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Selective Oxidation of Acetophenones Bearing Various Functional Groups to Benzoic Acid Derivatives with Molecular Oxygen

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Abstract: Acetophenones substituted by alkyl, alkoxy, acetoxy, and halogen groups were selectively oxidized with molecular oxygen to the corresponding benzoic acids by using the *N*,*N*′,*N*″-trihydroxyisocyanuric acid (THICA)/cobalt(II) acetate [$Co(OAc)_2$] and THICA/$Co(OAc)_2$/manganese(II) acetate [$Mn(OAc)_2$]. For example, 4-methylacetophenone was selectively oxidized with molecular oxygen to 4-acetylbenzoic acid (85%) by THICA/$Co(OAc)_2$ and to 4-methylbenzoic acid (93%) by $Mn(OAc)_2$, while terephthalic acid was obtained in 93% with the THICA/$Co(OAc)_2$/$Mn(OAc)_2$ catalytic system. It is interesting that the acetyl group on the aromatic ring is efficiently converted by a very small amount of $Mn(OAc)_2$ to the corresponding carboxylic acid, and that the present method provides a versatile route to acetylbenzoic acids which are difficult to prepare by conventional methods.

Keywords: acetophenones; aerobic oxidation; benzoic acids; *N*-hydroxyphthalimide; *N*,*N*′,*N*″-trihydroxyisocyanuric acid

Introduction

Benzoic acids are very important raw materials for the synthesis of preservatives, dyes, synthetic resins, etc. There have been a variety of methods for the synthesis of benzoic acids. Among them, the transition metal-catalyzed carbonylation of aryl halides in the presence of a nucleophile like water is often used as an important methodology for the synthesis of benzoic acids. In particular, Pd complexes have been widely used for this purpose.[1] Quite recently, Boyarskii et al. have prepared *p*-acetylbenzoic acid by carbonylation of *p*-bromoacetophenone with CO in the presence of $Co_2(CO)_8$.[2] In order to avoid the use of toxic carbon monoxide, Cacchi et al. obtained various benzoic acids by the Pd-catalyzed hydroxycarbonylation of aryl halides or triflates in the presence of acetic anhydride and lithium formate.[3] Silvani et al. used $Mo(CO)_6$ as a commercially available stable CO source for the Pd-catalyzed hydroxycarbonylation of aryl triflates.[4] On the other hand, benzoic acids are also prepared by the oxidation of alkylbenzenes with powerful oxidants such as $KMnO_4$[5] and ozone.[6] However, it is difficult to selectively oxidize methylbenzenes bearing several functional groups by these oxidants. The conversion of alkyl aryl ketones to aromatic carboxylic acids with molecular oxygen by the use of $Mn(NO_3)_2$ and $Co(NO_3)_2$ has been reported by Minisci et al.[7] The simplest method is thought to be the direct aerobic oxidation of methylbenzenes, exemplified by the conversion of toluene to benzoic acid or *p*-xylene to terephthalic acid by using a Co catalyst or a Co/Mn/Br system, respectively.[8]

Although there have been several approaches for preparing substituted benzoic acids, a new selective route to various substituted benzoic acids from substituted benzenes is thought to be still important. In particular, a method for the preparation of acetylbenzoic acids is important, since the preparation of these compounds is not an easy task.[9] In this paper, we wish to report a new selective method for the synthesis of benzoic acid derivatives by the aerobic oxidation of aromatic compounds bearing an acyl group by a catalytic system consisting of $Mn(OAc)_2$, *N*,*N*′,*N*″-trihydroxyisocyanuric acid (THICA)/$Co(OAc)_2$, or THICA/$Co(OAc)_2$/$Mn(OAc)_2$.[10] Fortunately, acetophenones are easily available from commercially sources or are easily prepared by the *N*-hydroxyphthal-

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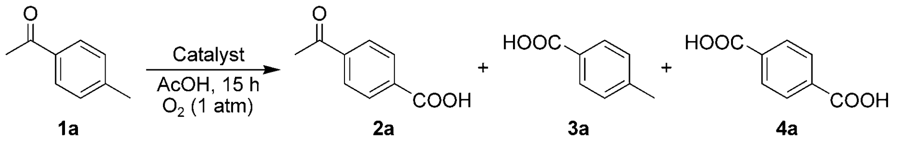
imide (NHPI)-catalyzed aerobic oxidation of alkylbenzenes.[11]

Results and Discussion

The oxidation of 4-methylacetophenone (**1a**) with O_2 (1 atm) was chosen as a model reaction and was carried out by the use of several catalysts under various conditions (Table 1).

