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Catalytic Radical Addition of Carbonyl Compounds to Alkenes by Mn(II)/Co(II)/O_2 System

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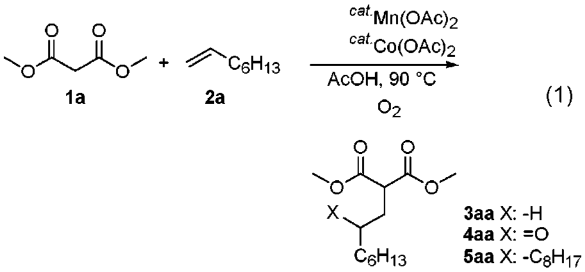
The radical addition of enolizable carbonyl compounds such as malonates and malononitrile to alkenes was successfully achieved through a catalytic process using the Mn(II)/Co(II)/O_2 system to afford the corresponding adducts in fair to good yields. Dimethyl malonate added to 1,5-cyclooctadiene to produce a fused bicycle compound.

The carbon−carbon bond-forming reaction through a radical process has attracted wide interest in synthetic organic chemistry, and the rapid development in this area made it possible for chemists to apply a variety of synthetic reactions.[1] It is known that a number of carbon−carbon bond-forming free-radical reactions are mediated by transition metals, and high oxidation state metal ions such as Mn(III), Ce(IV), Co(III), Ag(II), and Pb(IV) promote the addition of α-keto radicals derived from ketones to alkenes.[2] Among these metal oxidants, $Mn(OAc)_3$ is widely used as a powerful reagent for various types of organic synthesis,[3] but most reactions are carried out with the use of a large amount of a metal reagent except for a few methods mediated by $AgNO_3/Na_2S_2O_3$[4] and $Mn(OAc)_3/KMnO_4$[5] systems. Nowadays, from an environmental and practical point of view, organic synthesis using a stoichiometric amount of a metal reagent may be restricted to a small-scale reaction.

We have recently developed a catalytic radical addition of simple ketones to alkenes by the use of a novel redox system consisting of Mn(II)/Co(II)/O_2.[6] Thus, α-alkylated ketones, which are conventionally prepared by the reaction of enolates with alkyl halides, could be prepared by the radical addition of ketones to alkenes in the presence of catalytic amounts of Mn(II) (0.5 mol %) and Co(II) (0.1 mol %) under air or dioxygen as a terminal oxidant. This method can be applied to large-scale synthesis of various types of α-alkylated ketones. The Mn(II)/Co(II)/O_2 redox system may enable catalytic accesses to Mn(III)-promoted radical reactions, which are carried out by the use of a stoichiometric amount of Mn(III) reagents.

We have examined a catalytic radical addition of enolizable methylene compounds such as malonates and α-keto esters to alkenes using the Mn(II)/Co(II)/O_2 redox system.

The addition of dimethyl malonate (**1a**) to 1-octene (**2a**) was chosen as a model reaction and was carried out in the presence of a catalytic amount of $Mn(OAc)_2$ combined with $Co(OAc)_2$ in a mixed gas of O_2 and N_2 in acetic acid under various reaction conditions (eq 1 and Table 1).



(1)

The reaction of **1a** (30 mmol) with **2a** (2 mmol) in the presence of $Mn(OAc)_2$ (0.04 mmol) and $Co(OAc)_2$ (0.02 mmol) under a mixed gas of O_2/N_2 (0.1 atm/0.9 atm) in acetic acid (2 mL) at 90 °C for 3 h produced dimethyl octylmalonate (**3a**) (60%) and a diadduct, dimethyl 2-(2-hexyldecyl)malonate (**5aa**) (10%), as major products at 96% conversion of **2a** (Table 1, run 1). The reaction at 100 °C under these conditions gave almost the same results as that at 90 °C, but the yield of **3aa** considerably decreased in the reaction at 80 °C (Table 1, runs 2 and 3). The reaction in the absence of either $Mn(OAc)_2$ or $Co(OAc)_2$ led to **3aa** in poor yield (Table 1, runs 4 and 5). To know the influence of oxygen concentration on the present reaction, the reaction was examined under varying oxygen pressure (Table 1, runs 6−9). The reaction under 1 atm of O_2 gave **3aa** (43%) and dimethyl 2-(2-oxooctyl)malonate (**4aa**) (5%) along with a complex mixture of undesired oxygenated products (Table 1, run 6). The formation of the oxygenated product **4aa** is due to the trapping of O_2 by an adduct radical derived from **1a** and **2a** as discussed later. When the amount of Co-

