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Selectivity in Organic Group Transfer in Reactions of Mixed Diorganomanganese(II) and Triorganomanganate(II) with 2-Cyclohexen-1-one or Cyclohexanecarbaldehyde

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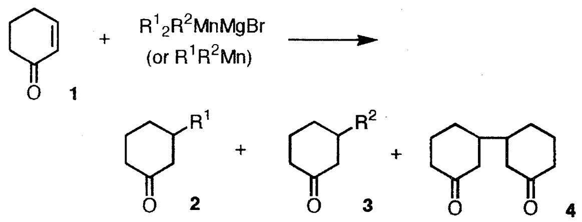
The unsymmetrical diorganomanganeses(II) (R^1R^2Mn) and magnesium triorganomanganates(II) ($R^1_2R^2MnMgX$) reacted with 2-cyclohexen-1-one to produce the 1,4-addition products in moderate to good yields. The approximate reactivity order obtained from the product distribution was $CH_2{=}CHCH_2 > PhS > n\text{-Bu} > Ph > Me$, Me_3SiCH_2, $n\text{-}C_6H_{13}\text{–}C{\equiv}C$. In contrast, the reactivity order for the addition of these reagents to cyclohexanecarbaldehyde was $CH_2{=}CHCH_2 > Ph > Me > n\text{-Bu} > n\text{-}C_6H_{13}C{\equiv}C > Me_3SiCH_2$.

Diorganocuprate(I) reagents are widely used in organic synthesis.[1)] These compounds are particularly well-suited for substitution reactions on an extremely wide range of saturated haloalkanes and unsaturated electrophiles (allylic and propargylic derivatives) as well as for 1,4-addition to α,β-unsaturated carbonyl compounds. Generally only one of the two R groups in a cuprate(I) of the stoichiometry R_2CuLi (or R_2CuMgX) can be introduced into a substrate; mixed cuprates(I) of the type R_tR_rCuLi have been used, in which R_t is an easily transferred ligand and R_r is a tightly held, nontransferable "dummy ligand". Several groups R_r such as alkynyl- and thiolatocuprate(I) have been used for this purpose. Only little attention has been paid to the related reactions of diorganomanganese(II) and triorganomanganate(II),[2)] and their scope remains to be established.[3)] We became interested in mixed manganates(II)[4)] in connection with our work on the allylmanganation of acetylenes.[5)] We report here the results of a survey of the selectivities exhibited by a number of mixed organomanganate(II) reagents in the transfer of their organic moieties to substrates in two reactions: conjugate addition to 2-cyclohexen-1-one and nucleophilic addition to cyclohexanecarbaldehyde.

(1) Addition Reaction of Mixed Organomanganese(II) Reagents to 2-Cyclohexen-1-one. Diorganomanganese(II) compounds and triorganomanganates(II) were prepared according to the reported procedure.[6)] Diorganomanganese(II) reagents were generated in THF at 0 °C by an addition of R^1MgX and R^2MgX (1 equimolar amount each) to a suspension of $MnCl_2$. Triorganomanganates(II) were prepared in THF at 0°C by an addition of 2 molar amounts of R^1MgX to 1 molar amount of manganese(II) chloride, followed by an addition of 1 molar amount of a second Grignard reagent (R^2MgX). The resulting homogeneous solutions of organomanganate(II) reagents will be referred to for convenience simply as solutions of diorganomanganeses(II) R^1R^2Mn and triorganomanganates(II) $R^1_2R^2MnMgX$, although they probably contain mixtures of several different manganates(II).[7)] These solutions were treated with 2-cyclohexen-1-one at −78 °C and the resulting mixtures were stirred for 20 min at −78 °C and then quenched with 1 M HCl (1 M = 1 mol dm^{-3}). The distribution of the products was determined by the examination of ^{1}H NMR data of crude reaction mixtures and isolation of the products. The order in which the Grignard reagents were added to the suspension had no influence on the yields and distribution of the products. For instance, triorganomanganate(II), $n\text{-Bu}_2MeMgBr$ generated by two procedures, (A) an addition of 2 molar amounts of n-BuMgBr to 1 molar amount of $MnCl_2$ followed by an addition of 1 molar amount of MeMgBr, (Entry 5 in Table 1) and (B) an addition of 1 molar amount of MeMgBr followed by an addition of 2 molar amounts of n-BuMgBr, provided the same results to give 3-butylcyclohexanone in 50% yield and a trace amount of 3-methylcyclohexanone (< 1%) upon treatment with 2-cyclohexen-1-one.