The oxidation of **1a** was conducted under O_2 (1 atm) in the presence of a catalytic amount of NHPI in AcOH at 100 °C for 15 h. In this reaction, the methyl group was oxidized in preference to the acetyl group to give 4-acetylbenzoic acid (**2a**) selectively, although the conversion of **1a** was low (entry 1). Interestingly, the same oxidation by $Mn(OAc)_2$ (0.5 mol%) under these conditions afforded *p*-toluic acid (**3a**) in which the acetyl group is selectively oxidized in 93% yield (82% isolated yield) (entry 2). The oxidation proceeded smoothly to give **2a** in high yield (90%) even when the amount of $Mn(OAc)_2$ was halved (entry 3). However, no oxidation was induced by $Co(OAc)_2$ (0.5 mol%) (entry 4). It is very attractive to note that $Mn(OAc)_2$ catalyzed the oxidation of the acetyl group with O_2 in high selectivity even in the presence of the methyl group. Oxidation by the $Co(OAc)_2/Mn(OAc)_2$ system gave almost the same result as that by $Mn(OAc)_2$ alone (entry 5), while the oxidation by $Mn(OAc)_2$ in the presence of NHPI produced selectively **2a** rather than **3a** (entry 6). This shows that the oxidation of the methyl group with O_2 by NHPI was accelerated by the addition of $Mn(OAc)_2$. Similar phenomena were also observed in the oxidation by $Co(OAc)_2$ in the presence of NHPI (entry 7). On the other hand, the reaction was found to be markedly accelerated by the NHPI/$Co(OAc)_2$/$Mn(OAc)_2$ catalytic system, leading to terephthalic acid (**4a**) (52%) and **3a** (35%) as major products (entry 8). Oxidation results using the NHPI system at 120 °C were similar to those at 100 °C (entries 9 and 10). Previously, we showed that THICA possesses a higher oxidizing ability than NHPI for the aerobic oxidation of polymethylbenzenes.[10] Therefore, THICA was used in place of NHPI (entries 11–15). As expected, the oxidation of **1a** by THICA/$Co(OAc)_2$ afforded selectively **2a** in good yield (85%) (entry 11). When the amount of the THICA/$Co(OAc)_2$ was halved, **2a** was formed still in substantial yield (77%) (entry 12). In a similar way as the reaction using the NHPI/Mn-

Table 1. Oxidation of 4-mthylacetophenone (**1a**).[a]



Entry	Catalyst	Temperature [°C]	Conversion [%]	Yield [%][b]		
				2a	**3a**	**4a**
1	NHPI	100	16	12	1	nd[c]
2	$Mn(OAc)_2$	100	99	nd[c]	93 (82)	4
3[c]	$Mn(OAc)_2$	100	99	nd[c]	90	6
4	$Co(OAc)_2$	100	2	trace	2	nd[c]
5	$Co(OAc)_2/Mn(OAc)_2$	100	98	nd	91	3
6	NHPI/$Mn(OAc)_2$	100	62	59	1	2
7	NHPI/$Co(OAc)_2$	100	43	33	2	4
8	NHPI/$Co(OAc)_2/Mn(OAc)_2$	100	99	4	35	52
9	NHPI/$Co(OAc)_2$	120	62	56	trace	2
10	NHPI/$Co(OAc)_2/Mn(OAc)_2$	120	99	3	55	38
11	THICA/$Co(OAc)_2$	120	92	85 (72)	nd[c]	7
12[d]	THICA/$Co(OAc)_2$	120	82	77	trace	4
13	THICA/$Mn(OAc)_2$	120	26	24	2	trace
14	THICA/$Co(OAc)_2/Mn(OAc)_2$	120	99	5	2	93 (91)
15[e]	THICA/$Co(OAc)_2/Mn(OAc)_2$	120	99	5	3	91

