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Catalysis Today 23 (1995) 69–158

CATALYSIS TODAY

Methodology and scope of metal/bromide autoxidation of hydrocarbons

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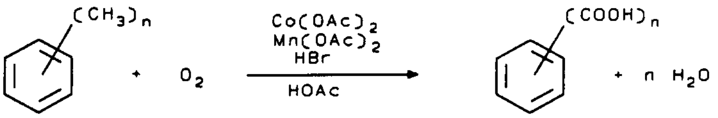
1. Introduction

1.1. Definition

The general definition of the Amoco MC method can be given as follows:

$$\text{hydrocarbon} + \text{dioxygen} \xrightarrow[\text{solvent}]{\text{catalyst = metal(s)/bromide}} \text{oxygenate} + \text{water} \qquad (1.1)$$

with the most common example being polymethylbenzenes in which every methyl group is converted to a carbonyl group:



(1.2)

The value of $n = 1$ to 4. It is a homogeneously catalyzed, liquid phase oxidation with gaseous oxygen being pumped through the liquid consisting of the soluble hydrocarbon, soluble metal salt and soluble bromide salt. This system is characterized by:

(1) High activity as compared to other autoxidation catalysts.

(2) High selectivity over a very large operating temperature range (from 25°C to 300°C). This allows one to accommodate very large differences in reactivity of the hydrocarbon and accounts for the large number of reported products using this method (Table 1.1), and the number of major industrial processes (Table 1.2).

(3) Many of the carboxylic acid products are relatively insoluble in the acetic acid solvent at, or near, room temperature. The system therefore provides for a separation of the product from the solvent and catalyst.

1.2. Scope

The author is unaware of any review articles on this class of catalysts and their application since their discovery in 1954. This review will emphasize the preparative aspects of this method for incorporation

Table 1.1
Types of reagents that have oxidized using the AMOCO MC method

Category	Reagents No.	Type of products
Alkylaromatic		
Methylbenzenes (often substituted)	73	Aromatic acids, benzylic acetates, benzylic alcohols, benzaldehydes
Ethylbenzenes	14	Acetyl derivatives, aromatic acids
Others (isopropyl, tetralins, biphenyls, etc.)	38	Aromatic acids
Oligomerics $(R)_nPh\text{-}X\text{-}Ph(R)_n \rightarrow (HOOC)_nPh\text{-}X\text{-}Ph(COOH)_n, X = -S-, -CH_2-, -O-$, *etc.*	52	Aromatic acids
Alkylnaphthalenes	26	Aromatic acids, benzylic acetates, benzylic alcohols, benzaldehydes
Heterocyclics	21	Aromatic acids
Organometallics	14	Aromatic acids
Aliphatics	34	Alcohols, aldehydes ketones, carboxylic acids
Total = 251 reagents (feedstocks)		

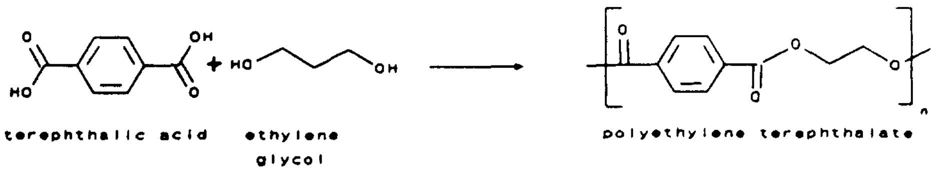
of oxygen atoms into organic substances. A concise summary illustrating the large number of different reagents that have been oxygenated by this method is given in Table 1.1.

This review will summarize the types of catalysts, solvents, and experimental conditions that have been used and suggest ways to pick the proper conditions for the oxidation of a given substrate. Mechanistic suggestions as they apply to the preparative methods will be given but the numerous other mechanistic papers will not be discussed. A few selected leading references discussing mechanism are available [1–11]. Good summaries are available for the formation of by-products during the oxidation of *p*-xylene [12,13], isopropylbenzenes [14], and naphthalenes [15]. The engineering aspects of liquid phase oxidation have been discussed [16,17].

Related commercially interesting reactions will also be compared to the MC method. These will be restricted to dioxygen as the primary oxidant because of its availability and cost considerations necessary for large scale operations.

1.3. Historical

The impetus for the discovery of the Amoco MC catalysts was the industrial preparation of aromatic polyesters which required a cheap source of aromatic acids. In 1941, Whinfield and Dickson first prepared a polyester from the reaction of terephthalic acid (1,4-dicarboxybenzene) and ethylene glycol [18]:



(1.3)

They showed that the product, polyethylene terephthalate (usually abbreviated PET) could be fabricated into an excellent fiber. This led to a search to find a suitable reagent of sufficient availability and a suitable oxidation method to prepare terephthalic acid. The key, of course, was to find a catalyst which will selectively control the incorporation of dioxgen into the hydrocarbon. In 1938, the use of cobalt salts, manganese salts, and acetic acid as a solvent was disclosed by DuPont for the partial oxidation of toluene to benzoic acid (40% yield at 46% conversion) [19]. This knowledge led to the first commercial autoxidation process to produce terephthalic acid in 1951. Dubbed the Witten or Imhausen process, it

Table 1.2
Capacities to produce aromatic acids at Amoco chemical corporation

Reagent	Product	Catalyst	Mode	Yield (%)	Capacity (million lbs)
p-Xylene	Terephthalic acid	Co/Mn/Br	CSTR[a]	>90	3060
m-Xylene	Isophthalic acid	Co/Mn/Br	CSTR	>90	445
Pseudocumene	Trimellitic acid	Co/Mn/Br/Zr	Batch	>90	105
–	2,6-NDA[b]	–	–	–	100

[a] Continuously stirred tank reactor.

[b] 2,6-NDA = 2,6-naphthalenedicarboxylic acid. Starting material has not been announced.Start-up of this plant is scheduled in 1995 (see Chemical Marketing Reporter, March 1, 1993).

was based on the cobalt catalyzed oxidation of *p*-xylene and gave terephthalic acid in 15% per pass yield [20]. In 1954, the MC catalyst was discovered apparently independent of DuPont, Amoco and others by Landau, Saffer and Barker of Scientific Design [21] and it was patented in 1958 [22]. Landau et. al. were attempting to oxidize *p*-diisopropylbenzene to terephthalic acid. They went to acetic acid because they thought the acetic acid would acetylate the alcohols and help the oxidation. After scouring the entire periodic chart for metals that would work better than cobalt, it occurred to them to vary the anion. Their breakthough came when they used manganese bromide as a catalyst and subsequently obtained a terephthalic acid yield of 60%. *p*-Xylene had just become available as a viable oxidation feedstock and hence they tried the manganese bromide catalyst with it — and immediately obtained a 77% yield — much greater than the 15% yield obtainable with a cobalt catalyst.

Standard Oil of Indiana (later Amoco), who had been interested in the oxidation of alkylaromatic compounds for some time, recognized the significance of the discovery, purchased the patent rights to the new catalyst and went through the pain of developing a new oxidation technology. From 1965 to 1991, Amoco has placed nine different reactors on line, with capacities ranging from 40 to 1000 million pounds per year, to produce terephthalic acid. It has formed a number of joint ventures [23] and has taken advantage of the flexibility of the method to produce a number of different aromatic acids (see Table 1.2). A large number of pilot plant and experimental samples of other aromatic acids have been prepared by Amoco. Some of these will be discussed and, of course, are available for commercial evaluation.

Terephthalic acid is currently ranked 11th in volume of the U.S. production of organic chemicals and has been growing at a double-digit pace as demand for polyester film and resins continues to grow [24].

1.4. Comparison of the MC method to other methods for the preparation of aromatic acids

The first methods developed for the preparation of aromatic acids used stoichiometric reagents [25]. Permanganate and dichromate oxidations require large amounts of reagents and yield copious amounts of salts that must be disposed of. Using permanganate, one pound of benzoic acid from toluene generates 0.71 pounds of manganese dioxide (assuming 100% yield). In contrast, the MC method yields water as the major product. Nitric acid oxidations give good yields to aromatic acids but also yield nitrated by-products [20] and produce nitrous oxide emissions [26]. Although nitration was the first industrial method used to prepare terephthalic acid [20] it was eventually displaced by autoxidation methods; i.e., reaction of dioxygen with *p*-xylene. Yields using the MC method (see Sections 4.3 and 4.5), are comparable or exceed those using stochiometric methods [25].

There are two competing methods for the Amoco MC method — both based on cobalt salts [1,20]. The 'Witten' method involves the partial oxidation of *p*-xylene and a separation of the *p*-toluic acid and terephthalic acid as their methyl esters. The other method co-oxidizes the *p*-xylene with acetaldehyde, methylethylketone, or paraldehyde. Both methods use much higher catalyst metal concentrations (by roughly an order of magnitude) and have about twice the reactor residence times as the Amoco MC method [27,28]. The major disadvantage of the Amoco method is the necessity to use titanium clad equipment to combat the corrosive nature of metal/bromine/acetic acid mixtures.