The representative results are summarized in Table 1. It is worth some brief comments. The yields of 1,4-addition product were moderate, since bicyclic ketone **4**, which results from the β-reductive dimerization of cyclohexenone, was produced in 25—35% yields[2)] in all cases examined. Triorganomanganates(II) provided slightly better yields of 1,4-addition product compared to diorganomanganeses. However, the reactivity order was almost the same for both reagents. The reactivity order was $CH_2{=}CHCH_2 > PhS > n\text{-Bu} > Ph > Me$, Me_3SiCH_2, $n\text{-}C_6H_{13}C{\equiv}C$. The order is very similar to that for organocuprates(I), with the exception of manganate(II) containing phenylthio moiety. Phenylthio group migrates more easily than butyl group (Entries 3 and 13). This shows sharp contrast to the hetero cuprates(I) (RCu(SPh)Li) in which phenylthio moiety is retained on copper.[4)] Allylic moiety was transferred most easily among the organic moieties examined. 1,2-Addition of allyl group competed with ordinary conjugated addition (Entries 2 and

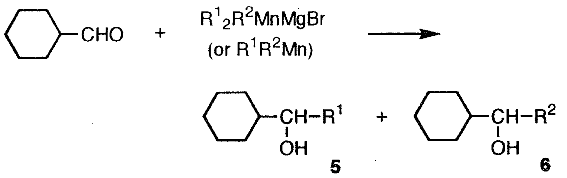
Table 1. 1,4-Addition of Organomanganese Reagents to 2-Cyclohexen-1-one[a]



Entry	Manganese reagent		Yield (%) of	
	R^1	R^2	**2**	**3**
	$R^1_2R^2$MnMgBr			
1	*n*-Bu	*n*-Bu	59	—
2	*n*-Bu	$CH_2{=}CHCH_2$	1	36[b]
3	*n*-Bu	PhS	17	27
4	*n*-Bu	Ph	51	8
5	*n*-Bu	Me	50	<1
6	*n*-Bu	*i*-C_3H_7	16	<1
7	*n*-Bu	Me_3SiCH_2	61	<1
8	*n*-Bu	*n*-$C_6H_{13}C{\equiv}C$	72	<1
9	*n*-$C_6H_{13}C{\equiv}C$	*n*-Bu	1	14
10	Ph	*n*-Bu	10	27
	R^1R^2Mn			
11	*n*-Bu	*n*-Bu	29	—
12	*n*-Bu	$CH_2{=}CHCH_2$	<1	22[c]
13	*n*-Bu	PhS	3	60
14	*n*-Bu	Ph	37	2
15	*n*-Bu	Me	43	1
16	*n*-Bu	Me_3SiCH_2	33	<1
17	*n*-Bu	*n*-$C_6H_{13}C{\equiv}C$	13	<1

a) Bicyclic ketone **4** was obtained in 25—35% yields in all experiments. b) Contaminated by 1,2-addition product (19%). c) 1,2-Addition product was obtained as a main product (49%).

Table 2. Addition of Organomanganese Reagents to Cyclohexanecarbaldehyde



Entry	Reagent		Yield (%) of	
	R^1	R^2	**5**	**6**
	$R^1_2R^2$MnMgBr			
1	*n*-Bu	*n*-Bu	98	—
2	*n*-Bu	$CH_2{=}CHCH_2$	<1	89
3	*n*-Bu	Me	35	36
4	*n*-Bu	Ph	44	54
5	*n*-Bu	*n*-$C_6H_{13}C{\equiv}C$	70	7
6	*n*-Bu	Me_3SiCH_2	97	<1
	R^1R^2Mn			
7	*n*-Bu	Me	35	49
8	*n*-Bu	Ph	14	70
9	*n*-Bu	*n*-$C_6H_{13}C{\equiv}C$	58	9
10	*n*-Bu	Me_3SiCH_2	89	<1

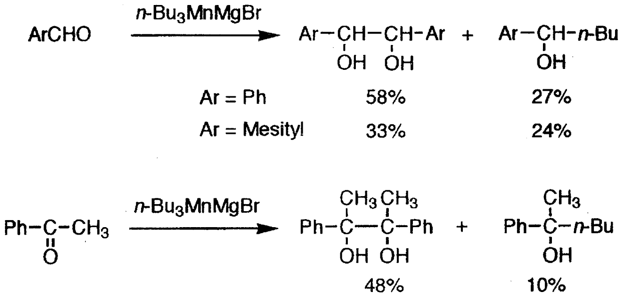
12). The selectivity in alkyl group transfer characterizing mixed manganese(II), in which R^1 is butyl and R^2 is methyl, was high (Entries 5 and 15). The use of *i*-PrMgBr (Entry 6) instead of methyl also provided butylated product selectively, but the yield decreased dramatically. The low yield might be ascribed to the instability of the manganese reagent derived from secondary Grignard reagent.[6f] 1-Octynyl and trimethylsilylmethyl[8] clearly resist transfer as well as methyl group (Entries 7, 8, 9, 16, and 17). The transfer ability of phenyl group is one-third to one-fifth of that of butyl group (Entries 4, 10, and 14).