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Table 1. Reaction of Dimethyl Malonate (1a) with 1-Octene (2a) by $Mn(OAc)_2$ and $Co(OAc)_2$ under Various Conditions[a]

run	$Mn(OAc)_2$ (mol %)	$Co(OAc)_2$ (mol %)	time (h)	convn[b] (%)	yield[c] (%)		
					3aa	**4aa**	**5aa**
1	2	1	3	96	60	1	10
2[d]	2	1	3	99	63	1	12
3[e]	2	1	3	78	39	1	12
4	2	-	2	20	3	<1	<1
5	-	1	2	5	n.d.	n.d.	n.d.
6[f]	2	1	2	98	43	5	5
7[g]	2	1	2	97	55	3	10
8[h]	2	1	2	82	44	1	12
9[i]	2	1	2	73	42	<1	14
10	2	0.5	2	80	43	1	10
11	1	1	2	93	54	2	9
12[d,j]	2	1	3	95	49	1	8
13[d,j,k]	2	1	3	100	87	<1	11

[a] Compound **2a** (2 mmol) was allowed to react with **1a** (30 mmol) under $N_2/O_2 = 0.9/0.1$ atm in the presence of $Mn(OAc)_2$ and $Co(OAc)_2$ in AcOH (2 mL) at 90 °C. [b] Conversion of **2a**. [c] Based on **2a** reacted. [d] 100 °C. [e] 80 °C. [f] O_2 (1 atm). [g] $N_2/O_2 = 0.5/0.5$ atm. [h] Air (1 atm). [i] $N_2/O_2 = 0.95/0.05$ atm. [j] Without AcOH. [k] **1a** (87 mmol) was used.

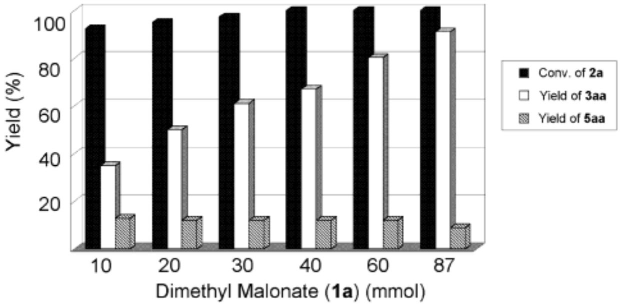


Figure 1. Effect of the amount of **1a**. Reaction conditions: **1a** (10−87 mmol), **2a** (2 mmol), $Mn(OAc)_2$ (2 mol %), $Co(OAc)_2$ (1 mol %), AcOH (2 mL), 100 °C, 3 h, $N_2/O_2 = 0.9/0.1$ atm.

$(OAc)_2$ or $Mn(OAc)_2$ was halved, the yield of **3aa** decreased to 43% or 54%, respectively (Table 1, runs 10 and 11). It is interesting to note that the present reaction could be successfully carried out without any solvent, when **1a** was used instead of a solvent, to form **3aa** in 87% yield (Table 1, run 13). After the reaction, unreacted **1a** was recovered in over 80% yield from a reaction mixture by distillation.

Figure 1 shows the influence of the ratio of **1a** to **2a** on the yield of **3aa** and **5aa**. The yield of the **3aa** increased with increasing the concentration of **1a** to **2a**. When alkene **2a** was allowed to react with excess **1a** (87 mmol), **2a** was completely converted into adducts **3aa** (91%) and **5aa** (9%).

Table 2 shows the reactions between several enolizable methylene compounds and alkenes by the Mn(II)/Co(II)/O_2 redox-couple under selected reaction conditions.

