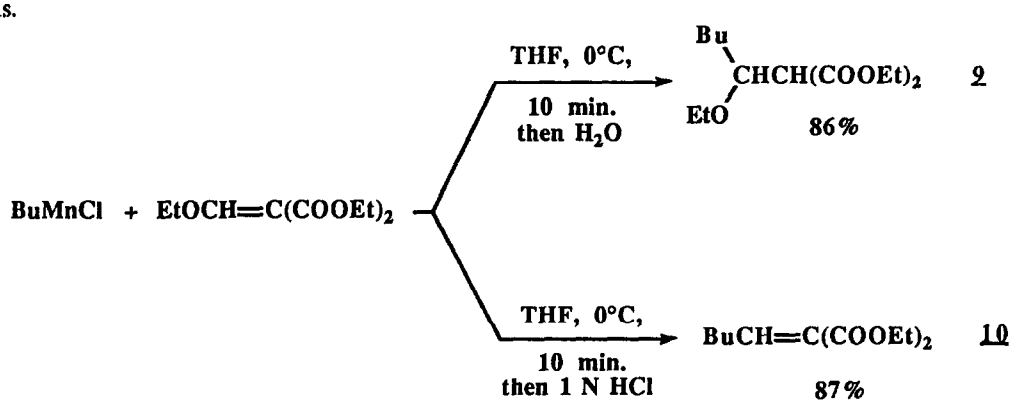
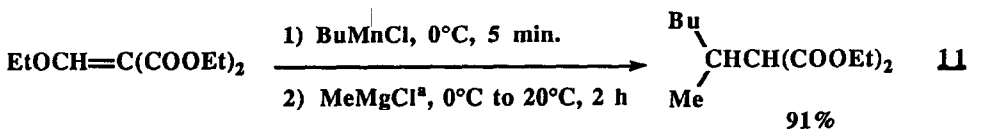
With the organomanganese reagents such a drawback was never observed and it is possible to prepare, at 0°C, the monoaddition product **9** (neutral hydrolysis) or the addition-elimination product **10** (acid hydrolysis) in good yields.

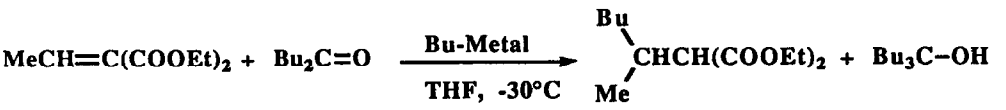


Furthermore, two different R groups can be added according to the following one-pot procedure.

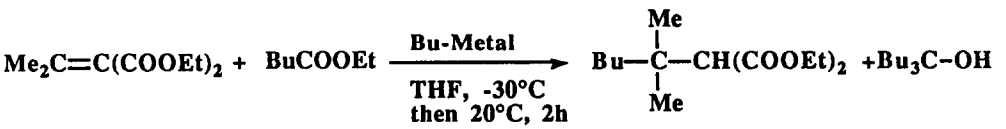


a) This procedure allows MeMgCl to be converted to MeMnCl before the elimination step.

Finally, organomanganese reagents are also interesting for their chemoselectivity. This is exemplified hereunder.



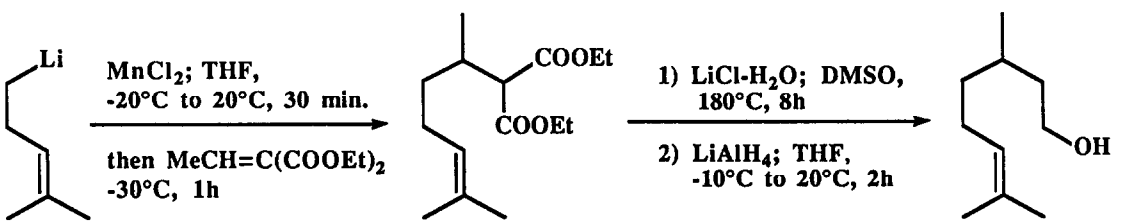
BuMgCl :	71%	16%
BuMnCl :	87%	0%



BuMgCl :	45%	15%
BuMnCl :	71%	0%

For practical purposes, let us recall that organolithium or organomagnesium compounds are readily and quantitatively transformed into their organomanganese counterparts, at room temperature, by simple addition of a stoichiometric amount of manganese chloride, a very inexpensive material[6].

In conclusion, the conjugate addition of organomanganese reagents to alkylidenemalonic esters proceed in good yields. It is worthy of note that alkylidenemalonic esters can be used as valuable synthetic equivalents of α,β-unsaturated esters. This is illustrated by the short synthesis of the citronellol outlined in the following scheme.



Overall yield : 76%

Further studies on the reaction of organomanganese reagents with conjugated unsaturated carbonyl compounds will be reported shortly.

EXPERIMENTAL

I- Manganese Salts:

1°) Manganese Iodide.