Some aromatic acids can be prepared by gas phase oxidation over metal oxide catalysts, most notably the commercial production of *o*-phthalic anhydride from *o*-xylene [20]. Quite pure product at high yields (about 78 mol-% to *o*-phthalic anhydride) is produced this way. The disadvantages of gas-phase over liquid phase oxidation will be discussed in Section 1.10.

1.5. Mechanism

A few selected leading references on mechanism are summarized [1–11]. This section is meant to give a brief introduction to the subject from the point of view of the author. To a first approximation, the MC system can be treated as a free radical chain mechanism. Free radicals have been observed during the MC oxidation of cumene [29]. Using toluene as an example and 'I' to indicate a radical initiating species the usual scheme [30] is:
Initiation:

$$PhCH_3 + I \rightarrow PhCH_2^{\cdot} + IH \tag{1.4}$$

Propagation:

$$PhCH_2^{\cdot} + O_2 \rightarrow PhCH_2O_2^{\cdot} \tag{1.5}$$

$$PhCH_2O_2^{\cdot} + PhCH_3 \rightarrow PhCH_2OOH + PhCH_2^{\cdot} \tag{1.6}$$

Termination:

$$PhCH_2^{\cdot} + PhCH_2O_2^{\cdot} \rightarrow PhCH_2OOCH_2Ph \tag{1.7}$$

$$PhCH_2O_2^{\cdot} + PhCH_2O_2^{\cdot} \rightarrow PhCH_2O_4CH_2Ph \tag{1.8}$$

At temperatures above 50°C, the primary peroxides would slowly thermally decompose:

$$PhCH_2OOH \rightarrow PhCH_2O^{\cdot} + OH^{\cdot} \tag{1.9}$$

The above scheme is strongly modified by the presence of the metals. Cobalt performs at least three functions:

(1) It enhances the rate of oxidation by quickly reacting with the primary peroxides via the Haber–Weiss cycle [30]:

$$Co(II) + PhCH_2OOH \xrightarrow{k_1} Co(III)OH + PhCH_2O^{\cdot} \tag{1.10}$$

$$Co(III)OH + PhCH_2OOH \xrightarrow{k_2} Co(II) + PhCH_2OO^{\cdot} + H_2O \tag{1.11}$$

(2) The cobalt(III) is a radical initiating species since it is well known to oxidize methylbenzenes to benzylic radicals ($PhCH_2^{\cdot}$), [3]. Hence, it enhances the rate by participating in the initiation step.

(3) It reacts very rapidly and selectively with peracids, which are formed from benzaldehydes. The dimeric nature of cobalt(II) in acetic acid/water mixtures provides for a non-radical, very fast, highly selective generation of acids from the peracids [2]:

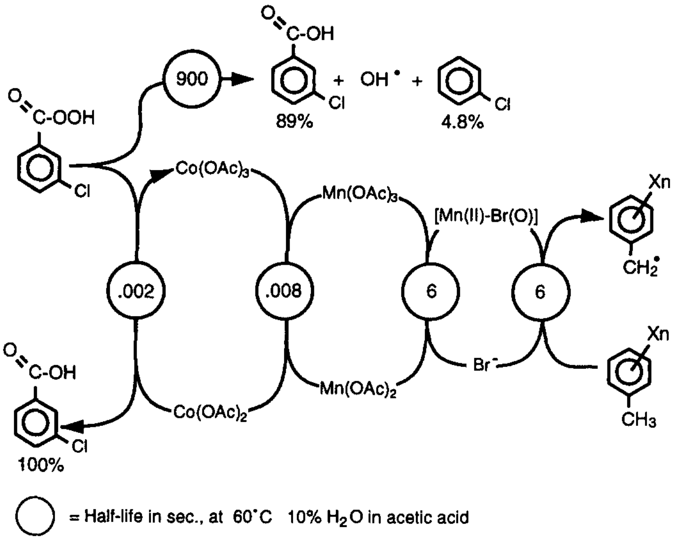


Fig. 1.1. A model of the Amoco MC catalyst, based on data from ref. [2].

Table 1.3

Changes in reactivity of *para*-substituted methylaromatic compounds and estimated necessary temperatures and pressures to produce the corresponding aromatic acids in 1–2 h

Substitutent	Reactivity[a]	Controlling factors[b]	
		Temperature	Pressure
$-OMe$	5.5	100°C	1 atm air
$-CH_3$	2.0		
$-CMe_3$	1.8	↓	↓
-H	1.0	150°C	10 atm air
-Cl	0.79		
-CN	0.24	↓	↓
$-NO_2$	0.18	200°C	25 atm air

[a] Using $\sigma +$ values from Jerry March, Advanced Organic Chemistry, McGraw-Hill, New York, 2nd edn., p. 253 and a ρ value of −0.95.

[b] These are estimated from the authors experience using a Co/Mn/Br catalyst at catalyst concentration of [Co] = [Mn] = 2 × [Br] of 0.010 M.

Table 1.4

Estimate of the reactivity of methylaromatics as the methyl groups are consecutively oxygenated to carboxylic acids[a]

n = No. of carboxyl groups	$n=0$	$n=1$	$n=2$	$n=3$	$n=4$	$n=5$
Toluene	1.0					
p-Xylene	3.9	0.39				
m-Xylene	2.5	0.49				
o-Xylene	3.9	0.39				
1,3,5-Trimethylbenzene	4.6	1.2	0.25			
1,2,4-Trimethylbenzene (peudocumene)	8.8	1.6	0.19			
1,2,3-Trimethylbenzene	6.4	1.4	0.18			
1,2,4,5-Tetramethylbenzene	19	3.3	0.78	0.079		
1,2,3,4-Tetramethylbenzene	19	3.7	0.35	0.079		
1,2,3,4,5-Pentamethylbenzene	39	7.4	1.6	0.29	0.039	
1,2,3,4,5,6-Hexamethylbenzene	71	13	7.8	0.51	0.12	0.016

[a] Assumptions are that Hammett substitutent constants: (1) in the *ortho*-position are the same as in the *para*-position, (2) substitutents constants are additive, and (3) the arithmetic average was taken where geometrical isomers of similar activity are possible.

Table 1.5
Predicted and observed initial rates of oxygenation for selected hydrocarbon[a]

	Rate of O_2 uptake (ml O_2/min)	Predicted by Hammett Eq.	Difference
Toluene	0.49	0.49	0.0
m-Xylene	1.43	1.39	+0.04
p-Xylene	2.26	2.25	+0.01
o-Xylene	3.82	2.25	+1.57
1,3,5-$(CH_3)_3Ph$	2.64	2.70	−0.06
1,2,4-$(CH_3)_3Ph$	4.96	3.98	+0.98

[a] Measured using 0.966 M hydrocarbon concentration, cobalt(II) acetate = manganese(II) acetate = 0.0201 M, NaBr = 0.0402 M using air at ambient atmospheric pressure in 13% water/acetic acid solution. Values were measured in the authors laboratory.

Table 1.6
Reactivity differences between MC type oxidations and cobalt catalyzed oxidations[a]

		Reactivity relative to toluene		
		$n=1$	$n=2$	$n=3$
Toluene	MC type	1.0		
Toluene	Co catalyst	1.0		
p-Xylene	MC type	3.9	0.39	
p-Xylene	Co catalyst	7.3	0.17	
m-Xylene	MC type	2.5	0.49	
m-Xylene	Co catalyst	3.0	0.26	
1,2,4-Trimethylbenzene	MC type	8.8	1.6	0.20
1,2,4-Trimethylbenzene	Co catalyst	24	1.1	0.041

[a] A ρ of -0.95 was used for the MC catalyst and -1.81 for the Co only catalyst. The latter value was calculated from the values in C.F. Hendriks, H.C.A. Beek and P.M. Heerjes, Ind. Eng. Chem. Prod. Res. Dev., 17 (1978) 266. The latter report a value of -1.9 but did not account for the number of equivalent hydrogen atoms.

