

Addition of Carboxyalkyl Radicals to Alkenes through a Catalytic Process, Using a Mn(II)/Co(II)/O₂ Redox System

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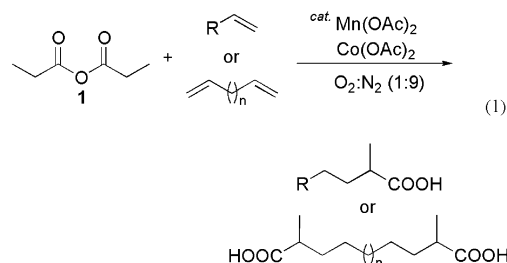
A novel strategy for production of mono- and dicarboxylic acids by the addition of carboxyalkyl radicals to alkenes and dienes, respectively, was successfully developed through a catalytic process with use of Mn(II)/Co(II)/O₂ system. Thus, a variety of carboxylic acids were prepared by the reaction of alkenes and dienes with acid anhydrides in the presence of a very small amount of Mn(OAc)₂ (0.5 mol %) and Co(OAc)₂ (0.1 mol %) under dilute dioxygen.

Carbon–carbon bond-forming reactions through carbon radical generation by the action of higher valence transition metal ions such as Mn(III), Co(III), Cu(II), Fe(III), Ag(II), Pb(IV), Ce(IV), etc., are used as a powerful means in organic synthesis.¹ Among many metal oxidants, Mn(II) is often used as a unique oxidant for a variety of synthetic reactions. Pioneering work in this chemistry has been done by Bush and Finkbeiner² and Heiba and Dessau,³ who reported that the oxidative addition of acetic acid to alkenes in the presence of Mn(OAc)₃ produces γ -lactones. In this reaction, acetic acid is oxidized by Mn(OAc)₃ to a carboxymethyl radical, which adds to an alkene to form an adduct radical. Subsequent further oxidation of the adduct radical by additional Mn(OAc)₃ affords a carbocation whose intramolecular cyclization gives a γ -lactone. Although the Mn(III)-mediated reactions are very attractive as a synthetic tool, a serious drawback of this method is that a large excess of Mn(III) ions must be used to complete the reactions in satisfactory yields. Therefore, if the Mn(III)-promoted free-radical reactions can be carried out via a catalytic process of the metal ions, the importance of the reactions would vastly increase from the synthetic and environmental viewpoints.

Recently, we have succeeded in catalytic free-radical addition of ketones to alkenes using a Mn(II)/Co(II)/O₂ redox system. Thus, α -keto radicals derived from aliphatic and cyclic ketones added to alkenes such as 1-oc-

tene in the presence of very small amounts of Mn(OAc)₂ (0.5 mol %) and Co(OAc)₂ (0.1 mol %) under atmospheric dioxygen (1 atm) give the corresponding α -alkylated ketones in fair to good yields.⁴ The application of this system to the reaction of enolizable carbonyl compounds such as malonates with alkenes led to adducts in which alkyl groups are incorporated to the α -position of malonates.⁵

In this paper, we wish to report a novel catalytic method for the synthesis of mono- and dicarboxylic acids by the addition of carboxyalkyl radicals, generated in situ from acid anhydrides, using a Mn(II)/Co(II)/O₂ redox couple, to alkenes (eq 1).



The reaction of propionic anhydride (**1**) with 1-decene (**2**) was chosen as a model reaction and was carried out under various conditions to confirm optimum reaction conditions (Table 1).

2 (1 mmol) was allowed to react in **1** (60 mmol) without solvent in the presence of Mn(OAc)₂ (5 μ mol, 0.5 mol %) and Co(OAc)₂ (1 μ mol, 0.1 mol %) under a mixed gas of O₂ (0.1 atm) and N₂ (0.9 atm) at 130 °C for 5 h followed by hydrolysis with aqueous sulfuric acid to give 2-methyldodecanoic acid (**3**) in 90% yield (Run 1). This is the successful carboxyalkyl radical addition to alkenes through a catalytic process. When the amount of **1** decreased to 30 and 15 equiv, the yield of **3** decreased to 86% and 74%

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TABLE 1. Reaction of Propionic Anhydride (**1**) with 1-Decene (**2**) Catalyzed by Mn(OAc)₂/Co(OAc)₂/O₂ under Various Conditions^a