The anhydrous manganese iodide must be prepared since, presently, the commercial manganese iodide is very expensive and, moreover, not usable to prepare organomanganese reagents suitably. This salt is conveniently obtained as follows :

Under a nitrogen atmosphere, 256.5 g of powdered iodine are added at 0°C, under vigorous stirring, to 55 g (1 mole) of granulated manganese i.e. Fluka Puriss. granular, purity ≥ 99% in 400 ml of anhydrous ether (the use of micronized manganese powder which contains very often a large amount of manganese oxides should be avoided). The addition rate is adjust in order to keep the temperature of the reaction mixture below 25 to 30°C. Next, the stirring is continued at room temperature until the coloration due to the presence of iodine disappears (about 4 h). The precipitate of manganese iodide is then filtered on a sintered glass and washed twice with 100 ml of ether. After 2 h under reduced pressure (10^{-2} torr), 300 g of pure anhydrous manganese iodide (97% yield)are obtained. This product must be kept in darkness and in the absence of moisture.

Important note: It should be underlined that it is possible to prepare manganese iodide, then to convert it directly, without isolation, in an organomanganese reagent by adding an organolithium or magnesium compound to the reaction mixture (see below). Very often, this "one-pot" procedure give better result than the two steps one described above.

2°) Manganese Chloride.

The commercial anhydrous manganese chloride (purity ≥ 99%) available from Fluka, Strem Chemical, Alfa Inorganic or Janssen can be generally used without preliminary treatment. However, for the most part, the experiments described herein have been achieved by using an anhydrous manganese chloride furnished by Chemetals Inc., Baltimore, USA (manganese chloride regular, flakes) which is very cheap and works particularly well. Sometimes, manganese chloride should be dried (2 h at 180°C) before using.

3°) Solubilization of Manganese Chloride in THF: Preparation of the Soluble Dilithiumtetrachloromanganate Complex $MnCl_4Li_2$.

Under a nitrogen atmosphere, a suspension of 50 mmoles of anhydrous manganese chloride and 100 mmoles of anhydrous lithium chloride in 80 ml of THF is stirred at room temperature until obtaining of a clear yellow solution of the "ate complex" $MnCl_4Li_2$. The rate of dissolution is very depending of both the origin and the granular size of the lithium and manganese salts. Thus the preparation time varied from 30 min. to 12 h.

In most cases, the milkiness suspension which is obtained after 1 to 2 h can be used in place of the expected clear solution without drawback.

II- Preparation of Organomanganese Compounds: General Procedures.

Organomanganese reagents must be prepared and used under a nitrogen atmosphere

1°) In Ether.

a) Preparation of RMnI.

To 52 mmoles of manganese iodide in 80 ml of anhydrous ether are added between -10 to 0°C (-40°C for R= s or t-alkyl), under stirring, a solution of 50 mmoles of an organolithium compound in ether or in a hydrocarbon or 50 mmoles of an organomagnesium compound in ether. The organomanganese reagent RMnI is quantitatively obtained after 30 min of stirring at 10°C (1 to 2 h at -35°C for R= s or t-alkyl). The reaction mixture appears as a dark red-brownish solution or a beige to brownish suspension (a dark greenish coloration is often observed when R= aryl and sometimes for R= alkenyl).

b) Preparation of R_2Mn.

Symmetrical organomanganese compounds R_2Mn are less stable than organomanganese iodide reagents RMnI. They are obtained from 25 mmoles of manganese iodide and 50 mmoles of an organolithium or magnesium compounds in ethereal solution. For R= alkenyl, aryl or alkynyl (no β-eliminable hydrogen atom), they are sufficiently stable to be quantitatively prepared according to the previous procedure. On the other hand, the reaction must be performed at -10°C for 45 min (addition at -30°C) when R= n-alkyl and at -30°C for 1 h when R= s or t-alkyl. Moreover, in this last case (R= s- or t-alkyl) the partial decomposition of the symmetrical organomanganese compound cannot be avoided.

c) Preparation of R_3MnLi.

Lithium organomanganates are quantitatively prepared from 16.7 mmoles of manganese iodide and 50 mmoles of an

organolithium compound (prepared in ether or in a hydrocarbon) according to the procedure described above for RMnI. A red-brownish solution is generally obtained. Lithium organomanganates are more stable than the corresponding organomanganese reagents RMnI.

note: Let us recall that magnesium organomangates R_3MnMgX cannot be prepared in ether.

2°) In THF.

a) Preparation of RMnCl from RLi.

A solution of 50 mmoles of an organolithium compound in ether or a hydrocarbon is added, under stirring, to 52 mmoles of anhydrous manganese chloride in 80 ml of THF, between -35°C and 0°C (*see the following note).* After 30 min. of stirring at room temperature the organomanganese chloride reagent is quantitatively obtained as a brownish solution (formation of an "ate complex" with the lithium salts present in the reaction mixture).

In THF, all organomanganese compounds are stable at room temperature. However, with the less stable organomanganese compounds (t- and s-alkylMnCl), decomposition can occur at this temperature when some low grade manganese chloride is used as starting material.

note: the reaction mixture must be cooled before to add the organolithium compound in order to avoid the metallation of the THF by this one. Thus, the temperature should be choosen according to the reactivity of the organolithium compound, for instance, -35°C for BuLi and 0°C for the less reactive methyl, alkenyl or aryllithium.

b) Preparation of RMnCl from RMgX.

b-1) From $MnCl_2$.