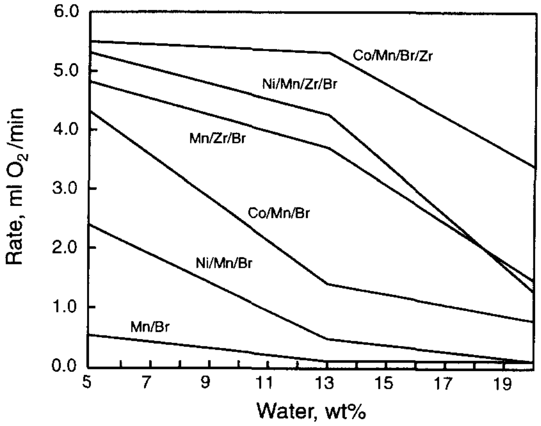
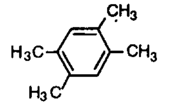
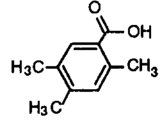
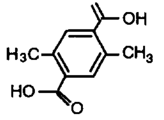
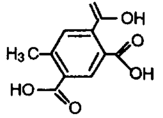
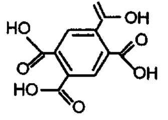


Fig.1. 2. The activity of selected MC catalysts as a function of water concentration. Data from ref. [83].

$$m\text{-chloroperbenzoic} + \mathrm{Co(II)}_2 \rightarrow m\text{-chlorobenzoic acid} + \mathrm{Co(III)}_2 \quad (1.12)$$

As illustrated in Fig. 1.1, the rate of *m*-chloroperbenzoic acid disappearance is catalyzed by a factor of 900/0.002 = 45000! Furthermore, virtually 100% yield to 3-chlorobenzoic acid is obtained in the presence of cobalt while only 89% yield is obtained in its absence. 4.8% of chlorobenzene results during the thermal decomposition of MCPBA while none is detected in the presence of cobalt. The reaction is much

	Reactivity (1)	Time, min	Temp, °C	Pressure, atm	Catalyst, mmole (2)
			138	10	20
1,2,4,5-tetramethylbenzene $+O_2$ ▼ $-H_2O$	19				
		(4)	144	10	22
1-carboxy-2,4,5-trimethylbenzene $+O_2$ ▼ $-H_2O$	3.3				
		(26)	156	14	25
1,4-dicarboxy-2,5-dimethylbenzene $+O_2$ ▼ $-H_2O$	0.78				
					
1,2,4-tricarboxy-3-methylbenzene $+O_2$ ▼ $-H_2O$	0.08	50	204	24	30
					
1,2,4,5-tetracarboxybenzene	--	110	224	31	156

1. Only carboxylic acid intermediates shown. Many of these will have geometrical isomers which are not shown.
2. Sum of Co, Mn, and Br.

Fig. 1.3. Experimental conditions necessary for the MC reaction of durene to pyromellitic acid. Data from ref. [34].

more selective. The selectivity is enhanced with cobalt presumably because MCPBA is a two-electron oxidant which can react with the cobalt(II) dimer which is a two-electron reductant. The formation of the hydroxyl radical, OH˙ is thus avoided [2].

Most liquid phase industrial oxidation processes are based on cobalt catalyzed oxidations [16]. It is particularly instructive to observe the changes when bromine and manganese are added into a cobalt catalyzed oxidation of a methylaromatic compound. Five dramatic changes result [1]:

(1) The catalyst is 16 times more active [1,31,32].

(2) The vent carbon dioxide and carbon monoxide concentration, which are indicative of the selectivity of the reaction, are reduced by a factor of 10, along with the higher activity.

(3) The steady state concentration of Co(III) is reduced from 11% of the total cobalt present to only 0.6%.

(4) Cobalt catalyzed oxidations are limited in their maximum operating temperature — about 150°C. MC catalysts can operate at much higher temperatures giving comparable yields to aromatic acids [1].

(5) Long induction times are absent [1] except for highly purified hydrocarbons [11].

Table 1.7
Increase in water concentration when methyl groups are consecutively oxygenated to an aromatic acid[a,b]

	$n=1$	$n=2$	$n=3$	$n=4$	$n=5$	$n=6$
Toluene	6.5					
Dimethylbenzene	5.6	11.3				
Trimethylbenzene	5.0	10.0	15			
Tetramethylbenzene	4.4	8.9	13	17		
Pentamethylbenzene	4.0	8.1	12	16	20	
Hexamethylbenzene	3.7	7.4	11	14	18	22

[a] n = No. of methyl groups oxidized to the carboxyl group.
[b] Assumed reaction is 33.0 g of hydrocarbon in 100.0 g of anhydrous acetic acid. Assumes 100% yield, no water formation due to side-reactions, and no water loss from the reactor.

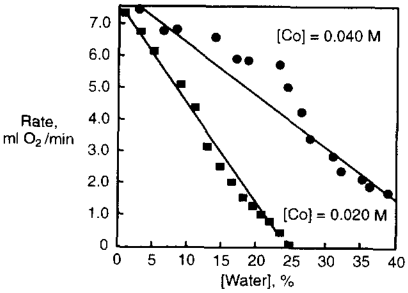


Fig. 1.4. Results of adding water into a Co/Mn/Br catalyzed oxidation of pseudocumene [65].

Table 1.8
Concentration of aromatic carboxylic acids groups, M, as polymethylbenzenes are consecutively oxygenated to carboxylic acids[a,b]

	$n=1$	$n=2$	$n=3$	$n=4$	$n=5$	$n=6$
Toluene	3.58					
Dimethylbenzene	3.11	6.22				
Trimethylbenzene	2.75	5.50	8.25			
Tetramethylbenzene	2.46	4.92	7.38	9.85		
Pentamethylbenzene	2.22	4.45	6.68	8.91	11.14	
Hexamethylbenzene	2.03	4.07	6.11	8.14	10.18	12.22

[a] n = No. of carboxyl groups.
[b] Assumed reaction is 33.0 g of hydrocarbon in 100.0 g of anhydrous acetic acid. Assumes 100% yield, no water formation due to side-reactions, and no water loss.

These five changes clearly indicate that new catalytic pathways are now available. Some of these new pathways are indicated in Fig. 1.1 which are from kinetic studies performed in our laboratory [2]. Addition of *m*-chloroperbenzoic acid (MCPBA) to a mixture of cobalt(II) acetate, manganese(II) and sodium bromide in acetic acid/water mixtures results in three consecutive reactions. The cobalt(II) is oxidized to cobalt(III); the latter then oxidizes manganese(II) to manganese(III); and finally manganese(III) oxidizes bromide to dibromine. The thermodynamics in this sequence are interesting. The most easily oxidizable substance is bromide, followed by Mn(II), and finally Co(II). However the experimentally observable sequence is cobalt(II) first (the least favorable oxidation by MCPBA), then manganese(II) and then bromide. It may be that we may be in the 'inverted region' in Marcus–Hush theory. Many of the characteristics of an MC oxidation, given above, have been rationalized via this diagram [1,2].

Table 1.9
Degree of precipitation (in %) of selected aromatic acids in acetic acid

	Formed during reaction (g)[a]	Degree of precipitation (%)[b]		
		25°C	100°C	200°C
o-Xylene to *o*-phthalic acid	47	–	74	–
p-Xylene to terephthalic acid	47	99.93	99.4	96.2
m-Xylene to isophthalic acid	47	99.5	97.7	72
1,2,4-Trimethylbenzene to trimellitic acid	52	98.1	–	–

[a] Assuming typical values in which 33 g of reagent is placed in 100 g of acetic acid and oxygenated under MC conditions. A 90% yield is assumed.

[b] Solubilities taken from ref. [17] in 100% acetic acid. Products from oxidation will really be in a mixture of about 10% water/acetic acid.

The steady state concentration of cobalt(III) is reduced because of a rapid reaction of cobalt(III) with manganese(II) (see Fig. 1.1). This partially avoids the decarboxylation of acetic acid ($R = CH_3$) and aromatic acids (R = phenyl):

$$\mathrm{Co(III)OH + RCOOH \rightarrow Co(II) + R^{\cdot} + CO_2 + H_2O} \tag{1.13}$$

and at least partially accounts for the lower vent carbon oxides since the rate of reaction of Mn(III) with acetic acid is much slower than with Co(III). The greatly enhanced activity can be rationalized by the much higher rate of initiation since the bromine atom (which is probably a complex with Mn) abstracts hydrogen from the aromatic methyl group atoms much faster than Co(III). The much lower steady state concentration of cobalt(III) makes reaction 1.11 much less important than in catalysts which employ only cobalt.

1.6. Selectivity considerations

We will consider four principles:

(1) All organic substances present in an MC oxidation will be partially destroyed — they will be oxidized to carbon dioxide and methyl acetate. The degree to which they become 'over-oxidized' to carbon dioxide will vary however and is specific to the reagent being oxidized. The most important point is that the acetic acid solvent, essential to the method (see Section 2), will be oxidized *but normally at a rate much less than the reagent hydrocarbon.* Acetic acid is relatively inert. In a recent patent, it is stated that 0.07 lb of acetic acid was lost per pound of terephthalic acid produced [33].

(2) The alkylperoxy radicals and bromine-atom like transients in the MC system are quite selective and preferentially abstract only the most weakly bound hydrogen; i.e., the selectivity is strongly related to the C–H bond strength [30]. Thus methylaromatic compounds can be oxidized to aromatic carboxylic acids because the C–H bond of the methyl group (85 kcal/mol) is much less than that of the benzene ring C–H bond (104 kcal/mol). Any C–H bond directly attached to aromatic rings (benzylic carbon atom) is stabilized by resonance and has an accompanying lower bond strength [15]. When this bond exists, it is always preferentially oxidized and is the basis for a large number of products reported during MC oxidations. Thus, the methylenic bond (i.e., $-CH_2-$) attached directly an aromatic ring is preferentially oxidized to one which is not (see reactions 6.2, 8.3 and 8.6). Similarly, a benzylic methyl group (i.e., $-CH_3$) is preferentially oxidized to an aliphatic one. This is typified by the preferential oxidation of a benzylic methyl groups over the methyl group in *t*-butyl derivatives (i.e., $-C(CH_3)_3$) (see reactions 2.1 and 3.3). The *t*-butyl group will be oxidized (see Section 4.5), but at a much slower rate than the

benzylic methyl group. Other examples are compounds which can be considered as substituted *t*-butyl derivatives (see reactions 4.13, 4.15, 4.22, 4.25, and 11.2).