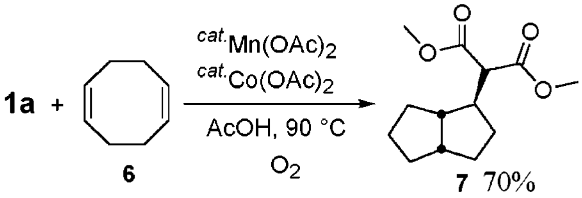
Compound **1a** reacted with some difficulty to methyl-substituted alkene, 2-methyl-1-heptene (**2b**), compared with that to the normal alkene **2a**, giving adduct **3ab** in slightly lower yield and several unidentified products were produced (Table 2, run 1). In general, the addition of an attacking radical to methyl-substituted alkene is known to inhibit the reaction owing to the steric hindrance. The reaction of **1a** with 2-norbornene (**2c**) afforded an adduct, **3ac**, in 80% yield (Table 2, run 2). Hydrolysis of the resulting **3ac** led to the corresponding dicarboxylic acid whose X-ray analysis indicated that **1a** approaches the exo direction of **2c** to give **3ac** having an exo configuration (Table 2, run 2, and Figure 2, Supporting Information). It is reported that the peroxide-initiated radical addition of aldehyde to **2c** takes place stereoselectively to form the corresponding exo adduct.[7]

When 1-octyne (**2d**) was used as the alkyne, about a 1:1 isomeric mixture of adduct **3ad** was obtained in 55% yield (Table 2, run 3). It was found that diethyl malonate (**1b**) adds smoothly to **2a** to form the corresponding adduct, **3ba**, in 80% (Table 2, run 4). We next examined the reaction of α-diketo compounds such as acetoacetic ester with **2a** (Table 2, run 5). Ethyl acetoacetate (**1c**) was less reactive than malonic esters **1a** and **1b**. The addition of α-acetyl-γ-butyrolactone (**1d**) to **2a** proceeded even in the presence of a very small amount of $Mn(OAc)_2$ (0.5 mol %) and $Co(OAc)_2$ (0.1 mol %) to form adduct **3da** in 60% yield (Table 2, run 6). Malononitrile (**1e**) was a sluggish substrate, but *n*-octyl malonitrile (**3ea**) was obtained in good yield (78%) by allowing it to react with **2a** using $Mn(OAc)_2$ (5 mol %) and $Co(OAc)_2$ (1 mol %) (Table 2, run 7).

A plausible reaction path of the present reaction of **1a** to **2a** is illustrated in Scheme 1.

In a previous paper,[6] we showed that Mn(II) can be continuously reoxidized to Mn(III) by the action of a Co(III)−dioxygen complex like a superoxocobalt(III) generated in situ from Co(II) and O_2.[8] The Mn(III) oxidizes **1a** to give a radical species (**A**) that readily adds to the alkene **2a** to form an adduct radical (**B**). The resulting radical intermediate **B** reacts with **1a**, O_2, or **2a** to lead to **3aa**, **4aa**, or **5aa**, respectively.

The reaction of **1a** with 1,5-cyclooctadiene (**6**) led to the formation of a fused product **7** (70%) via intramolecular radical cyclization (eq 2). The structure of **7** was found to be a cis-fused product by comparing its spectral data with those of literature values.[5] The formation of **7** was rationally explained by Scheme 2. An adduct radical (**C**) derived from **1a** and **6** undergoes intramolecular cyclization followed by hydrogen atom abstraction from the substrate affording the fused adduct **7**.



(2)

In summary, we have succeeded in the catalytic radical-addition of enolaziable compounds to alkenes by an Mn(II)/Co(II)/O_2 redox system to form the corresponding adducts in fair to good yields.

Experimental Section

General Procedure. ^1H and ^{13}C NMR spectra were measured at 270 and 67.5 MHz, respectively, in $CDCl_3$ with TMS as the internal standard. IR spectra were measured as films on NaCl plates. GLC analysis was performed with a flame ionization detector using a 1 mm × 30 m capillary column (OV-1). All starting materials were commercially available and used without any purification.