Organomanganese chloride reagents are prepared by adding between -10°C to 0°C, under stirring, a solution of 50 mmoles of an organomagnesium halide in ether or better in THF (RMgX; X= Cl, Br, I) to a suspension of 52 mmoles of anhydrous manganese chloride in 80 ml of THF. The reaction is quantitative after stirring for 30 min. to 3 h.at room temperature. A brownish solution or suspension is thus obtained.

b-2) From the Soluble Dilithiumtetrachloromanganate Complex $MnCl_4Li_2$.

Interestingly, the previous procedure should be improved by using of the soluble dilithium tetrachloromanganate complex $MnCl_4Li_2$ (52 mmoles) instead of the insoluble manganese chloride. Thus, the reaction mixture is homogeneous and the desired organomanganese chloride reagent is quantitatively formed, at 0°C, as soon as the addition of the organomagnesium compound (50 mmoles, solution in ether or THF) is completed. Furthermore, the organomanganese reagents thus prepared are always soluble (formation of an "ate complex" with the lithium salts).

c) Preparation of R_2Mn.

Symmetrical organomanganese reagents are quantitatively prepared from 50 mmoles of organolithium or organomagnesium compound and 25 mmoles of anhydrous manganese chloride (or its "ate complex" $MnCl_4Li_2$) according to the procedure described above for the preparation of organomanganese chloride reagents. They are soluble in THF in the presence of lithium salts.

d) Preparation of R_3MnLi and R_3MnMgX.

To a suspension of 16.7 mmoles of anhydrous manganese chloride in 80 ml of THF is added, under stirring, a solution of 50 mmoles of organolithium compound in ether or in hydrocarbon or a solution of 50 mmoles of organomagnesium compound in ether or better in THF. The addition is performed between -30°C and 0°C for organolithium compound (see above the note in II-2-a)) and at 0°C for organomagnesium compound. After 30 min. of stirring at room temperature, the expected lithium or magnesium organomanganate is quantitatively obtained. Lithium or magnesium organomanganates are always soluble in THF (brownish solution).

III) Addition of Organomanganese Reagents to Alkylidenemalonic Esters and Related Compounds.

1°) Addition of Organomanganese Chloride RMnCl to β-Monosubstituted Alkylidenemalonic Esters $RCH=C(COOEt)_2$ in THF.

A solution of 50 mmoles of β-monosubstituted alkylidenemalonic ester in 10 ml of THF was added dropwise at -30°C, under stirring, to 50 mmoles of organomanganese chloride RMnCl (in 80 to 100 ml of THF) prepared as described above (II-2-a and II-2-b). After stirring for 2 h

- at room temperature for the organomanganese reagents which do not contain β-eliminable hydrogen atom (R= Me, aryl, alkenyl, alkynyl ...)
- at -30°C for the organomanganese reagents which contain one or many β-eliminable hydrogen atoms (R= n-, s- or t-alkyl),

the reaction mixture was hydrolyzed, at -10°C, with 60 ml of a 1 N HCl solution. The aqueous layer was then decanted and extracted twice with 50 ml of ether. After drying of the combined organic layers with magnesium sulfate and evaporation of solvents under vacuo, the product was isolated by distillation.

2°) Addition of Organomanganese Chloride RMnCl to β,β-Bisubstituted Alkylidenemalonic Esters $R_2C=C(COOEt)_2$ in THF.

a) Organomanganese chloride RMnCl Having No β-Eliminable Hydrogen Atom.

To 50 mmoles of organomanganese chloride in 80 to 100 ml of THF (see above) was added at 0°C,under stirring, a solution of β,β-bisubstituted alkylidenemalonic ester in 10 ml of THF. Stirring was continued for 2 h at room temperature, then, the reaction mixture was hydrolyzed with 60 ml of a 1 N HCl solution. After decantation and extraction of the aqueous layer twice with 50 ml of ether, the combined organic layers was dried with magnesium sulfate and solvents were removed under vacuo.The product was isolated by distillation.

b) Organomanganese Chloride RMnCl Having One or Many β-Eliminable Hydrogen Atoms.

The procedure is the same as above (III-2-a) excepted that:
- the addition of β,β-bisubstituted alkylidenemalonic esters was performed at -30°C
- the reaction mixture was stirred for 3 h at -30°C then for 2 h at room temperature before to be hydrolyzed

3°) Addition of Organomanganese Reagents R_2Mn, R_3MnLi and R_3MnMgX to Alkylidenemalonic Esters in THF.

The addition of these organomanganese reagents to β-mono or β,β-bisubstituted alkylidenemalonic esters has been achieved according to the procedure used for the addition of the organomanganese chloride RMnCl (see above III-1 and III-2)

4°) Addition of Organomanganese Reagents to Alkylidenemalonic Esters in Ether.

In ether, the addition of organomanganese reagents to alkylidenemalonic esters was carried out in the same conditions that in THF (see III-1, III-2 and III-3).