Stabilization by hyperconjugation accounts for the well-established reactivity sequence that tertiary C–H bonds ($H–CR_3$) are more reactive than second C–H bonds ($H–CR_2H$), which are more reactive than primary C–H bonds ($H–CH_2R$). Thus, the *initial* oxidation of isopropyl derivatives (Section 7) are higher than ethyl derivatives (Section 5), which are higher than methyl (Sections 4.3 and 4.5) derivatives.

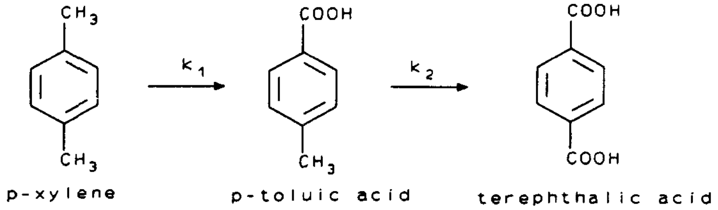
(3) Relative rates of reactions are a measure of the selectivity of a process. The rate of oxidation of most methylaromatic compounds follows the Hammett structure–reactivity relationship [34,35]:

$$\log(k/k_o) = \sigma \times \rho \tag{1.14}$$

where k = the rate constant for the disappearance of a given compound, k_o = the rate constant for the disappearance of toluene, σ = the constant characteristic of the substituent on the ring, and ρ = the constant for given set of conditions.

Many values of ρ for metal/bromine catalyzed oxygenations have been reported [34,35]. They are all very similar and range from -0.60 to -1.34. We will use the reported value of -0.95 because it was measured in 10% water/90% acetic acid solutions, which is a typical solvent for MC reactions. The absolute magnitude of ρ indicates that hydrocarbons will differ substantially in activity; for example 4-nitrotoluene is 31 times less active than 4-methoxytoluene (see Table 1.3). The negative sign indicates that electron withdrawing substituents are less active. One could easily oxidize *p*-methoxytoluene to *p*-methoxybenzoic acid in the presence of 4-nitrotoluene. 4-Nitrotoluene would remain relatively inert under these while *p*-methoxytoluene becomes oxidized to *p*-methoxybenzoic acid.

The industrially important case are polymethylbenzenes being autoxidized to their polycarboxylic compounds. When a methyl group becomes oxidized to a carboxylic acid, the *para*-sigma+ Hammett substituent constant changes from -0.31 to $+0.42$. This reduction in ring electron density results in the oxygenation of the second methyl group *para* to the first to be 4.9 times slower. Since there are twice as many oxidizable hydrogen atoms in *p*-xylene than in *p*-toluic acid, *p*-xylene is $2 \times 4.9 = 9.8$ times more reactive than *p*-toluic acid (see Table 1.4). Thus during the oxidation of *p*-xylene high yields of *p*-toluic acid are formed before the oxidation of the second methyl group commences (see Table 4.2):



(1.15)

where $k_1 = 4.9 \times k_2$.

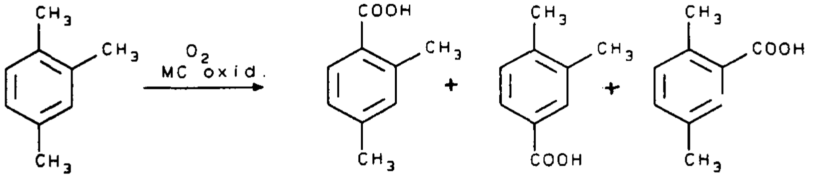
The difference in selectively is less in *m*-xylene — 5.1 (see Table 1.4). Hence, the theoretical isolatable yields to *m*-toluic acid would not be as high as with *p*-toluic acid.

We have assumed that *ortho*-substituents have the same Hammett substituent constants as *para*. This is only partially true (see Table 1.5). Table 1.5 was derived by plotting the rate of oxygen uptake versus the sum of Hammett substitute constants for toluene, *m*-xylene, *p*-xylene, and 1,3,5-trimethylbenzene since these molecules do not contain *o*-methyl groups. The resultant line is:

$$\text{Predicted rate} = (-2.03 \times \text{sum of substituent constants} + 0.495) \times \text{No. of } CH_3 \text{ groups}$$

We find that *o*-substituents, as indicated by the data for *o*-xylene and 1,2,4-trimethylbenzene, are more reactive than predicted (see Table 1.5).

For 1,2,4-trimethylbenzene we expect to see three geometric isomers of the monoacids because the reactivity of the three symmetrically different methyl groups are similar. The predicted reactivity of the methyl groups in the 1, 2, and 4 position are 3.9, 2.5 and 2.5, respectively:

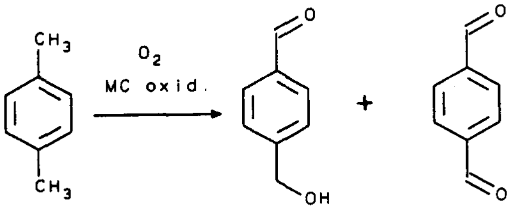


(1.16)

These three isomers have been observed [36].

The Hammett ρ value is a slope of the log(rate k) vs. the substituent constants. Larger values of the slope would denote a greater selectivity since a larger difference in rate constants occurs with changes in the substituent constant. The selectivity for cobalt catalyzed oxidations for the oxidation of first methyl group to a carboxylic acid is greater than for MC oxidations because of the significantly larger ρ value of -1.81 as compared to -0.95 (see Table 1.6). The difference in reactivity of p-xylene going to p-toluic acid is $7.3/0.17=43$ for a cobalt catalyst and $3.9/0.39=10$ for a MC type catalyst. We can conclude that if one wants to prepare p-toluic acid from p-xylene one would use a cobalt catalyzed system rather than an MC system to take advantage of the better selectivity. Similarly if one wanted to prepare terephthalic acid from p-xylene one would use to the MC system because the difference of k_1 and k_2 (see reaction 1.15) is smaller.

Although, to the first approximation, the oxidation of one methyl group to a carboxylic acid group occurs before the next group methyl group becomes oxidized, small amounts of compounds where both methyl groups of p-xylene are functionalized, are expected. Hydroxymethylbenzaldehyde and terephthaldehyde have been detected [37–39] during the oxidation of p-xylene:



from ref. 38: 1.5% 4.1%
from ref. 40: 8% (as the acetate)

(1.17)

(4) Intermediate formation-free radical autoxidations, in which the propagation step involves benzylic peroxy radicals, typically have the intermediate benzylic alcohols, benzylic acetates, and benzaldehydes of significantly higher reactivity than the methyl group. The reactivity difference of Ph–CH_3, Ph–CH_2OH and Ph–CHO is 1.0, 5.5 and 6000 [30]. This is consistent with the observations that in MC oxidations the methyl group is the least reactive and that the maximum concentration of any single intermediate is relatively low, typically 10–30% (see Section 4.2 for examples).

1.7. Controlling factors in the MC method

The selectivity and activity can be controlled by variation of:

(1) Pressure. The oxygen concentration in solution will increase with pressure as well as the boiling point of the solvent–solute mixture.

(2) Concentration of the reagent.

(3) Concentration of oxygen in the gas entering the reactor. Most often air, which contains 20.9% dioxygen, is used because of its ready availability. Higher oxygen contents can be achieved by mixing air with 100% oxygen. The use of 100% oxygen has been reported (see Tables 4.1–14.1). The latter two options are expensive commercially since an oxygen plant must be installed or tanks of 100% oxygen purchased. *Caution: pressurized air and especially mixtures containing oxygen concentration higher than air can be very dangerous. Special equipment is required for safe operations.*

(4) Temperature. The normal operating range is from 80 to 230°C. The catalyst is active at 25°C and can be used to at least 260°C. The normal boiling point of acetic acid, is 116–118°C; hence, pressurized vessels must be used if higher temperatures than this are desired.

(5) Catalyst concentration. Activity normally increases with concentration up to a maximum value then sometimes decreases. Not necessarily related, but often true, is the yield to aromatic carboxylic acid increases with catalyst concentration. For example for the oxidation of *p*-acetoxyacetophenone to *p*-acetoxybenzoic acid, tripling the catalyst concentration results in yield increase from 81 to 87% [73]. The vent carbon dioxide and carbon monoxide concentration are normally reduced as well. In solventless *o*-xylene oxidation to phthalic acid, the overoxidation of *o*-xylene was reduced from 8.8 to 5.8% by increasing the catalyst concentration by a factor of seven [77].