[a] **1a** (3 mmol) was allowed to react in the presence of catalysts [NHPI (10 mol%) or THICA (5 mol%), $Mn(OAc)_2$ (0.5 mol%) and/or $Co(OAc)_2$ (0.5 mol%)] under O_2 (1 atm) in AcOH (3 mL) at 100–120 °C for 15 h.

[b] Yields based on GC analysis after the esterification with MeOH (20 mL) and H_2SO_4 (50 mg) at 100 °C for 24 h. Numbers in parentheses show isolated yields.

[c] Not detected.

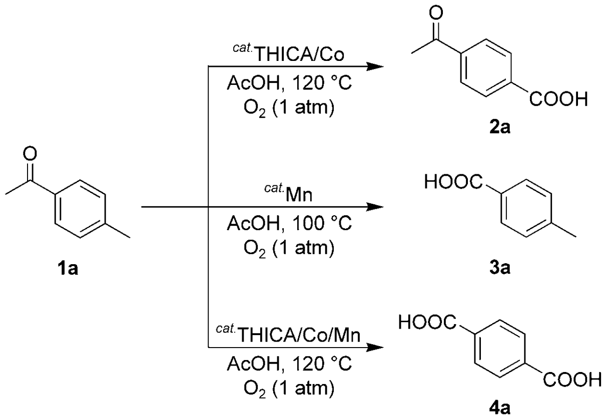
[d] THICA (2.5 mol%)/$Co(OAc)_2$ (0.25 mol%) was used.

[e] THICA (2.5 mol%)/$Co(OAc)_2$ (0.25 mol%)/$Mn(OAc)_2$ (0.25 mol%) was used.

$(OAc)_2$ system, **1a** was oxidized to **2a** in low conversion (24%) by the THICA/$Mn(OAc)_2$ system (entry 13). However, **1a** was converted into **4a** in high yield (93%) by adding a small amount of $Co(OAc)_2$ to the THICA/$Mn(OAc)_2$ system (entry 14). Even by the use of a half amount of the THICA/$Co(OAc)_2$/$Mn(OAc)_2$ system, **1a** was converted to **4a** in almost the same yield (91%) (entry 15).

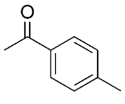
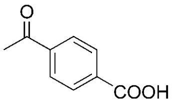
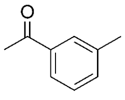
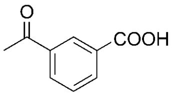
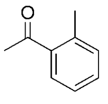
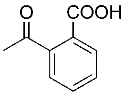
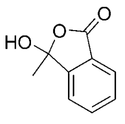
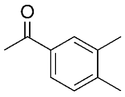
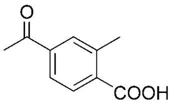
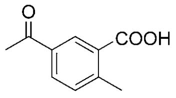
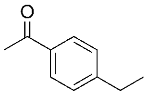
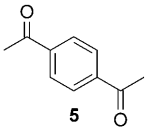
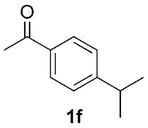
By selecting the combination of THICA, $Co(OAc)_2$, and $Mn(OAc)_2$, we now provide a new selective route to different substituted benzoic acids like **2a**, **3a**, and **4a** from **1a** as shown in Scheme 1.

Table 2 shows the oxidation results of various acetophenones having alkyl substituents with O_2 (1 atm) by THICA/$Co(OAc)_2$ in acetic acid at 120 °C for 15 h. It is attractive that the THICA/$Co(OAc)_2$ system



Scheme 1. Selective oxidation of 4-methylacetophenone (**1a**).