5°) Addition of Organomanganese Reagents to Various Compounds Related to Alkylidenemalonic Esters.

The addition of butyl manganese chloride to ethyl butylidene acetoacetate (entry 36), butylidene acetoacetone (entry 37) and ethyl ethylidene cyanoacetate (entry 38) was achieved according to the procedure previously described in the case of the β-monosubstituted alkylidenemalonic ester (III-1)

IV) Copper-Catalyzed Addition of Organomanganese Reagents to Alkylidenemalonic Esters in THF.

The addition was performed according to the procedure reported above (III-2) except that 2.5 mmoles of cuprous chloride (5%) were added, at 0°C, just before the addition of the ethyl isopropylidene malonate.

V) Addition of Organomanganese Reagents to Ethyl β-Ethoxymethylidenemalonate.

A solution of 50 mmoles of ethyl β-ethoxymethylidenemalonate in 10 ml of THF was added at 0°C, under stirring, to 50 mmoles of butylmanganese chloride in 80 ml of THF. Next:
- to obtain the addition products **9**, the reaction mixture was stirred at 0°C for 10 min. then hydrolyzed at this temperature with 60 ml of H_2O
- to obtain the addition-elimination product **10**, the reaction mixture was stirred at 0°C for 10 min.before to be hydrolyzed at -10°C with 60 ml of a 1 N HCl solution. After work-up (cf III-2), the crude product was heated at 180-200°C for 2 h in order to complete the conversion of **9** to **10** (elimination)
- to obtain the addition-elimination-addition product **11**, stirring was continued at 0°C for 5 min.then a solution of 50 mmoles of methyl magnesium chloride in THF was added. The reaction mixture was then allowed to warm to room temperature, stirred for 2 h and hydrolyzed with 60 ml of a 1 N HCl solution.

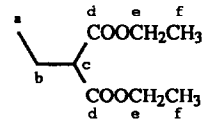
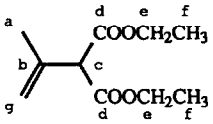
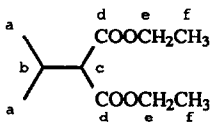
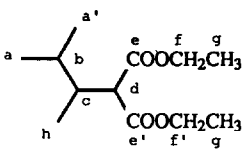
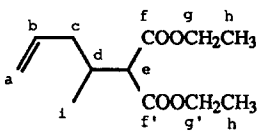
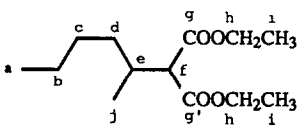
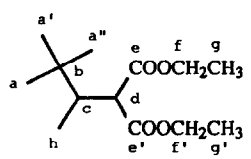
The products were then isolated as above (III-2).

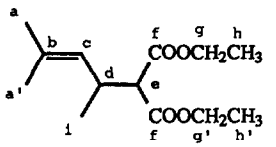
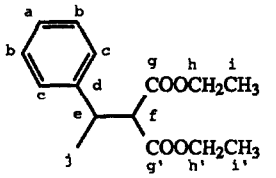
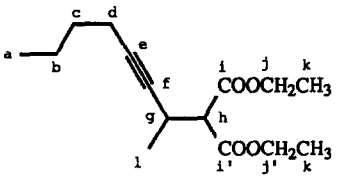
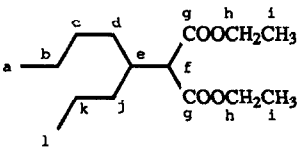
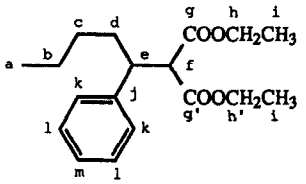
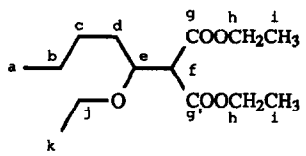
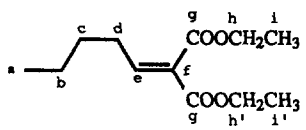
VI) Synthesis of the Citronellol.

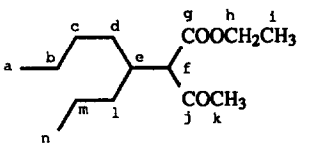
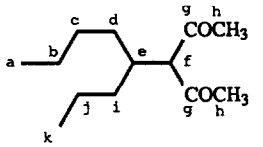
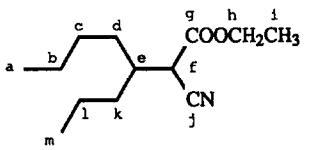
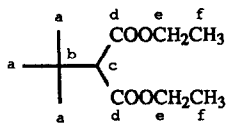
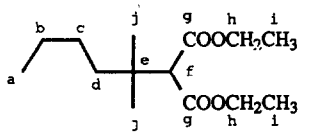
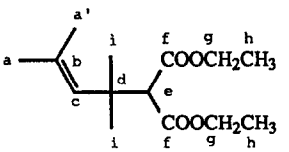
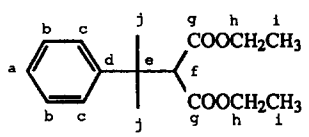
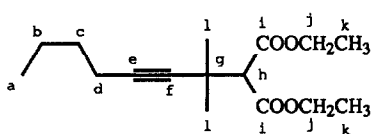
The addition of the organomanganese reagent $Me_2C=CHCH_2\ CH_2MnCl$ to the alkylidenemalonate $MeCH=C(COOEt)_2$ was performed on a 50 mmoles scale according to the general procedure (see III-1). The malonate $Me_2C=CHCH_2CH_2(Me)CHCH(COOEt)_2$, isolated by distillation, was thus obtained in 90% yield.
The decarboxylation of this malonic ester into ethyl citronellate was then achieved in 87% yield (bp: 68°C/0.01 torr) according to the method of Krapcho[7] (0.6 eq. LiCl, 0.6 eq. H_2O; DMSO, 180°C, 8 h). Next, ethyl citronellate was reduced by treatment with $LiAlH_4$ (THF, -10°C to 20°C, 2 h) into citronellol which was isolated by distillation (bp: 105°C/10 torr) in 97% yield.