(2) Addition of Mixed Organomanganese(II) Reagents to Cyclohexanecarbaldehyde. Similar experiments were carried out to determine the selectivity with which organic groups are transferred in the reaction with cyclohexanecarbaldehyde.[9] The results are summarized in Table 2.

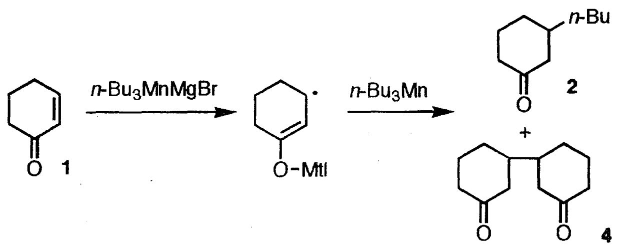
Several features of these data deserve comment. (1) The yields of adducts are higher than those for 1,4-addition products[10] described in Section (1). (2) The reactivity order was $CH_2{=}CHCH_2 > Ph > Me > n\text{-}Bu > n\text{-}C_6H_{13}C{\equiv}C > Me_3SiCH_2$. The selectivity with which organic groups are transferred is different from that in the reaction with 2-cyclohexen-1-one. For example, a methyl group, which is retained in the 1,4-addition reaction, transfers more easily than butyl group (two times, Entries 3 and 7).[11] Phenyl moiety, which is more sluggish than butyl group to migrate in the conjugate addition reaction, migrates 2.5—5 times more easily than butyl moiety (Entries 4 and 8). (3) The reaction of manganese(II) compounds (*n*-Bu_3MnMgBr or *n*-Bu_2Mn) with a ketone such as cyclohexanone did not proceed at −78 °C and ketone was recovered unchanged.[12]

The use of benzaldehyde in place of cyclohexanecarbaldehyde resulted in formation of pinacol coupling products. For instance, treatment of benzaldehyde with tributylmanganate(II) provided benzpinacol in 58% yield (*meso*/*dl* = 1/1) in addition to butylated product, PhCH(OH)–*n*-Bu (27%). Acetophenone also afforded the corresponding pinacol coupling product (48%) and butylated compound (10%) (Scheme 1).

The difference between the reactivity order in the reaction of 2-cyclohexen-1-one and that in the reaction of cyclohexanecarbaldehyde could be attributed to the different mechanisms between these two reactions. We are tempted to assume the following mechanisms for the two types



Scheme 1.



Scheme 2.

of the reactions, based on the findings described above. Organomanganese(II) compounds have two characteristic features and they act either as nucleophilic reagents or one-electron donating reagents depending on the substrates employed.[13] The reaction with cyclohexanecarbaldehyde would be explained by a nucleophilic attack of an alkyl group on manganese, whereas 1,4-addition reaction and pinacol coupling reaction might be modeled by a radical reaction mediated by one-electron donation[14] from organomanganese(II) reagents to 2-cyclohexen-1-one or aromatic carbonyl compounds (Scheme 2).[15]

Experimental

General Procedure for 1,4-Addition of Mixed Manganese Compounds to 2-Cyclohexen-1-one. The reaction of 2-cyclohexen-1-one with dibutylmethylmanganate(II) is representative. A suspension of manganese(II) chloride (151 mg, 1.2 mmol) in THF (10 ml) was sonicated for 10 min under argon atmosphere. With stirring, to this suspension at 0 °C were added a solution of butylmagnesium bromide in THF (2.4 ml, 1.0 M, 2.4 mmol) and a solution of methylmagnesium bromide in THF (1.2 ml, 1.0 M, 1.2 mmol) at intervals of 3 min. After being stirred for 20 min, the resulting dibutylmethylmanganate(II) was cooled to −78 °C and a solution of 2-cyclohexen-1-one (96 mg, 1.0 mmol) in THF (3 ml) was dropped into it. After 20 min, the starting material was consumed completely. Hydrochloric acid (1.0 M) was added to quench the reaction and the products were extracted with ethyl acetate (20 ml×3). The combined organic layer was concentrated. Purification by silica gel column chromatography afforded 3-butylcyclohexanone (77.6 mg, 0.50 mmol) in 50% yield and only a trace amount of 3-methylcyclohexanone was detected by ^{1}H NMR.