Table 2. Oxidation of the alkyl group of acetophenones (**1**) with O_2.[a]

Entry	Substrate	Conversion [%]	Product	Yield [%][b]
1	 **1a**	92	 **2a**	85 (72)
2	 **1b**	98	 **2b**	88 (72)
3	 **1c**	74	 **2c** +  **2c'**	(66)[c]; (31)[d]
4[e]	 **1d**	91	 **2d** +  **2d'**	83 (75)[f]
5	 **1e**	91	 **5**	73; 87 (73)[g]
6	 **1f**	62	**5**	45 (36)[h]

[a] **1** (3 mmol) was allowed to react in the presence of THICA (5 mol%) and $Co(OAc)_2$ (0.5 mol%) under O_2 (1 atm) in AcOH (3 mL) at 120 °C for 15 h.

[b] Yields based on GC analysis after the esterification with MeOH (20 mL) and H_2SO_4 (50 mg) at 100 °C for 24 h. Numbers in parentheses show isolated yields.

[c] **2c** and **2c′** were obtained as an equilibrium mixture.

[d] NHPI (10 mol%) was used in place of THICA (5 mol%) at 100 °C.

[e] For 6 h.

[f] **2d**:**2d′** = 52:48 (^{1}H NMR analysis).

[g] NHPI (10 mol%) was used in place of THICA (5 mol%) in CH_3CN (3 mL) at 75 °C.

[h] **2a** (14%) was obtained along with **5**.

prompted the oxidation of the alkyl groups on the acetophenones in high selectivity in preference to the acetyl groups which are easily oxidized by $Mn(OAc)_2$ under these conditions as mentioned later. The reactivities of the three regioisomeric methylacetophenones, **1a**–**1c**, were compared with each other. The reactivities of 4- and 3-methylacetophenones (**1a** and **1b**) were found to be similar, giving 4- and 3-acetylbenzoic acids (**2a** and **2b**) in 85% and 88%, respectively (entries 1 and 2). However, 2-methylacetophenone (**1c**) was a reluctant substrate for the oxidation and afforded a mixture of 2-acetylbenzoic acid (**2c**) and 3-hydroxy-3-methylphthalide **2c′** which exist as an equilibrium mixture in 66% isolated yield (entry 3). From the ^{1}H NMR spectrum of the mixture, the ratio of **2c** to **2c′** was estimated to 1:9.[12] From 3,4-dimethylacetophenone (**1d**), a mixture of 4-acetyl-2-methylbenzoic acid (**2d**) and 3-acetyl-6-methylbenzoic acid

Table 3. Oxidation of the acetyl group of acetophenones (**1**) with O_2.[a]

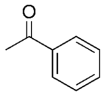
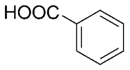
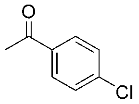
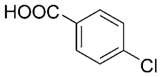
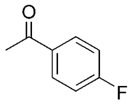
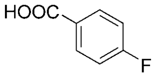
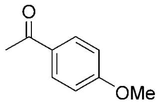
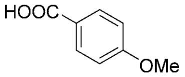
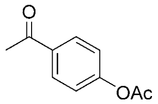
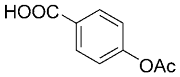
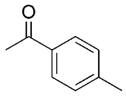
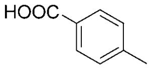
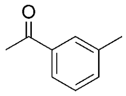
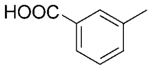
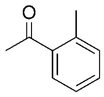
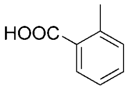
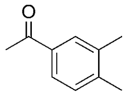
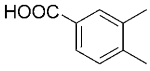
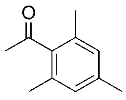
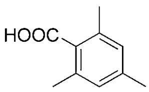
Entry	Substrate	Conversion [%]	Product	Yield [%][b]
1	 **1g**	99	 **3g**	97 (93)
2	 **1h**	98	 **3h**	96 (90)
3[c]	 **1i**	98	 **3i**	96 (88)
4[c]	 **1j**	96	 **3j**	93 (84)
5[c]	 **1k**	97	 **3k**	86 (74)
6	 **1a**	99	 **3a**	93 (82)
7	 **1b**	99	 **3b**	88 (75)
8	 **1c**	96	 **3c**	85 (81)
9	 **1d**	99	 **3d**	95 (87)
10[c]	 **1l**	98	 **3l**	82 (78)