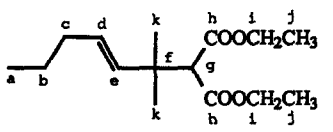
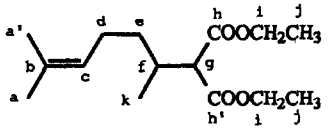
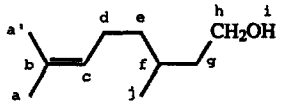
The physical and spectral data of the above products are given at the end of the Table IV.

Table IV. Physical and Spectral Data of Products.

Product	bp (°C/torr) and Refractive Index / °C	IR (cm^{-1}), ^1H and ^{13}C NMR (δ, $CDCl_3$, TMS), Microanalysis
	35-36/10^{-2} 1.4160/26	ν C=O : 1725-1745; ν C-O-C : 1025 ^1H: 4.30 (q, 4 H, e); 3.30 (t, 1 H, c); 2.00 (dq, 2 H, b); 1.30 (t, 3 H, f); 1.00 (t, 3 H, a) ^{13}C: 169.40 (d); 61.20 (e); 53.63 (c); 22.35 (b); 14.20 (f); 11.90 (a) Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.62; H, 8.53
	96-97/10 1.4340/20	ν C=O : 1730-1750; ν C=C : 1645; ν C-O-C : 1035 ^1H: 5.15 (d, 2 H, a); 4.30 (q, 4 H,e); 4.20 (s, 1 H, c); 2.00 (s, 3 H, g); 1.40 (t, 6 H, f) ^{13}C: 167.50 (d); 137.90 (b); 116.95 (a); 61.40 (e); 59.50 (c); 20.85 (g); 14.05 (f) Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.79; H, 8.21
	98-100/10 1.4170/26	ν C=O: 1725-1750; ν C-O-C: 1030 ^1H: 4.30 (q, 4 H, e); 3.15 (d, 1 H, c); 2.40 (m, 1 H, b); 1.25 (t, 6 H, f);1.05 (d, 6 H, a) ^{13}C: 168.65 (d); 61.00 (e); 59.10 (c); 25.80 (b); 20.40 (a); 14.20 (f) Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97. Found: C, 59.58; H, 9.22
	51-52/10^{-2} 1.4286/26	ν C=O : 1725-1750; ν C-O-C : 1030 ^1H: 4.25 (q, 4 H, ff'); 3.35 (d, 1 H, d); 2.20 (m, 1 H, c); 1.70 (m, 1 H, b); 1.30 (t, 6 H, g); 0.90 (m, 9 H, aa'h) ^{13}C: 169.00 and 168.80 (ee'); 61.10 and 61.00 (ff '); 56.45 (d); 38;95 (c); 29.85 (b); 21.35 (h); 16.75 and 11.80 (aa'); 14.20 (g) Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.40; H, 9.97
	65-66/10^{-2} 1.4371/20	ν C=O : 1735-1755; ν C=C : 1645; ν C-O-C : 1035 ^1H: 5.80 (m, 1 H, b); 5.10 and 4.95 (2s, 2 H, a-trans and a-cis); 4.20 (q, 4 H, gg'); 3.25 (d, 1 H, e); 2.40 to 1.90 (m, 3 H, cd); 1.25 (t, 6 H, h); 1.00 (d, 3 H, i) ^{13}C: 168.75 and 168.55 (ff'); 135.95 (b); 117.10 (a); 61.10 and 61.00 (gg'); 56.85 (e); 38.90 (c); 33.20 (d); 16.90 (i); 14.15 (h) Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 62.81; H, 9.07
	60-61/10^{-2} 1.4270/27	ν C=O : 1730-1750; ν C-O-C : 1035 ^1H: 4.30 (q, 4 H, h); 3.30 (d, 1 H, f); 2.30 (m, 1 H, e); 1.30 to 1.00 (m, 18 H, abcdi) ^{13}C: 168.90 and 168.70 (gg'); 61.00 (h); 57.80 (f); 34.15 (d); 33.40 (e); 29.20 (c); 22.80 (b); 17.00 (j); 14.20 (i); 14.10 (a) Calcd for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.62; H, 10.07
	110/13 1.4347/20	ν C=O : 1730-1755; ν C-O-C : 1030 ^1H: 4.19 and 4.18 (2q, 4 H, ff'); 3.52 (d, 1 H, d); 2.25 (dq, 1 H, c); 1.29 and 1.28 (2t, 6 H, gg'); 1.04 (d, 3 H, h); 0.95 (s, 9 H, a) ^{13}C: 169.90 and 169.25 (ee'); 61.15 and 60.80 (ff'); 53.35 (d); 42.70 (c); 33.65 (b); 27.60 (a); 14.10 (g); 12.05 (h) Calcd for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.71; H, 10.11