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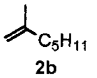
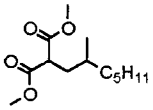
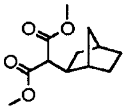
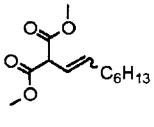
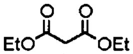
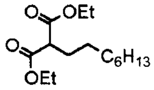
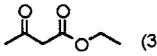
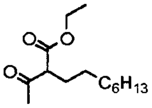
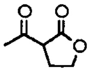
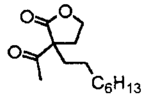
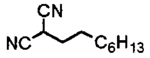
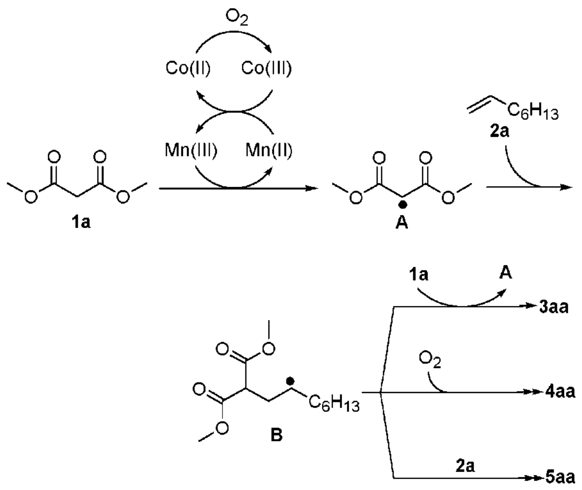
(8) Redox potentials of Mn(III)/Mn(II) (1.51 eV) and Co(III)/Co(II) (1.82 eV) in water were reported the following paper: Sheldon, R. A.; Kochi, J. K. *Oxid. Combust. Rev.* **1973**, *5*, 135.

Table 2. Addition of Various Enolizable Compounds to Alkenes[a]

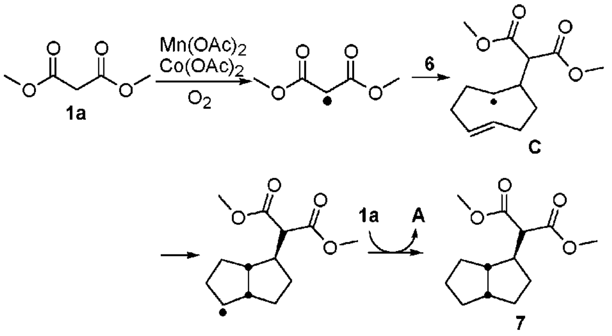
Run	Enolizable compounds	(mmol)	Alkenes	Product	Conv.(%)[b]	Yield (%)[c] 3	Yield (%)[c] 5
1[d,e]	**1a**	(87)	 **2b**		77	**3ab** 34	**5ab** 2
2[f]	**1a**	(87)	 **2c**		99	**3ac** 80	**5ac** 4
3[g]	**1a**	(87)	$\equiv$—C_6H_{13} **2d**		97	**3ad** 55 (E/Z = 1/1)	
4[d,h]	 **1b**	(87)	**2a**		98	**3ba** 80	**5ba** 11
5	 **1c**	(30)	**2a**		83	**3ca** 50	**5ca** 9
6	 **1d**	(30)	**2a**		83	**3da** 60	**5da** 10
7[d]	NC$\smallsmile$CN **1e**	(60)	**2a**		84	**3ea** 78	**5ea** trace

[a] Alkenes (2 mmol) were allowed to react with enolizable compounds in the presence of $Mn(OAc)_2$ (2 mol %) and $Co(OAc)_2$ (1 mol %) in AcOH (2 mL) at 90 °C for 5 h under N_2/O_2 = 0.9/0.1 atm. [b] Conversion of alkenes. [c] Based on alkenes used. [d] 100 °C. [e] 8 h. [f] See Figure 2. [g] 50 °C, 48 h. [h] 3 h.

Scheme 1



Scheme 2



General Procedure for the Reaction of 1a and 2a. To a solution of **1a** (30 mmol), $Mn(OAc)_2$ (2 mol %), and $Co(OAc)_2$ (1 mol %) in AcOH (2 mL) in a two-necked flask equipped with a balloon filled with an appropriate concentration of O_2 was added **2a** (2 mmol), and the mixture was stirred at 90 °C for 3 h. After evaporation of AcOH, the product **3aa** was isolated by flash chromatography on silica gel (*n*-hexane–AcOEt = 5:1).