(6) Type of catalyst. There are a large variety of catalysts of different reactivity and selectivity, which will be discussed in detail in Section 3. Some examples at different water concentrations are illustrated in Fig. 1.2. The rate is being expressed in ml of oxygen reacted per minute.

(7) Variation of composition of a given catalyst. For example for a Co/Mn/Br catalyst, the activity and selectivity will vary somewhat with the Co/Mn and Br/(Co+Mn) molar ratios (see Section 3).

(8) Variation of the reactor water concentration (see Section 1.8). The use of temperature, pressure, and catalyst concentration variation during the preparation of 1,2,4,5-tetracarboxybenzene (pyromellitic acid) from 1,2,4,5-tetramethylbenzene (durene) has been discussed in detail [34]. It illustrates the use of these controlling factors (see Fig. 1.3). Durene itself is very reactive (relative reactivity = 19) hence one initiates the reaction at relatively low temperatures and pressures (150 psi and 138°C) (see Fig. 1.3). When the first methyl group is oxidized to 1-carboxy-2,4,5-tetramethylbenzene, the reactivity drops to 3.3. The temperature, pressure and catalyst concentrations are therefore increased to accommodate this change. The sequence is repeated for the oxidation of the third, then the fourth methyl group which drop in reactivity from 3.3 to 0.78 to 0.08. One ends up at a final pressure of 450 psi and temperature of 204°C [34].

1.8. Deactivation mechanisms

This is defined as a substance which decreases the rate of oxygen uptake. In theory, anything which affects: (a) the steady state concentration of the benzylic radicals, (b) the steady state concentrations of Co(III) and Mn(III), and (c) and the chemical form of the catalyst can potentially deactivate the system.

(1) Anti-oxidants. The free radical nature of the MC method is best illustrated by the strong deactivation that occurs when trace amounts of substances such as phenols, sulfides, primary amines, etc. are added to an MC oxidation. Phenols deactivate by replacing the short-lived benzylic radicals by long-lived phenolic radicals. Phenols are constantly forming as by-products during an MC oxidation [12] hence a constant depression of the rate constantly occurs. If a given reagent does not initiate under MC conditions, it should be checked for the presence of trace amounts of these anti-oxidants. Reagents which are themselves anti-oxidants can be masked to allow the methyl group to be oxidized. This has been done via acetylation for phenols [73] and amines [44,45] and via methylation for phenols [162].

(2) Water is a strong deactivator in MC oxidations (see Figs. 1.2 and 1.4). The reduction in rate, as the water concentration is increased from 5 to 20%, varies from 35 to 77% depending upon the type of catalyst. Similar examples from the oxidation of *p*-xylene and *m*-xylene can be found in reference [46]. Since one mole of water is generated for every methyl group that becomes oxidized to an aromatic acid, the problem is intrinsic to the method. The concentration of water will increase during a batch oxidation and the maximum amount of water deactivation will be present at the end of the reaction — at the time when maximum catalyst activity is normally desired since the reagent is at its lowest concentration. Polymethylbenzenes can form very high concentrations of water during their reaction (see Table 1.7). This problem can be partially overcome by: (1) increasing the catalyst concentration (see Fig. 1.4), (2) by withdrawing and condensing the vapor above the liquid during the reaction since it will be water rich, and (3) by using the most active catalyst (see Section 3 and Fig. 1.2). Continuous addition of acetic anhydride is also reported [47]. The mechanism of water poisoning is not known. There is evidence that hydrogen bonding of the water in acetic acid decreases the reactivity of peroxides [48]. Increasing water concentration also decreases the rates at which Co(III) oxidizes Mn(II) and Mn(III) oxidizes bromide [6,65].

(3) Catalyst metal precipitation by aromatic acids. The MC method is dependent upon the concentration of soluble forms of cobalt and manganese. The intermediates and product aromatic acids can potentially react and precipitate the catalyst metals and hence reduce the rate of reaction or terminate it. For example 1,2,3-tricarboxy-, 1,2,4-tricarboxy-, and 1,2,4,5-tetracarboxybenzene (hemimellitic, trimellitic and pyromellitic acid respectively) are known to precipitate the catalyst metals. Pyromellitic acid forms very insoluble cobalt and manganese salts which, under the proper circumstances, can completely terminate a MC reaction [49]. The precipitation can be avoided by: (a) increasing the water concentration in the reactor, (b) by decreasing the pH and (c) by increasing the bromide concentration [34,50].

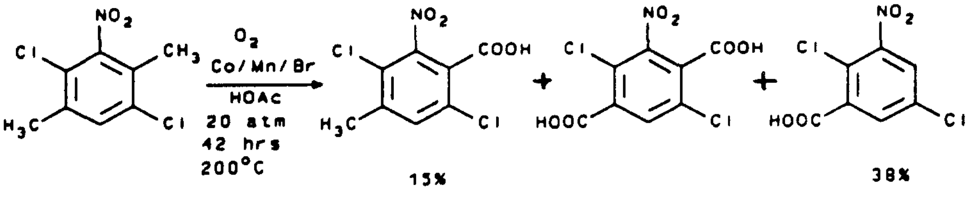
The driving force for precipitation is not chelation, but rather hydrogen bonding [34,51]. The crystal structure of the cobalt(II) complex of acetate (which is very soluble in acetic acid) has been compared with the trimellitate, and pyromellitate compounds. Interestingly, the coordination sphere of cobalt(II) of the trimellitate compound is essentially the same as cobalt(II) acetate tetrahydrate — four water molecules in a square planar array around the cobalt and a single carboxylate oxygen from each trimellitate monoanion in the trans positions. Why then, is cobalt(II) acetate very soluble in acetic acid/water solutions while cobalt(II) trimellitate is relatively insoluble? The answer lies in the fact that 26 hydrogen bonds exist in each cobalt-trimellitate moiety. All six of the carboxylate oxygens in both trimellitic anions are involved in hydrogen bonding interactions. This extensive hydrogen bonded array links together adjacent molecules and undoubtedly is the cause of the TMLA complex of cobalt being more insoluble than the acetate. Since hydrogen bonding interactions are 3–10 kcal/mol, the driving force for precipitation can be 78–260 kcal/mole. The crystal structure of cobalt(II) pyromellitate is similar to the trimellitate. There is no chelation of the *ortho*-carboxylic acid groups with the metals. Instead the cation consists of hexaaquo metal cations, $[M(H_2O)_6]^{+2}$, and the dianion of pyromellitate with an extensive hydrogen bonding network [51].

(4) Deactivation by aromatic acids. Even if the aromatic acids do not precipitate the catalyst metals, their presence can reduce the rate of reaction. This was first reported during the oxidation of *o*-toluic acid with and without the presence of benzoic and *ortho*-phthalic acids [5e]. This has also been shown by spiking selected aromatic acids into an MC oxidation and observing decreased rates of oxidation [5a]. Two carboxylic acid groups in the *ortho*-position on the ring deactivate more strongly as do increasing number of carboxylic acids on the ring. Labeling experiments and correlations between the aromatic acid concentration and vent carbon dioxide concentration suggest that the mechanism is decarboxylation of the aromatic acids. Decarboxylation (see reaction 1.13 above), reduces the steady state concentration of

the cobalt(III) in the catalytic cycle (see Fig. 1.1). Decarboxylation also occurs from manganese(III) but the rate is much less than of cobalt [1]. The concentration of carboxylic acid groups can build up to very high concentrations when polymethylbenzenes are being oxygenated (see Table 1.8). The water generated from the reaction is considered to be part of the solvent in Table 1.8.

Many aromatic acids are relatively insoluble in acetic acid [17] and precipitate during the reaction (see Table 1.9). This is a desirable because it avoids some of the decarboxylation and should be maximized if possible. If the desired product is an aromatic acid and this acid has only partial solubility in the reaction mixture, one should attempt to perform the experiment at a temperature as low as possible to minimize its concentration in solution. For example, the degree of precipitation of isophthalic acid increases from 72 to 97.7% from 200 to 100°C.