General Procedure for the Reaction of Mixed Manganese(II) Reagents with Cyclohexanecarbaldehyde. The reaction of cyclohexanecarbaldehyde with dibutylphenylmanganate(II) is representative. The manganate(II) (1.2 mmol) was prepared from 2BuMgBr, PhMgBr, and MnCl$_2$ according to the procedure described above for the generation of dibutylmethylmanganate(II). The resulting dibutylphenylmanganate(II) was cooled to −78 °C and a solution of cyclohexanecarbaldehyde (112 mg, 1.0 mmol) in THF (3 ml) was added. After being stirred for 20 min, the mixture was poured into 1 M HCl and the products were extracted with ethyl acetate (20 ml×3). Silica-gel column purification provided 1-cyclohexyl-1-pentanol (75 mg, 44%) and cyclohexylphenylmethanol (103 mg, 54%).

Pinacol Coupling Reaction of Benzaldehyde with Tributylmanganate. A suspension of manganese(II) chloride (151 mg, 1.2 mmol) in THF (10 ml) was sonicated for 10 min under argon atmosphere. Butylmagnesium bromide (1.0 M THF solution, 3.6 ml, 3.6 mmol) was added to the resulting suspension of MnCl$_2$ at 0 °C. The mixture was stirred for 20 min and then cooled to −78 °C. A THF solution of benzaldehyde (106 mg, 1.0 mmol) was added and the whole was stirred for 1 h at −78 °C. Extractive work up (1 M HCl, ethyl acetate) followed by silica gel column chromatography gave benzpinacol (62 mg, 58% yield). Spectral data of pinacol coupling products derived from 2,4,6-trimethylbenzaldehyde and acetophenone were identical with those reported in the literature.[16]

References

1) a) N. Krause and A. Gerold, *Angew. Chem., Int. Ed. Engl.*, **36**, 186 (1997); b) R. J. K. Taylor, "Organocopper Reagents, A Practical Approach," Oxford University Press, Oxford (1994); c) B. H. Lipshutz and S. Sengupta, *Org. React.*, **41**, 135 (1992); d) B. H. Lipshutz, in "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press, New York (1991), Vol. 1, Chap. 1.4, p. 107; e) B. H. Lipshutz, in "Encyclopedia of Inorganic Chemistry," ed by R. B. King, Wiley, New York (1994); f) Y. Yamamoto, *Angew. Chem., Int. Ed., Engl.*, **25**, 947 (1986); g) E. Nakamura, *Synlett*, **1991**, 539; h) P. Knochel and R. D. Singer, *Chem. Rev.*, **93**, 2117 (1993).

2) G. Cahiez and M. Alami, *Tetrahedron Lett.*, **27**, 539 (1986).

3) The related reactions of diorganozinc compounds and triorganozincates have been reported. a) J.-L. Luche, C. Petrier, J.-P. Lansard, and A. E. Greene, *J. Org. Chem.*, **48**, 3837 (1983); b) A. E. Greene, J.-P. Lansard, J.-L. Luche, and C. Petrier, *J. Org. Chem.*, **49**, 931 (1984); c) M. Isobe, S. Kondo, N. Nagasawa, and T. Goto, *Chem. Lett.*, **1977**, 679; d) D. Seebach and W. Langer, *Helv. Chim. Acta*, **62**, 1701 and 1710 (1979).

4) Mixed cuprate(I): W. H. Mandeville and G. M. Whitesides, *J. Org. Chem.*, **39**, 400 (1974); B. H. Lipshutz, R. S. Wilhelm, and J. A. Kozlowski, *J. Org. Chem.*, **49**, 3938 (1984). Mixed zincate(II): W. Tückmantel, K. Oshima, and H. Nozaki, *Chem. Ber.*, **119**, 1581 (1986).

5) K. Okada, K. Oshima, and K. Utimoto, *J. Am. Chem. Soc.*, **118**, 6076 (1996).