	55-56/10^{-2} 1.4385/27	ν C=O : 1730-1750; ν C=C : 1650; ν C-O-C : 1025 ^{1}H: 5.10 (d, 1 H, c); 4.25 and 4.15 (2q, 4 H, gg'); 3.25 (m, 2 H, de); 1.70 (s, 6 H , aa'); 1.25 and 1.20 (2t, 6 H, hh'); 1.05 (d, 3 H, i) ^{13}C: 168.40 (f); 132.55 (b); 126.70 (c); 61.05 and 61.00 (gg'); 58.35 (e); 33.40 (d); 25.00 and 19.95 (aa'); 19.20 (i); 14.20 (hh') Calcd for $C_{13}H_{22}O_4$; C, 64.44; H, 9.15. Found: C, 64.16; H, 9.23
	100-105/10^{-2} 1.4820/26.5	ν C=O : 1725-1750; ν C=C : 1365-1450-1600; ν C-O-C : 1025 ^{1}H: 7.35 (s, 5 H, abc); 4.25 and 3.95 (2q, 4 H, hh'); 3.65 (m, 2 H, ef); 1.30 (d, 3 H, j); 1.25 and 0.95 (2t, 6 H, ii') ^{13}C: 168.25 and 167.80 (gg'); 143.25 (d); 128.40 (b);127.50 (c); 126.80 (a); 61.30 and 60.95 (hh'); 59.30 (f); 40.15 (e); 20.20 (j); 14.10 and 13.75 (ii') Calcd for $C_{15}H_{20}O_4$; C, 68.16; H, 7.63. Found: C, 68.14; H, 7.82
	95-97/10^{-2} 1.4428/27	ν C≡C : 2020; ν C=O : 1730-1750; ν C-O-C : 1035 ^{1}H: 4.25 (q, 4 H, jj'); 3.30 (m, 2 H, gh); 2.10 (m, 2 H, d); 1.50 to 1.20 (m, 13 H, bckl); 0.90 (t, 3 H, a) ^{13}C: 167.65 and 167.50 (ii'); 82.20 (f); 80.85 (e); 61.35 and 61.30 (jj'); 58.25 (h); 31.15 (c); 26.55 (g); 21.90 (b); 19.35 (l); 18.40 (d); 14.20 (k); 13.65 (a) Calcd for $C_{15}H_{24}O_4$; C, 67.14; H, 9.01. Found: C, 66.81; H, 9.29
	77-78/10^{-2} 1.4331/20	ν C=O : 1730; ν C-O-C : 1035 ^{1}H: 4.20 (q, 4 H, h); 3.35 (d, 1 H, f); 2.05 (m, 1 H, e); 1.50 to 1.20 (m, 10 H, bcdjk); 1.25 (t, 6 H, i); 0.90 (t, 6 H, al) ^{13}C: 168.95 (g); 60.95 (h); 55.55 (f); 38.10 (e); 33.75 (j); 31.05 (d); 29.15 (c); 23.05 (b); 20.10 (k); 14.25 (i); 14.05 (a) Calcd for $C_{15}H_{28}O_4$; C, 66.14; H, 10.36. Found: C, 66.13; H, 10.60
	- 1.4845/20	ν C=O : 1730-1750; ν C=C : 1365-1450-1490-1600; ν C-O-C : 1030 ^{1}H: 7.25 (s, 5 H, klm); 4.25 and 3.85 (2q, 4 H, hh'); 3.65 (d, 1 H, f); 3.40 (m, 1 H, e); 1.65 (m, 2 H, d); 1.25 and 0.90 (2t, 6 H, ii'); 1.15 (m, 4 H, bc); 0.80 (t, 3 H, a) ^{13}C: 168.45 and 167.80 (gg'); 141.10 (j); 128.85 (l); 128.40 (k); 128.25 (m); 61.35 and 60.95 (hh'); 58.95 (f); 45.65 (e); 33.70 (d); 29.25 (c); 22.40 (b); 14.10 (i); 13.85 (a) Calcd for $C_{18}H_{26}O_4$; C, 70.56; H, 8.55. Found: C, 70.31; H, 8.73
	90-92/10^{-2} -	ν C=O : 1740-1760; ν C-O-C (ester) : 1035; ν C-O-C (ether) : 1100 ^{1}H: 4.20 (q, 4 H, h); 3.90 (m, 1 H, e); 3.55 (q, 2 H, j); 3.50 (d, 1 H, f); ^{13}C: 167.70 and 167.35 (gg'); 78.00 (e); 66.15 (f); 61.15 (h); 57.10 (j); 32.55 (d); 27.25 (c); 22.85 (b); 15.50 (k); 14.10 (ai) Calcd for $C_{14}H_{26}O_5$; C, 61.29; H, 9.55. Found: C, 61.50; H, 9.27
	138-140/12 1.4428/20	ν C=O : 1725; ν C=C : 1645; ν C-O-C : 1050 ^{1}H: 7.00 (t, 1 H, e); 4.30 and 4.25 (2q, 4 H, hh'); 2.30 (dq, 2 H, d); 1.35 and 1.30 (2t, 6 H, ii'); 1.50 to 1.20 (m, 4 H, bc); 0.90 (t, 3 H, a) ^{13}C: 165.35 and 163.90 (gg'); 148.90 (e); 129.25 (f); 61.00 (hh'); 30.65 (d); 29.45 (c); 22.45 (b); 14.20 (i); 13.75 (a) Calcd for $C_{12}H_{20}O_4$; C, 63.14; H, 8.83. Found: C, 62.70; H, 8.92