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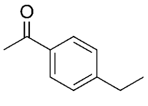
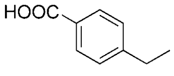
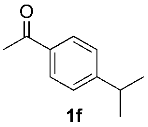
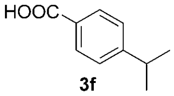
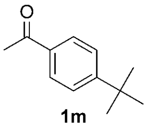
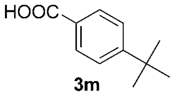
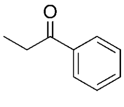
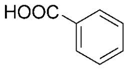
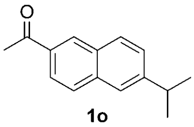
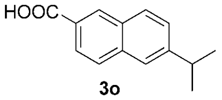
Table 3. (Continued)

Entry	Substrate	Conversion [%]	Product	Yield [%][b]
11[c,d]	 **1e**	82	 **3e**	64 (63)[e]
12[c,d]	 **1f**	72	 **3f**	50 (47)[f]
13	 **1m**	99	 **3m**	99 (94)
14	 **1n**	90	 **3g**	88 (80)
15[c]	 **1o**	99	 **3o**	93 (92)

[a] **1** (3 mmol) was allowed to react in the presence of $Mn(OAc)_2$ (0.5 mol%) under O_2 (1 atm) in AcOH (3 mL) at 100 °C for 15 h.

[b] Yields based on GC analysis after the esterification with MeOH (20 mL) and H_2SO_4 (50 mg) at 100 °C for 24 h. Numbers in parentheses show isolated yields.

[c] $Co(OAc)_2$ (0.5 mol%) was added.

[d] For 6 h.

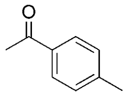
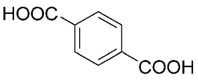
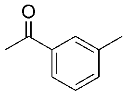
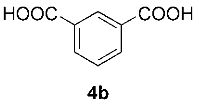
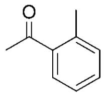
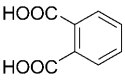
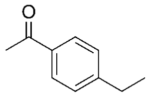
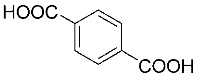
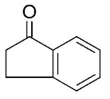
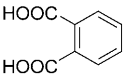
[e] **2a** (5%) and **4a** (9%) were obtained as by-products.

[f] **2a** (8%) and **4a** (6%) were formed along with **3f**.

(**2d′**) was obtained in 83% total yield (entry 4). It is important that the present method provides a very simple route to acetylbenzoic acids, in particular, 3-acetylbenzoic acid **2b**, since the preparation of **2b** calls for several stepwise reactions. For instance, **2b** is prepared from acetophenone by nitration, reduction, diazotation, reaction with cuprous cyanide and hydrolysis.[9] In addition, Camps reported a method for **2b** based on the Claisen condensation of isophthalic acid with methylene carboxylic esters.[13] The oxidation of 4-ethylacetophenone (**1e**) and 4-isopropylacetophenone (**1f**) gave rise to 1,4-diacetylbenzene (**5**) in 87% and 45% yields, respectively, under optimized reaction conditions (entries 5 and 6).