Compounds **3aa**,[9] **3ad**,[10] **3ba**,[11] **3ca**,[12] and **3ea**[13] were reported previously.

Dimethyl 2-(2-hexyldecyl)malonate (5aa): ^1H NMR δ 0.85–1.25 (m, 34H), 1.86 (t, 2H, J = 8.3 Hz), 3.70 (s, 3H), 3.73

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(s, 3H); ^{13}C NMR δ 13.8, 22.3, 23.6, 25.9, 28.8, 28.9, 29.2, 29.3, 29.5, 29.6, 31.5, 32.0, 32.8, 35.1, 49.4, 51.8, 51.9, 52.0, 52.1, 57.3, 169.7, 172.0; IR 2924, 1738, 1462, 1229, 1173 cm^{-1}; MS (70 eV) *m*/*e* = 55, 132, 145, 179, 307.

Dimethyl 2-(2-methylheptyl)malonate (3ab): ^{1}H NMR δ 0.86−0.89 (m, 6H), 1.13−1.28 (m, 9H), 1.64−1.71 (m, 1H) 1.92−2.03 (m, 1H), 3.47 (t, 1H, J = 6.8 Hz), 3.73 (s, 6H); ^{13}C NMR δ 14.1, 19.2, 22.6, 30.8, 32.0, 35.9, 36.6, 49.7, 49.8, 52.3, 52.4, 52.5, 169.9, 170.0; IR 2925, 1738, 1434, 1199, 1154, 1011 cm^{-1}; MS (70 eV) *m*/*e* = 55, 132, 145, 173.

Dimethyl 2-(2-norbornyl)malonate (3ac): ^{1}H NMR δ 1.07−1.29 (m, 6H), 1.48−1.56 (m, 3H), 2.01 (br, 1H), 2.16−2.33 (m, 2H), 3.13 (d, 1H, J = 11.7 Hz), 3.70 (s, 3H), 3.74 (s, 3H); ^{13}C NMR δ 28.2, 29.5, 35.2, 35.9, 36.5, 39.5, 41.7, 52.2, 52.2, 57.2, 168.9, 169.2; IR 2953, 1756, 1436, 1220 cm^{-1}; MS (70 eV) *m*/*e* = 59, 95, 132, 157, 195.

2-(2-Norbornyl)malonic acid: ^{1}H NMR (CD_3OD) δ 1.12−1.36 (m, 5H), 1.44−1.62 (m, 3H), 2.05−2.14 (m, 2H), 2.99 (br, 1H), 3.02 (d, 1H, J = 11.5 Hz); ^{13}C NMR (CD_3OD) δ 29.5, 30.8, 36.1, 37.3, 38.0, 41.0, 43.1, 59.0, 172.2, 172.6; IR 2950, 1693, 1419, 1240 cm^{-1}.

α-Acetyl-α-octyl-γ-butyrolactone (3da): ^{1}H NMR δ 0.87 (t, 3H, J = 7.3 Hz), 1.18−1.25 (m, 12H), 1.77 (dt, 1H, J = 4.7, 12.0 Hz), 1.98−2.06 (m, 1H), 2.09−2.17 (m, 1H), 2.32 (s, 3H), 2.90−2.96 (m, 1H), 4.13 (dq, 1H, J = 10.9, 9.1 Hz), 4.29 (dt, 1H, J = 2.9, 8.7 Hz); ^{13}C NMR δ 14.2, 22.8, 25.2, 25.6, 29.3, 29.3, 29.4, 29.8, 32.0, 35.3, 61.8, 66.4, 175.8, 202.7; IR 2925, 1769, 1465, 1359, 1026 cm^{-1}; MS (70 eV) *m*/*e* = 43, 55, 81, 128, 198.

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Supporting Information Available: Copies of ^{13}C and ^{1}H NMR and IR spectra for all of the products and Figure 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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