	69-71/10^{-2} 1.4410/20	ν C=O : 1720; ν C-O-C : 1020 ^{1}H: 4.25 (q, 2 H, h); 3.50 (d, 1 H, f); 2.20 (s, 3 H, k); 2.30 to 2.10 (m, 1 H, e); 1.30 to 1.20 (m, 13 H, bcdlmi); 0.90 (t, 6 H, an) ^{13}C: 203.00 (j); 169.45 (g); 63.90 (f); 60.95 (h); 37.70 (e); 33.25 (l); 30.55 (d); 29.10 (k); 28.65 (c); 23.05 (b); 19.70 (m); 14.20 (i); 14.05 (n); 11.40 (a) Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.18; H, 10.92
	60-61/10^{-2} 1.4440/28	ν C=O : 1690 ^{1}H: 3.80 (d, 1 H, f); 2.20 (s, 6 H, h); 1.40 to 1.20 (m, 11 H, bcdeij); 0.90 (t, 6 H, ak) ^{13}C: 204.20 (g); 73.60 (f); 38.00 (h); 32.85 (i); 30.20 (d); 29.65 (e); 28.15 (c); 23.05 (b); 19.20 (j); 14.35 (k); 14.00 (a) Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.63; H, 11.55
	78-80/10^{-2} 1.4398/20	ν C≡N : 2220; ν C=O : 1735; ν C-O-C : 1025 ^{1}H: 4.30 (q, 2 H, h); 3.70 (d, 1 H, f); 2.10 (m, 1 H, e); 1.60 to1.20 (m, 13 H, bcdilk); 0.90 (m, 6 H, am) ^{13}C: 166.50 (g); 115.60 (j); 62.50 (h); 42.10 (f); 39.10 (e); 34.25 and 34.05 (k); 31.70 and 31.40 (d); 29.00 (c); 22.75 (b); 20.00 (l); 14.10 (i); 14.00 (am) Calc for $C_{13}H_{23}O_2N$; C, 69.29; H, 10.29. Found: C, 69.18; H, 10.41
	104-105/10 1.4245/21	ν C=O : 1720; ν C-O-C : 1030 ^{1}H: 4.25 (q, 4 H, e); 3.25 (s, 1 H, c); 1.30 (t, 6 H, f); 1.10 (s, 9 H, a) ^{13}C: 168.20 (d); 61.30 (c); 60.70 (e); 33.55 (b); 20.05 (a); 14.15 (f) Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 60.97; H, 9.31
	75-76/10^{-2} 1.4353/26.5	ν C=O : 1725-1750; ν C-O-C : 1030 ^{1}H: 4.20 (q, 4 H, h); 3.30 (s, 1 H, f); 1.40 to 0.80 (m, 21 H, abcdij) ^{13}C: 168.30 (g); 60.70 (h); 59.65 (f); 40.95 (d); 36.25 (e); 26.10 (c); 25.15 (j); 23.50 (b); 14.15 (ai) Calcd for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14. Found: C, 64.91; H, 10.33
	65-67/10^{-2} 1.4490/20	ν C=O : 1730-1760; ν C=C : 1645; ν C-O-C : 1040 ^{1}H: 5.30 (m, 1 H, c); 4.15 (q, 4 H, g); 3.55 (s, 1 H, e); 1.75 (s, 3 H, a); 1.65 (s, 3 H, a'); 1.30 (s, 6 H, i); 1.25 (t, 6 H, h) ^{13}C: 168.15 (f); 131.95 (c); 131.80 (b); 60.95 (e); 60.70 (g); 37.80 (d); 28.15 and 19.15 (aa'); 27.10 (i); 14.20 (h) Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.63; H, 9.49
	112/10^{-2} 1.4910/21	ν C=O : 1730; ν C=C : 1360-1450-1600; ν C-O-C : 1025 ^{1}H: 7.40 (m, 5 H, abc); 4.10 (q, 4 H, h); 3.85 (s, 1 H, f); 1.60 (s, 6 H, j); 1.10 (t, 6 H, i) ^{13}C: 167.75 (g); 147.00 (d); 128.05 (b); 126.00 (a); 125.95 (c); 61.85 (f); 60.70 (h); 40.10 (e); 26.25 (j); 13.90 (i) Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.87; H, 8.12
	94/10^{-2} 1.4600/20	ν C≡C : 2235; ν C=O : 1730-1750; ν C-O-C : 1035 ^{1}H: 4.25 (q, 4 H, j); 3.45 (s, 1 H, h); 2.10 (m, 2 H, d); 1.45 (s, 6 H, l); 1.60 to 1.40 (m, 4 H, bc); 1.30 (t, 6 H, k); 0.90 (t, 3 H, a) ^{13}C: 167.40 (i); 85.00 (f); 81.30 (e); 61.00 (j); 60.85 (h); 32.85 (g); 31.15 (c); 27.70 (l); 21.85 (b); 18.40 (d); 14.15 (k); 13.70 (a) Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 67.70; H, 9.37