We next tried the oxidation of various acetophenones with O_2 (1 atm) by $Mn(OAc)_2$ in acetic acid at 100 °C for 15 h (Table 3). Fortunately, the $Mn(OAc)_2$-catalyzed oxidation of acetophenones proceeded very selectively to give the corresponding carboxylic acids in which the acetyl group was merely oxidized. Acetophenone (**1g**) was converted into benzoic acid (**3g**) in high yield (97%) (entry 1). Similarly, 4-chloroacetophenone (**1h**), 4-fluoroacetophenone (**1i**), 4-methoxyacetophenone (**1j**), and 4-acetoxyacetophenone (**1k**) were oxidized to the corresponding benzoic acid derivatives (**3h**–**3k**) in high yields (86–96%) (entries 2–5). The $Mn(OAc)_2$ catalyst was found to be effective to the oxidation of 4- and 3-methylacetophenones (**1a** and **1b**) as well as 2-methylacetophenone (**1c**) and gave the corresponding methylbenzoic acids, **3a**, **3b**, and **3c** in high yields (85–93%) (entries 6–8). Di- and trimethyl-substituted acetophenones such as 3,4-dimethylacetophenone (**1d**) and 2,4,6-trimethylacetophenone (**1l**) were also selectively oxidized to 3,4-dimethylbenzoic acid (**3d**) and 2,4,6-trimethylbenzoic acid (**3l**) in 95% and 82% yields, respectively (entries 9 and 10). However, in the oxidation of 4-ethylacetophenone (**1e**) and 4-isopropylacetophenone (**1f**), their alkyl groups were partly oxidized to form the corresponding benzoic acids (**3e** and **3f**) in moderate yields (entries 11 and 12). 4-*tert*-Butylacetophenone (**1m**) was converted to 4-*tert*-butylbenzoic acid (**3m**) in almost quantitative yield (entry 13). From propiophenone (**1n**), benzoic acid (**3g**) was obtained in 88%

Table 4. Oxidation of acetophenones (**1**) with O_2 by THICA/Co/Mn.[a]

Entry	Substrate	Conversion [%]	Product	Yield [%][b]
1	 **1a**	99	 **4a**	93(91)
2	 **1b**	98	 **4b**	94(89)
3[c]	 **1c**	99	 **4c**	88(73)
4	 **1e**	99	 **4a**	83(79)[d]
5[e]	 **1p**	99	 **4c**	90(82)

[a] **1** (3 mmol) was allowed to react in the presence of THICA (5 mol%), $Co(OAc)_2$ (0.5 mol%), and $Mn(OAc)_2$ (0.5 mol%) under O_2 (1 atm) in AcOH (3 mL) at 120 °C for 15 h.

[b] Yields based on GC analysis after the esterification with MeOH (20 mL) and H_2SO_4 (50 mg) at 100 °C for 24 h. Numbers in parenthesis show isolated yields.

[c] $ZrO(OAc)_2$ (0.5 mol%) and Ac_2O (0.02 mL) were added.

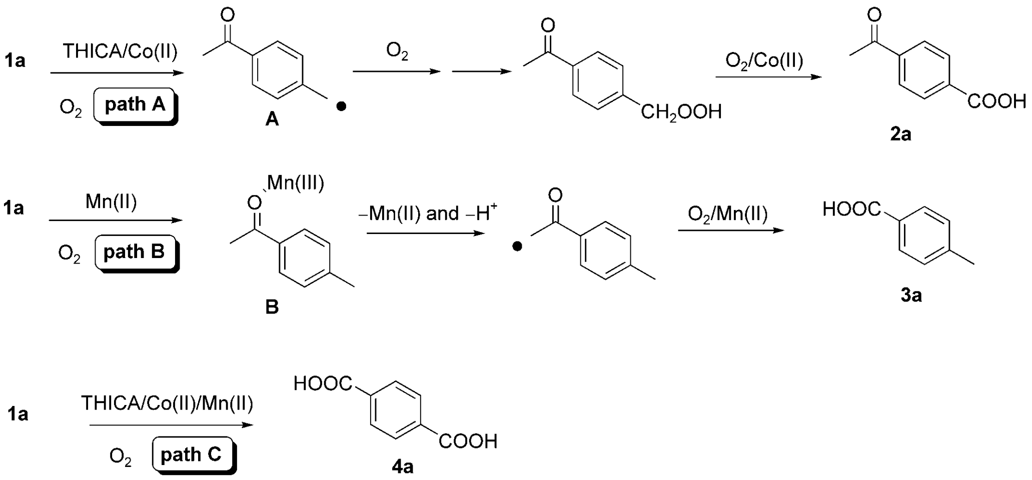
[d] **2a** (10%) was obtained along with **4a**.