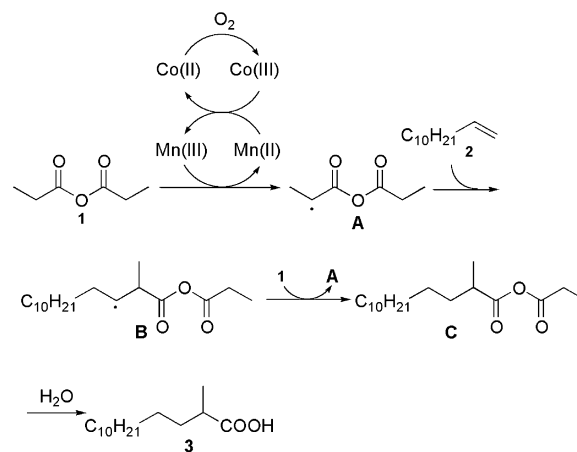
run	1 (mmol)	solvent/(mL)	temp.(°C)	conv (%)	3 (%) ^b
1	60	—	130	>99	90
2	30	—	130	>99	86
3	15	—	130	>99	74
4 ^c	30	—	130	>99	83
5 ^d	30	—	130	>99	70
6 ^e	30	—	100	10	—
7 ^{e,f}	30	—	100	96	80
8	30	EtCOOH/2	130	91	71
9	15	EtCOOH/2	130	78	49
10	30	MeCOOH/2	130	70	37 ^g

^a 1-Decene (**2**) (1 mmol) was reacted with propionic anhydride (**1**, 15–60 mmol) in the presence of Mn(OAc)₂ (5 μmol) and Co(OAc)₂ (1 μmol) under 0.1 atm of O₂ and 0.9 atm of N₂ at 130 °C for 5 h. ^b Based on **1** used. ^c The reaction was run under air. ^d The reaction was run under 0.5 atm of O₂ and 0.5 atm of N₂. ^e The reaction was run at 100 °C. ^f Mn(OAc)₂ (50 μmol) and Co(OAc)₂ (20 μmol) were used. ^g Dodecanoic acid (6%) was obtained.

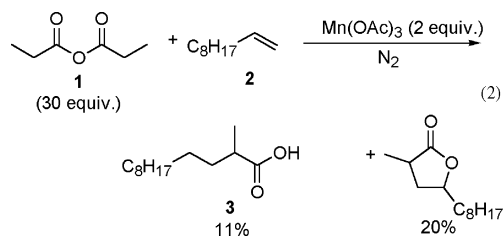
yields, respectively (Runs 2 and 3). The reaction under air led to **3** in 83% yield (Run 4). However, the reaction under a pressure of 0.5 atm of O₂ and 0.5 atm of N₂ resulted in considerable decrease of **3**, owing to the formation of unidentified polymeric products (Run 5). Although the addition was difficult at 100 °C under these conditions, **3** was obtained in 80% yield when Mn(OAc)₂ (50 μmol, 5 mol %) and Co(OAc)₂ (20 μmol, 2 mol %) were used (Runs 6 and 7). No coupling product was obtained when propionic acid was employed in place of propionic anhydride **1** (Run 8). It is interesting to note that the reaction in the presence of acetic acid produced **3** together with a small amount (6%) of dodecanoic acid (**4**) (Run 10). Since the reaction of **2** with acetic acid did not take place under these conditions, acetic anhydride (**5**), which is thought to be generated by the exchange reaction between acetic acid and **1** during the reaction course, reacted with **2** to form **4**.

It is well-known that a Co(II) species reacts with molecular oxygen to give a peroxocobalt(III) and/or superoxocobalt(III) species,⁶ and the resulting cobalt(III)–dioxygen complexes oxidize the Mn(II) to Mn(III), and then the Mn(III) oxidizes **1** to a carboxyalkyl radical. A plausible reaction path for the present reaction is illustrated as Scheme 1.

The reaction is initiated by the generation of Co(III)–dioxygen complexes from Co(II) and O₂, and the Mn(II) is oxidized to Mn(III) by the Co(III)–dioxygen complexes formed. Subsequently, **1** undergoes one-electron oxidation by Mn(III) to give a carboxyethyl radical (**A**), which then adds to alkene **2** to lead to an adduct radical (**B**). The radical **B** abstracts a hydrogen atom from **1** or another hydrogen donor to form an adduct (**C**) that then undergoes hydrolysis to give **3**. The formation of intermediate **C** was confirmed by the GC-MS spectrum. The **C** was found to be easily hydrolyzed into **3** under these conditions. Although the reaction seems to proceed through a chain process, the chain length of the reaction may be short.

SCHEME 1

The reaction with a stoichiometric amount of Mn(OAc)₃ in place of the Mn(II)/Co(II)/O₂ redox couple afforded **3** (11%) and 3-octyl-γ-butyrolactone (20%), which is formed through the well-known one-electron oxidation of the adduct radical by Mn(OAc)₃ followed by the intramolecular cyclization (eq 2).³


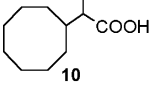
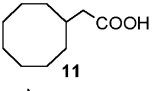

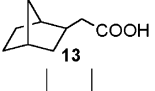

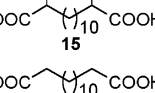
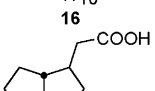

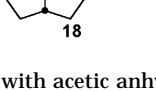


On the basis of these results, various alkenes and dienes were allowed to react with **1** and **5** in the presence of catalytic amounts of Mn(OAc)₂ and Co(OAc)₂ under dilute oxygen at 130 °C for 5 h (Table 2).