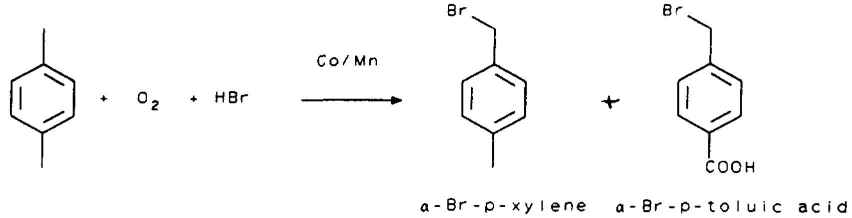
Increasing the number of carboxylic acids on the ring generally causes increasing decarboxylation of the aromatic acids. We may thus anticipate that any reagents with initially low electron density may be particularly prone to decarboxylation. A good case in point is the MC oxidation of 2,5-dichloro-3-nitro-*p*-xylene. MC oxidation results in the formation of 38% of the mono-decarboxylated product presumably via the ready decarboxylation of 2,5-dichloro-3-nitro-terephthalic acid [52]:



(1.18)

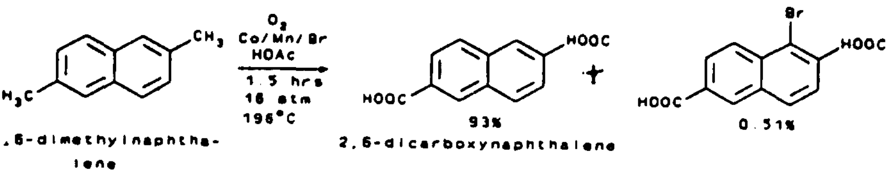
Extensive decarboxylation of *o*-nitrobenzoic during the oxidation of *o*-nitrotoluene above 182°C may be the reason for a decreased yield to this acid (see Section 4.5).

(5) Formation of organic bromides. The catalytic cycle depends upon the bromine existing in the ionic form. One should always expect to see benzylic bromides during an MC oxidation. During the oxidation of *p*-xylene both benzylic bromides are seen [12]:

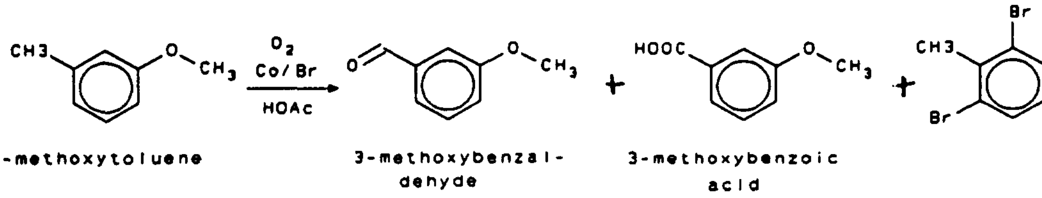


(1.19)

Additionally benzylic bromide formation has been observed during the oxidation of toluene (2.0% yield based on reagent [53,54]), 2-chlorotoluene (1.6–2.3%, [55]), 2,4-dichlorotoluene [56], *m*-phenoxytoluene [57], 4-nitrotoluene [58], and diphenylethane [59]. Under anhydrous conditions, the presence of these benzylic bromides do result in a decrease in catalytic activity [11]. Ring bromination, in trace amounts, can be found during the oxidation of *p*-xylene [12] but not enough to result in a significant reduction of the bromine concentration. Significant amounts of ring bromination occur where they are strongly favored — in naphthalene derivatives, where bromination in the 1-position is particularly favored [60] and in phenylethers because of their high electron density [39,61]:



(1.20)



(1.21)

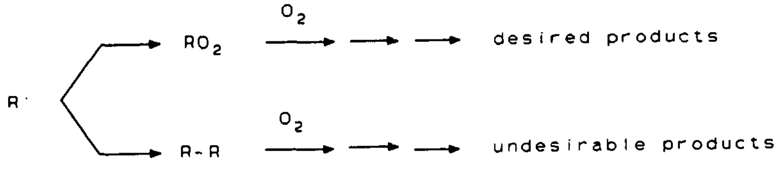
It is reported that the rate of oxidation of 2,6-dimethylnaphthalene decreased as the bromide ion was converted to the inactive form of organic bromide [62].

Ring bromination of *p*-xylene appears to occur much more extensively in water since bromoterephthalic acid is reported in 0.84% yield with a Co/Mn/Br catalyst but 0.0% in acetic acid [33]. It is also reported for V/Br systems (see Section 4.5).

(6) pH of the medium. The presence of strong acids, such as trichloroacetic acid [28], deactivate or terminate MC type oxidations. Thus, for example, the oxidation of alkyl derivatives of benzene sulfonic acid cannot be performed. However, MC oxidation of their salts have been reported (see Section 4.5).

(7) Specific metals. Metals such as vanadium and copper [64,65] are, in ppm concentrations, severe inhibitors to the oxidation. During the oxidation of *p*-xylene, the rate was reduced by 20% when the cobalt was replaced by copper [66]. Obviously, one must pay attention to the metallurgy in the process since mixtures of Co/Mn/Br and acetic are corrosive and copper containing metals could therefore severely inhibit the oxidation. The reason why certain metals are strong poisons is not known. They could react rapidly with the peroxy radicals in the chain mechanism (see reaction 1.6) or act as a shunt by reacting with the cobalt(II),(III), manganese(II),(III), Br^- species (see Fig. 1.1).

(8) Insufficient oxygen diffusion rate. The danger with easily oxidizable feedstocks such as *p*-methoxytoluene is that one may use too high a temperature or pressure which may result in depletion of the dissolved molecular oxygen and subsequent dimerization of the carbon centered radicals:

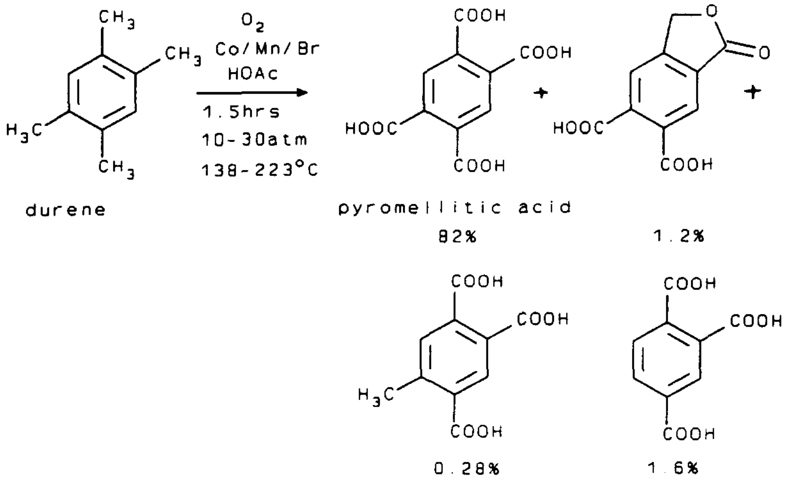


(1.22)

Low yields and, often, dark-colored products, result. In practice, one normally monitors the oxygen content in the vent and keeps it at a measurable amount — such as 4–5% [67]; i.e., a slight excess of oxygen over the stoichiometric amount is desirable. Semi-continuous or continuous operations are superior to batch operations from this point of view since oxygen depletion can occur more easily during the initial time period in batch oxidations. Inferior optical properties of the products from batch operation over continuous operations have been documented for the oxidation of *p*-xylene, *o*-xylene, mesitylene [67] and 4,4′-dicarboxydiphenylether [68].

1.9. Major by-products and intermediates normally encountered at the end of a MC oxidation

At least 32 different products have been reported for the MC oxidation of *p*-xylene to terephthalic acid. However most of these form in $<0.1\%$ yield [12]. The major by-products formed in higher yields than 0.1% are typically: (1) carbon dioxide, (2) methyl acetate, and (3) an aromatic acid containing one less carboxylic acid than expected from the reagent (for example benzoic acid from the oxidation of *p*-xylene). Two intermediates are also normally present associated with the oxidation of the last methyl group — the unreacted methyl group itself (1,2,4-tricarboxytoluene during the oxidation of 1,2,4,5-tetramethylbenzene) and the aldehyde. With *o*-methyl groups a phthalide (internal ester by the reaction of the alcohol on one methyl group with the carboxylic acid on the other) will also form. Typical is in the oxidation of durene where pyromellitic acid is obtained in 82% yield, the phthalide in 1.2% yield, the tricarboxytoluene in 0.28% yield and trimellitic acid in 1.6% yield [49]:



(1.23)

In the MC oxidation of *p*-xylene, 4-carboxybenzaldehyde is present in the product, typically 0.2–0.3% by weight [69]. Since 4-carboxybenzaldehyde is a chain-stopper during PET manufacture, great efforts are expended in reducing its concentration. Amoco uses hydrogenation in water to reduce the 4-carboxybenzaldehyde to *p*-toluic acid in very low concentrations [17]. The latter is usually called the Amoco PTA (purified terephthalic acid) process.

1.10. Comparison of gas and liquid phase oxidations

The advantage one has when performing liquid phase oxidations over gas phase oxidations is often not appreciated:

(1) Simpler engineering. Liquid phase oxidations can be performed in CSTR's (continuously stirred tank reactors) rather than multi-tubular reactors. The latter are necessary to effectively remove the heat from the solid catalyst during the exothermic oxidation and are expensive to fabricate.

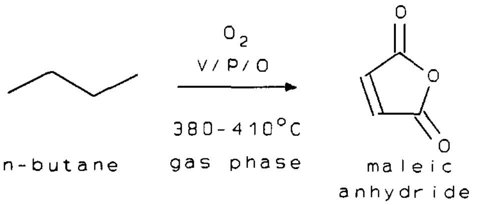
(2) Preparation of the catalyst. In the liquid phase, one adds the various catalyst components in the appropriate ratios. Solid state catalysts generally are multi-step, highly specific syntheses. The preparation of V/P/O catalysts used in maleic anhydride [70] is a good example.