[e] The $Co(OAc)_2$ (0.5 mol%)/$Mn(OAc)_2$ (0.5 mol%) system was used as the catalyst.

yield (entry 14). 6-Acetyl-2-isopropylnaphthalene (**1o**) was oxidized to 6-isopropyl-2-naphthoic acid (**3o**) in 93% yield.

When THICA/$Co(OAc)_2$/$Mn(OAc)_2$ system was employed as a catalyst, both alkyl and acetyl groups in methylacetophenones were efficiently oxidized with O_2 to give dicarboxylic acids like terephthalic and isophthalic acids (**4a**, **4b**, and **4c**) in 88–94% yields (Table 4, entries 1 and 2). Phthalic acid (**4c**) was similarly prepared from **1c**, when small amounts of $ZrO(OAc)_2$ and Ac_2O were added to the standard catalytic system (entry 3). 4-Ethylacetophenone (**1e**) and 1-indanone (**1p**) were also oxidized to **4a** and **4c** in good yields (entries 4 and 5).

The most important feature of the present selective aerobic oxidation of alkyl and acetyl groups on the aromatic ring is based on a favourable choice of THICA or $Mn(OAc)_2$ which plays the parts of a carbon-radical producing catalyst of the alkyl group or as a one-electron oxidation catalyst of the acetyl group, respectively. In a previous paper, we showed that *N*-hydroxy imides like NHPI and THICA serve as good catalysts for the generation of carbon radicals from sp^3 C–H bonds of alkanes under dioxygen and promote the autoxidation of alkylbenzenes to the corresponding benzoic acids.[10,14] On the other hand, it is well-known that Mn(III) species such as $Mn(OAc)_3$ possess a high one-electron oxidation ability for enolizable compounds like ketones to give a free radical which then reacts with O_2 or adds to alkenes and alkynes.[15] In addition, $Mn(OAc)_2$ is oxidized to $Mn(OAc)_3$ in acetic acid under the influence of O_2 and ketone.[15] In fact, we have reported that on the $Mn(OAc)_2$-catalyzed oxidative radical addition of enolizable compounds to afford unsaturated systems.[16]



Scheme 2. A plausible reaction pathway for selective oxidation of **1a** to **2a** (path A), **3a** (path B), and **4a** (path C).

Thus, a plausible reaction path for the present selective functional group oxidation is shown in Scheme 2.

When the THICA/Co(II) system was employed as the catalyst, the hydrogen atom of the methyl group of **1a** is abstracted to generate a benzyl radical **A** which then is trapped by O_2. The formed benzyl hydroperoxide is converted into benzoic acid **2a** (Scheme 2, path A). In contrast, when $Mn(OAc)_2$ was used as the catalyst, the Mn(II) species is oxidized to Mn(III) which coordinates to the acetyl group and then an acetyl radical intermediate (**B**) may be formed after the liberation of Mn(II) and H^+. Subsequently, the resulting radical **B** is oxidized under the influence of O_2 and Mn species to form **3a** (path B). When the THICA/$Co(OAc)_2$/$Mn(OAc)_2$ catalyst system was used, the oxidation *via* the path A and path B takes place simultaneously to give **4a** in which both the methyl and acetyl groups of **1a** are oxidized (path C).

Conclusions

The new protocol allowed for the selective oxidation of acetophenones with molecular oxygen in fairly good selectivity by tuning the catalytic system consisting of THICA, $Co(OAc)_2$, and $Mn(OAc)_2$. In particular, it is interesting that the selective conversion of the acetyl group to carboxylic acid group was efficiently achieved by a very small amount of $Mn(OAc)_2$ under O_2. This method provides a new route to various benzoic acids from substituted acetophenones by the oxidation with O_2 under the influence of a combined catalytic system consisting of THICA, $Co(OAc)_2$, and $Mn(OAc)_2$.