The reaction of **5** with **2** without any solvent afforded **4** in moderate yield (56%), but the same reaction in acetic acid led to **4** in good yield (80%) (Runs 2 and 3). **5** must be used in excess to obtain the adduct **4** in high yield, probably because the generation of a carboxymethyl radical from **5** is more difficult than that of a carboxyethyl radical from **1** by the Mn(III) ion, since the oxidation of the methylene group of **1** takes place more easily than that of the methyl group of **5**. 1-Octene (**6**) reacted with **1** and **5** to produce 2-methyldecanoic acid (**7**) (77%) and decanoic acid (**8**) (74%), respectively (Runs 4 and 5). Similarly, a cyclic alkene like cyclooctene (**9**) reacted with **1** and **5** to give the corresponding adducts, 2-cyclooctylpropionic acid (**10**) (62%) and cyclooctylacetic acid (**11**) (69%), respectively (Runs 6 and 7). Under these conditions, norbornene (**12**) afforded 2-norbornylacetic acid (**13**) in high yield (91%) (Run 8). It is noteworthy that **1** reacted with 1,9-decadiene (**14**) to lead to dicarboxylic acid, 2,13-dimethyltetradecanedionic acid (**10**), in fair yield (60%) (Run 9). This reaction provides a new simple catalytic route to α,ω-dicarboxylic acids which are difficult to prepare by conventional methods. However, the reaction of **5** with **14** was somewhat difficult and mono- and dicarboxylic acids were formed in low yields (Run 10). 1,5-Cyclooctadiene (**17**) afforded a fused carboxylic acid (**18**) (62%) rather than dicarboxylic acid (Run 11).

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TABLE 2. Reaction of Propionic Anhydride (1) and Acetic Anhydride (5) with Various Alkenes and Dienes Catalyzed by Mn(OAc)₂/Co(OAc)₂/O₂^a

Run	substrate	acid anhydride (mmol)	conv. (%) ^b	product	yield (%)
1	2	1 (30)	99	3	86
2	2	5 (150)	80	C ₁₁ H ₂₃ COOH 4	56
3 ^c	2	5 (150)	98	4	80
4	C ₆ H ₁₃ 6	1 (30)	99	C ₆ H ₁₃ 7	77
5 ^c	6	5 (150)	99	C ₉ H ₁₉ COOH 8	74
6		1 (30)	100		62
7 ^c	9	5 (150)	100		69
8 ^c		5 (150)	100		91
9		1 (60)	100		60
10 ^c	14	5 (150)	89		8 ^d
11 ^c		5 (150)	100		62

^a Substrate (1 mmol) was reacted with acetic anhydride (5) or propionic anhydride (1) in the presence of Mn(OAc)₂ (5 μmol) and Co(OAc)₂ (1 μmol) under 0.1 atm of O₂ and 0.9 atm of N₂ at 130 °C for 5 h. ^b Based on 1 or 5 used. ^c AcOH (2.5 mL) was used as a solvent. ^d Dodec-11-enoic acid (18%) was obtained.

This shows that intramolecular cyclization of the adduct radical takes place very fast compared with its coupling with the carboxymethyl radical. A similar fused product is obtained in the reaction of dimethyl malonate with 1,5-cyclooctadiene.⁷ The present reaction did not take place when alkenes bearing electron-withdrawing groups such

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as acrylates and acrylonitrile were employed, because carboxyalkyl radicals which are electrophilic in nature are undesirable for electron-poor alkenes.

In conclusion, we have developed a novel catalytic route to carboxylic acids from alkenes or dienes and acid anhydrides by using Mn(II)/Co(II)/O₂ as a redox couple.

Experimental Section

Starting materials and catalysts were purchased from commercial sources and used without further treatment. The products were isolated as their ester forms after the esterification of the products with MeOH under acidic conditions, and yields were estimated from the peak areas based on the internal standard technique by using GC. GC analysis was performed with a flame ionization detector, using a 0.2 mm × 30 m capillary column (OV-17). ¹H and ¹³C NMR spectra were measured at 400 and 100 MHz, respectively, in chloroform-*d* with Me₄Si as the internal standard. Infrared (IR) spectra were measured with NaCl or KBr pellets. GC-MS were obtained at an ionization energy of 70 eV. The products **3**,⁸ **7**,⁹ **10**,¹⁰ **11**,¹¹ **15**,¹² and **18**¹³ are known compounds, and **4**, **8**, **13**, and **16** are commercially available.

Procedure for Reaction of 1 with 2 under Dioxygen Atmosphere. To a solution of **1** (60 mmol), Mn(OAc)₂ (5 μmol, 0.5 mol %) and **X** (1 μmol, 0.1 mol %) in a two-necked flask equipped with a balloon filled with an appropriate concentration of O₂ was added **2** (1 mmol), and the mixture was stirred at 130 °C for 5 h. After the reaction, products were subjected to GC and GC-MS analyses.

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Supporting Information Available: Experimental data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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