(3) Gas phase processes have a fixed number of catalytic sites hence one cannot vary the catalyst concentration. The number of catalytic sites in liquid phase oxidations are limited only by the solubility of the catalyst components. The number of catalytic sites can be varied from reaction to reaction and during the reaction itself.

(4) Gas phase processes are energy intensive since the hydrocarbon must be vaporized and heated to typically 300–500°C and the hydrocarbon concentration is typically less than 3% in air.

(5) The space time yields, all else being equal, is about 10 times larger in liquid phase oxidations than in gas phase oxidations.

One advantage of gas phase over liquid phase processes, is that the product does not have to be separated from a solvent. As already mentioned, the insolubility of many aromatic acids in acetic acid/ water mixtures makes this a mute point in many MC type reactions (although removal of traces of acetic acid is still necessary). Because of the fixed sites in heterogeneous catalysis, occasionally very spectacular selectivity can be achieved. An example is the oxidation of n-butane to maleic anhydride in the gas phase, in which 50–55% mol yields can be achieved [70]:



(1.24)

In contrast the MC oxidation of n-butane yields acetic acid in about a 80% yield (see Section 14.1).

2. Solvents used in the MC method

For the last five years, the author has developed a database on the oxygenation of hydrocarbons which is carried on Molecular Design Limited's REACCS software. The database includes virtually all references on the preparative aspects of MC type oxidations. On 11/18/93, this database was searched for the solvents used for all of the MC type reactions; i.e., reactions where bromine is used in conjunction with other metals. The solvents used in these 680 reactions, with the number of citations in parenthesis, are in Table 2.1. The total number of citations is higher than 680 because more than one reference may be cited for each reaction. Specific references to many of these solvents will be found in the Tables in Sections 4–14.

Ninety-six percent of the solvents contain the carboxylic acid functional group. Even in 4% of the cases where a carboxylic acid is not used, carboxylic acids will be present almost immediately in the solvent for the following reasons:

(1) Where acetic anhydride is used as a solvent, it will quickly react with the water generated in the reaction to generate acetic acid.

(2) Often the initial reagent is itself a carboxylic acid, hence, the reagent provides the carboxylic acid group. An example is the oxidation of *p*-toluic acid to terephthalic acid.

(3) In 'solventless' reactions, where initially one adds only the liquid reagent and catalyst, carboxylic acids will be generated at quite low conversions. Also, the addition of small amounts of carboxylic acid material is claimed to activate solventless oxidation (see Section 3).

Thus virtually 100% of the solvents in MC systems partially or wholly consist of carboxylic acids. There is a complex synergy between the solvent and catalyst (see Section 3).

Table 2.1
Solvents used in MC type oxidations[a]

	Melting point (°C)	Boiling point (°C)
1. Acetic acid (816)	16	116–118
2. Proprionic acid (33)	−24	141
3. Acetic acid/acetic anhydride (25)	–	–
4. Acetic anhydride (15)	−73	138
5. Water (14)	0.0	
6. Benzoic acid (13)	122	249
7. Solventless (7)	–	–
8. *o*-Dichlorobenzene (4)	−18	179
9. Acetic acid/benzene (2)	–	–
10. Acetic acid/chlorobenzene (2)	–	–
11. 1-Hexanoic acid (2)	−3	202
12. Trichloroacetic acid/acetic acid (2)	–	–
13. 1-Hexanoic acid/benzene (1)	–	–
14. Proprionic acid/acetonitrile (1)	–	–
15. Acetic acid/*o*-dichlorobenzene (1)	–	–
16. Stearic acid (1)	67	183
17. Octanoic acid (1)	16	237
18. Acetic acid/benzoic acid (1)	–	–
19. Monochloroacetic acid (1)	62	189
20. Benzoic acid/benzene (1)	–	–
21. Acetic acid/benzophenone (1)	–	–
22. Acetic acid/heptane (1)	–	–

[a] From the Amoco Proprietary Database.

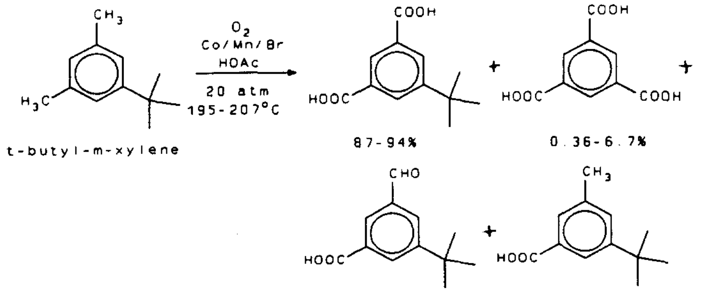
Acetic acid is the solvent of choice for the following reasons:

(1) MC catalysts are apparently significantly active only in solvents containing a carboxylic acid moiety, see above.

(2) Acetic acid is one of the most inert solvents in an autoxidation environment. The longer chained fatty acids, such as propionic acid, are as active as acetic acid, but they autoxidize much more easily to carbon oxides ($CO + CO_2$) and methyl acetate (see Section 14.1).

(3) The enormous volume of commercially produced aromatic acids requires that the solvent be readily available and inexpensive. The carbonylation and autoxidation routes to acetic acid produced 4.59×10^6 tonnes of acetic acid worldwide in 1991. 0.50×10^6 tonnes, 11% by weight, was required as a solvent in terephthalic acid and dimethylterephthalic acid manufacture in 1991 [71].

Acetic acid has a number of other virtues such as: (1) A good range of melting point and boiling point (16 and 116°C) allowing easy handing at room temperature. This can be contrasted, for example to benzoic acid with melting and boiling points of 122 and 249°C. (2) Many aromatic acids are significantly insoluble at room temperature making separation from the catalyst and the solvent easy (see Table 1.9). (3) Either acetic acid or acetic acid/water mixtures is normally a good recrystalization solvent for the products from an MC oxidation. Significant purification of the product occurs when the desired product precipitates. For example, for 5-*t*-butyl-*m*-xylene to 5-*t*-butylisophthalic acid (obtained in 87–94% yield):



(2.1)

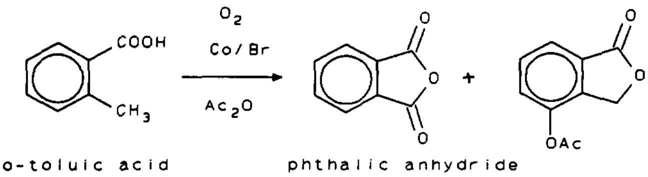
the undesirable 5-*t*-butyl-3-carboxybenzaldehyde, trimesic acid, and 5-*t*-butyl-*m*-toluic acid are all reduced by 90% when recrystallized from 15% water/acetic acid. In addition, the color was reduced by 80%. Water is a much poorer recrystallization solvent [72]. The simultaneous oxidation and precipitation often results in relatively pure products. For example, the MC reaction of *p*-acetoxyacetophenone to *p*-acetoxybenzoic acid is obtained in a 81% overall yield, but 75% of the product precipitates from solution in 96.4% purity [73].

The products from the oxidation of toluene and *o*-xylene, benzoic acid and *o*-phthalic acid respectively, can be used as oxidation solvents. Hence, commercial production of benzoic acid and *o*-phthalic acid can be performed using the products of the reaction as the solvent. There is an extensive patent literature in both areas.

The relative insolubility of the catalyst in solventless reactions can be overcome by using phase transfer compounds (see Section 3.11).

There are claims of higher yields when mixed solvents are used rather than acetic acid alone. The oxidation of *m*-xylene to isophthalic acid gives a 91% in a 1/3 v/v of acetic acid/*o*-dichlorobenzene mixture compared to acetic acid alone which gave a 80% yield. Similarly for acetic acid/benzene, the yields is 90% as compared to 80% for acetic acid alone. Addition of benzene to benzoic acid has a similar effect — increasing the yield from 75 to 90% [74].

Both oxidation and dehydration of *p*-toluic acid to phthalic anhydride occurred when acetic anhydride is used as the solvent. However, a large amount of 3-acetoxyphthalide was also produced. [75]:



(2.2)

Precipitation of the cobalt during the reaction as well as formation of bromoacetic acid occurred.

3. MC catalyst — different types and their function

3.1. Introduction

In retrospect, the combination of cobalt, manganese, and bromine — the most important MC catalyst — may have been anticipated prior to its discovery in 1954. In 1935, cobalt and manganese were known autoxidation catalysts [19]. In 1949, hydrogen bromide was known to strongly activate and reduce carbon oxide formation in gas phase oxidations of alkanes and alkylaromatic compounds [76]. The addition of hydrogen bromide to manganese or cobalt salts in the liquid phase; i.e., the MC catalyst, also results in much higher activity and reduced carbon oxide formation (see Section 1.5). However the catalyst was not discovered in such a scientific way — it was discovered quite by accident (see Section 1.3).