Experimental Section

General Experimental Methods

All starting materials were commercially available and used without any purification. All compounds except **2d′** are known compounds and have been reported previously.[17]

GLC analysis was performed with a flame ionization detector using a 0.22 mm × 25 m capillary column (BP-5). Mass spectra were determined at an ionizing voltage of 70 eV. Infrared (IR) spectra were measured as thin films on NaCl plate or KBr press disk. ^{1}H and ^{13}C NMR spectra were measured at 270 and 67.5 MHz, respectively, in DMSO-d_6 or $CDCl_3$ with Me_4Si as the internal standard. The products were characterized by ^{1}H NMR, ^{13}C NMR, and GC-MS. The yields of products were estimated from the peak areas based on the internal standard technique using GLC after the esterification with MeOH (20 mL) and H_2SO_4 (50 mg) at 100 °C for 24 h.

3-Acetyl-6-methylbenzoic acid (2d′) (methyl ester form): ^{1}H NMR (270 MHz, $CDCl_3$, Me_4Si): $\delta = 8.49$ (m, 1H), 7.96 (m, 1H), 7.33 (m, 1H), 3.93 (s, 3H), 2.66 (s, 3H), 2.62 (s, 3H); IR (KBr): $\nu = 2953$, 1723, 1688, 1436, 1258, 1099, 1075, 841, 781, and 700 cm^{-1}; MS (EI): *m/z* (relative intensity) = 192 (38) $[M]^+$, 177 (100), 161 (25), 149 (24), 134 (8), 117 (12), 105 (12), 89 (17), 77 (9); HR-MS (EI): *m/z* = 192.0787, calcd. for $C_{11}H_{12}O_3$ $[M]^+$: 192.0786.

General Procedure for the Oxidation of 1a in the Presence of THICA/$Co(OAc)_2$ (Table 1, entry 11)

A mixture of 4-methylacetophenone (**1a**) (403 mg, 3 mmol), THICA (27 mg, 0.15 mmol, 5 mol%) and $Co(OAc)_2 \cdot 4H_2O$ (3.7 mg, 0.015 mmol, 0.5 mol%) in acetic acid (3.0 mL) was placed in a pear-shaped flask equipped with a balloon filled with O_2. The mixture was stirred at 120 °C for 15 h. Removal of the solvent under reduced pressure afforded a crude mixture, which was extracted with $NaHCO_3$ solution followed by work-up with hydrochloric acid (1 mL) to give 4-acetylbenzoic acid (**2a**) isolated in the pure state; yield: 355 mg (2.16 mmol, 72%).

General Procedure for the Oxidation of 1a in the Presence of $Mn(OAc)_2$ (Table 1, entry 2)

A mixture of 4-methylacetophenone (**1a**) (403 mg, 3 mmol) and $Mn(OAc)_2 \cdot 4H_2O$ (3.6 mg, 0.015 mmol, 0.5 mol%) in acetic acid (3.0 mL) was placed in a pear-shaped flask equipped with a balloon filled with O_2. The mixture was stirred at 100 °C for 15 h. Removal of the solvent under reduced pressure afforded a crude mixture, which was extracted with $NaHCO_3$ solution followed by work-up with hydrochloric acid (1 mL) to give *p*-toluic acid (**3a**) isolated in the pure state; yield: 335 mg (2.46 mmol, 82%).

General Procedure for the Oxidation of 1a in the Presence of THICA/$Co(OAc)_2$/$Mn(OAc)_2$ (Table 1, entry 14)

A mixture of 4-methylacetophenone (**1a**) (403 mg, 3 mmol), THICA (27 mg, 0.15 mmol, 5 mol%), $Co(OAc)_2 \cdot 4H_2O$ (3.7 mg, 0.015 mmol, 0.5 mol%), and $Mn(OAc)_2 \cdot 4H_2O$ (3.6 mg, 0.015 mmol, 0.5 mol%) in acetic acid (3.0 mL) was placed in a pear-shaped flask equipped with a balloon filled with O_2. The mixture was stirred at 120 °C for 15 h. Removal of the solvent under reduced pressure afforded a crude mixture, which was extracted with $NaHCO_3$ solution followed by work-up with hydrochloric acid (1 mL) to give terephthalic acid (**4a**) isolated in the pure state; yield: 454 mg (2.73 mmol, 91%).

Supporting Information

Copies of ^{1}H/^{13}C NMR spectra of **2**–**5** are available as Supporting Information.

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