	80-81/10⁻² 1.4499/20	ν C=O : 1730-1760; ν C=C : 1645; ν C-O-C : 1040 ¹H: 5.50 to 5.10 (m, 2 H, de); 4.10 (q, 4 H, i); 3.50 (s, 1 H, g); 2.10 (m, 2 H, c); 1.35 (m, 2 H, b); 1.30 (s, 6 H, k); 1.25 (t, 6 H, j); 0.90 (t, 3 H, a) ¹³C: 168.05 (h); 136.30 (e); 130.50 (d); 61.25 (g); 60.80 (i); 38.50 (f); 30.80 (c); 27.10 (k); 23.25 (b); 14.15 (j); 13.85 (a) Calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.49; H, 9.86
	102-104/10⁻² 1.4482/22	ν C=O : 1735-1755; ν C=C : 1635; ν C-O-C : 1035 ¹H: 5.10 (t,1 H, c); 4.15 (q, 4 H, i); 3.20 (d, 1 H, g); 2.30 to 1.80 (m, 5 H, def); 1.70 (s, 3 H, a); 1.60 (s, 3 H, a'); 1.30 (t, 6 H, j); 1.00 (d, 3 H, k) ¹³C: 168.80 and 168.65 (hh'); 131.55 (b); 124.15 (c); 60.95 (i); 57.65 (g); 34.55 (d); 33.10 (f); 25.70 (a); 25.50 (e); 17.60 (a'); 16.90 (k); 14.20 (j) Calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.15; H, 10.01
	105/10 1.4556/21	ν C-O-H : 3320; ν C=C : 1635 ¹H: 5.10 (t, 1 H, c); 3.65 (t, 2 H, h); 3.55 (s, 1 H, i); 2.00 (dt, 2 H, d); 1.70 (s, 3 H, a); 1.60 (s, 3 H, a'); 1.65 to 1.10 (m, 5 H, feg); 0.90 (d, 3 H, j) ¹³C: 130.90 (b); 124.95 (c); 60.66 (h); 39.55 (g); 37.45 (d); 29.45 (f); 25.60 (ae); 19.60 (j); 17.60 (a') Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.80; H, 13.04

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REFERENCES

1. Part XIV: Cahiez, G.; Rivas-Enterrios, J. and Clery, P. *Tetrahedron Lett.* **1988**, *29*, 3659.
2. Cahiez, G. and Alami, M. *Tetrahedron Lett.* **1986**, *27*, 569.
3. For a closely related influence of lithium and magnesium salts on the 1,2- addition rate of organomanganese reagents to ketones see: Cahiez, G. and Figadère, B. *Tetrahedron Lett.* **1986**, *27*, 4445.
4. a) Ziegenbein, W.; in *Acetylenes*, Viehe, H.G.; Ed. Marcel Dekker Inc., New York, **1969**, 207 to 241. b) Ried,W. *Newer Methods Prep. Org. Chem.* **1968**, *4*, 95 to 138. c) Beumel, O. F. and Harris, R.F. *J. Org. Chem.* **1963**, *28*, 2775. d) House, H.O. and Fischer, W.F. *J. Org. Chem.* **1969**, *34*, 3615. e) Corey, E.J. and Beames, D.J. *J. Am. Chem. Soc.* **1972**, *94*, 7210. f) Hooz, J. and Layton, R.B. *J. Am. Chem. Soc.* **1971**, *93*, 7320. g) Schwartz, J.; Carr, D.B.; Hansen, R.T. and Dayrit, F.M. *J. Org. Chem.* **1980**, *45*, 3053 and references therein.
5. a) Gupte, S.D. and Sunthakar, S.V. *J.Org.Chem.* **1959**, *24*, 1334. b) Cuvigny, T. and Normant, H. *Bull. Soc. Chim. Fr.* **1961**, 2423.
6. Anhydrous manganese chloride costs about 2 to 3 $/Kg (Chemetals Inc. , Baltimore, Maryland, USA).
7. Krapcho, A.P. and Lovey, A.J. *Tetrahedron Lett.* **1973**, *12*, 957.