6) a) G. Cahiez, "Butylmanganese(II) Chloride and Related Reagents," in "Encyclopedia of Reagents for Organic Synthesis," ed by L. Paquette, Wiley, Chichester (1995), p. 925; b) G. Cahiez, "Manganese(II) Chloride," in "Encyclopedia of Reagents for Organic Synthesis," ed by L. Paquette, Wiley, Chichester (1995), p. 3227; c) G. Cahiez, *An. Quim.*, **91**, 561 (1995); d) E. J. Corey and G. H. Posner, *Tetrahedron Lett.*, **1970**, 315; e) G. Cahiez and J.-F. Normant, in "Modern Synthetic Methods 1983," ed by R. Scheffold, J. Wiley and Sons, Inc., Chichester (1983), Vol. 3, p. 173.

7) Exchange of alkyl groups between two different manganates could take place; thus in a mixture of 2 molar amounts of $\mathrm{R^1_3MnMgBr}$ and 1 molar amount of $\mathrm{R^2_3MnMgBr}$, the predominant species would be the mixed manganate, $\mathrm{R^1_2R^2MnMgBr}$ as in the case of organocuprate (B. H. Lipshutz, J. A. Kozlowski, and C. M. Breneman, *Tetrahedron Lett.*, **26**, 5911 (1985)). Indeed, the treatment of 2-cyclohexen-1-one (2.5 molar amounts) with the reagent, generated from 2 molar amounts of n-Bu$_3$MnMgBr and 1 molar of Me$_3$MnMgBr, afforded 3-butylcyclohexanone (45%) and 3-methylcyclohexanone (< 1%) along with bicyclic ketone **4** (25%).

8) The reaction of 2-cyclohexen-1-one with Me$_3$MnMgBr or $(n\text{-C}_6\text{H}_{13}\text{C}{\equiv}\text{C})_3\text{MnMgBr}$ afforded the corresponding 1,4-adduct in only < 5% or < 5% yield, respectively. In contrast, treatment of 2-cyclohexen-1-one with (Me$_3$SiCH$_2$)$_3$MnMgCl or (Me$_3$SiCH$_2$)$_2$Mn provided 1,4-addition product **7** (R. T. Taylor and J. G. Galloway, *J. Organomet. Chem.*, **220**, 295 (1981)) in 95 or 92% yield, respectively (Chart 1). Moreover, the reaction proceeded in the presence

of a catalytic amount of $MnCl_2$.

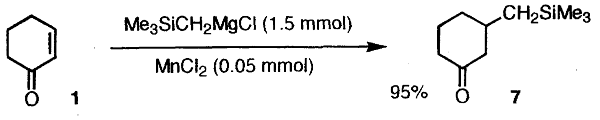


Chart 1.

9) The reaction of *n*-BuMnI with aldehydes and ketones has been reported. G. Cahiez and J. F. Normant, *Tetrahedron Lett.*, **1977**, 3383.

10) The reaction of cyclohexanecarbaldehyde with *n*-Bu_2CuLi at −78 °C gave the butylated adduct in 62% yield. Thus, manganese reagents seem to be more reactive than the corresponding cuprate(I) toward aldehydes.

11) Similar dependence of reactivity order on the substrates was observed in the addition reaction to aldehyde with mixed organocuprate. For instance, the methyl group, which is retained in the conjugate addition reaction, transfer as easily as a butyl group. Thus, treatment of cyclohexanecarbaldehyde with *n*-BuMeCuLi provided a mixture of butylated product (33%) and methylated one (27%).

12) The reaction at 0 °C for 1 h afforded butylcyclohexanol in 80% yield.

13) Recently we have found the third type reaction by manganates. Halogen–metal exchange reaction took place in the reaction of *gem*-dibromo compounds with triorganomanganates. R. Inoue, H. Shinokubo, and K. Oshima, *Tetrahedron Lett.*, **37**, 5377 (1996).

14) J. Nakao, R. Inoue, H. Shinokubo, and K. Oshima, *J. Org. Chem.*, **62**, 1910 (1997).

15) Although the relationship between different reaction mechanisms for these two types of reactions and different reactivity order are not clear at this stage, nucleophilicity of the corresponding anions could determine the reactivity order in the reaction of manganate(II) with cyclohexanecarbaldehyde. The stronger the nucleophilicity, the easier is the migration. In contrast, the reactivity order in the conjugate addition which might proceed via radical mechanism is much more difficult to explain. Studies on single electron transfer by means of trialkylmanganate(II) are underway.

16) A. Fürstner, R. Csuk, C. Rohrer, and H. Weidmann, *J. Chem. Soc., Perkin Trans. 1*, **1988**, 1729.