3.2. Types of catalysts

Using the REACCS oxidation database as before (Section 2), we can summarize the catalysts in MC type reactions as follows:

Table 3.1
Reactivity of the most common MC type catalysts [34]

	Relative reactivity	Typical metal/Br ratios (mol/mol)
Mn/Br	1.0	1/0.5–1.5
Co/Br	2.5	1/0.5–1.5
Co/Mn/Br	11	1/1–5/0.2–1.0
Co/Mn/Br/Zr	23	1/1–5/0.2–1.0/0.01

Catalysts with one metal and bromide (number of citations in parenthesis):

Co/Br (146)
V/Br (4)
Mn/Br (39)
Cu/Br (4)
Co/Br/acetate (9)
Ce/Br (1)
Co/Br/Cl (7)

Catalysts with two metals and bromide:

Co/Mn/Br (416)
Co/Mn/Br/Cl (4)
Co/Ca/Br (1)
Co/U/Br (1)
Co/Ce/Br (13)
Mn/Si/Br (4)
Mn/Fe/Br (1)
Co/Cu/Br (5)
Mn/Cu/Br (3)
Co/Te/Br (1)
Co/Mn/Br/acetate (4)
Ni/Mn/Br (2)
Co/Ni/Br (1)

Catalysts with three metals and bromide:

Co/Mn/Zr/Br (32)
Co/Ce/Zr/Br (2)
Co/Mn/Ru/Br (1)
Co/Mn/Mo/Br (1)
Co/Mn/Ce/Br (7)
Ni/Mn/Zr/Br (2)
Co/Mn/Cr/Br (1)
Co/Ce/Zn/Br (2)
Co/Mn/Hf/Br (1)
Co/Mn/Fe/Br (1)

Catalysts which are designated as having 'acetate' are usually prepared by addition of alkali metal acetates or ammonium acetate.

3.3. General characteristics of the catalysts

The reactivity of various catalysts are somewhat dependent upon the reagent used and the catalyst concentrations. A rough guide to the relative reactivity and to metal and bromide ratios is given in Table 3.1. The two most useful catalysts are the Co/Mn/Br and Co/Mn/Br/Zr combinations, vida infra.

91% of the quoted catalysts use cobalt as one of the components probably due to the well-established ability of cobalt to rapidly decompose the primary product of these reactions — the hydroperoxide (see

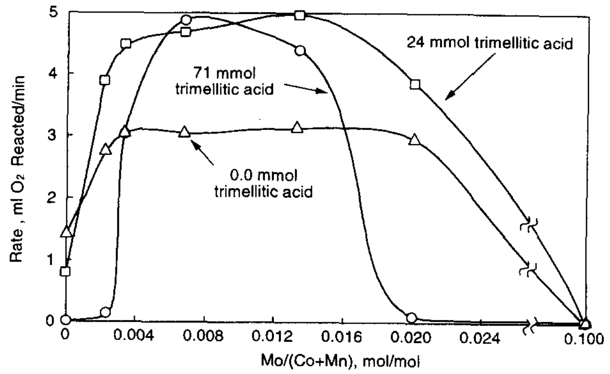


Fig. 3.1. Effect of trimellitic acid on the rate of oxidation of pseudocumene.

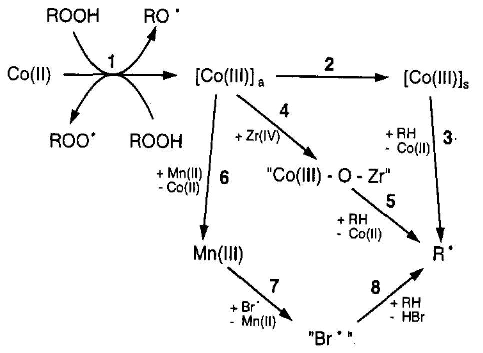


Fig. 3.2. Proposed scheme for Co/Zr and Co/Mn/Br catalysts.

Table 3.2
Examples illustrating the uniqueness of metal/bromide catalysts

Reagent	Br Catalyst	Non-Br catalyst	Reference No.
Toluene	Co/Br reactivity = 8	Co acetate reactivity = 1	[1]
p-Xylene to terephthalic acid	$MnBr_2$ yield = 75%	$MnCl_2$ yield = 30; MnF_2 yield < 30; $Mn(OAc)_2$ yield < 30; MnI_2 yield < 30; NH_4Br yield < 30	[22]
Ethylbenzene	Co/Br, reactivity = 275	Co, reactivity = 1.0; Co/Cl, reactivity = 1.3; Co/I reactivity = 0.0	[47]
Toluene to benzoic acid	Co/Mn/Br yield = 96%	Co/Mn, 0% yield, no oxygen uptake	[120]
Propane or n-butane or n-pentane	Co/Mn/Br, active	Co/Mn, much less reactive	[121]
1-isoAmynaphthalene to 1-naphthoic acid	Co/Mn/Br, yield = 50%	Co/Mn, yield = 37%	[122]
Fluorene to fluorenone	Co/Mn/Br, yield = 76%	Co/Mn, yield = 48%	[123]
p-Toluic acid to terephthalic acid	Co/Mn/Br, yield = 79%	Co/Mn yield = 12%	[40]
p-Tolualdehyde to benzoic	Co/Mn/Br, yield = 90%	Co/Mn yield = 1%	[84]
p-Xylene to terephthalic	Co/Mn/Br, yield = 92%	Co/Mn yield = 0.6%	[84]

Table 3.3
Selected thermodynamic and kinetic values related to the initiation of hydrocarbon oxidation

	$X=F^-$	$X=Cl^-$	$X=Br^-$	$X=I^-$
Reaction 3.4: ΔG, kcal/mol	44[a]	19	6.0	−9.1
Relative rate	no reaction[b]	0.002	1	>>1
ΔG, kcal/mol	−43[c]	−12	3.8	20

[a] These are calculated from the redox potential of cobalt(II)–(III) of −41.1 kcal/mol measured in water; from the values of the oxidation potentials of the halogens in water (66.2, 31.3, 25.1, and 14.1 kcal/mol for F, Cl, Br, I, respectively); and from the gas phase dissociation energies of 37.5, 57.8, 46.1, and 35.8 of F_2, Cl_2, Br_2, and I_2.

[b] Measured in the author's laboratory.

[c] These were calculated from from the bond dissociation energies of 128, 96.8, 81.0, and 65.0 kcal/mol for HF, HCl, HBr, and HI, respectively; and that for toluene of 85 kcal/mol.

Section 1.5). The bi-metallic catalysts were used 2.2 more frequently than the mono-metallic catalysts. Some of the reasons for the higher frequency of use of the bi-metallic compounds than the mono-metallics are:

(1) The bi-metallics in general have higher activity than the mono-metallic compounds. The best established case is with the Co/Mn/Br catalyst. Replacement of 20% of the cobalt by manganese results in an approximately five-fold increase in rate during the oxidation of *p*-toluic acid [8]. The activities of

Co/Br, Mn/Br, and Co/Mn/Br toward *p*-toluic acid are 0.66, 0.58 and 2.83 (in ml of dioxygen reacted/min) [1].

(2) The higher intrinsic activity of the Co/Mn/Br catalyst than the Co/Br allows one to use about 0.66/2.83 = 0.23 times less catalyst. This has an obvious cost advantage since five times less catalyst metals are being used.

(3) Use of lower concentrations of catalyst results in less of the catalyst components in the isolated solid products. Hence, less catalyst and product is lost when the product is separated and washed to remove these catalyst components.

(4) The Co/Mn ratio in the Co/Mn/Br can be varied widely with little loss of activity. Since manganese is currently 10–15 times less expensive than cobalt there is an economic incentive to vary this ratio.

The tri-metallic catalyst Co/Mn/Zr/Br is roughly three times more reactive than the Co/Mn/Br [34] and is commonly used for feedstocks which give unusually unreactive intermediates such as *o*-xylene [77], pseudocumene (1,2,4-trimethylbenzene) [78] and durene [34]. During the oxidation of *p*-xylene to terephthalic acid [69], a 22% reduction in catalyst concentration was possible, upon addition of hafnium to a Co/Mn/Br catalyst while still maintaining acceptable catalyst activity.

The addition of Mo, Zr, Hf have a remarkable catalytic effect since only trace amounts are effective. A Mo/(Co+Mn) mol/mol ratio as low as 0.0022 results in strong activation (see Fig. 3.1) [79]. Similarly in the oxidation of pseudocumene to trimellitic acid, a Zr/(Co+Mn) of 0.041 is reported [78]. In the oxidation of *p*-xylene to terephthalic acid, a Hf/(Co+Mn) ratio of 0.035 is used [69]. High decomposition rates to carbon dioxide and carbon monoxide occur when the zirconium is used in concentration similar to cobalt and/or manganese [78]. Part of the reason that Co/Mn/Br/Zr catalysts are used less frequently than Co/Mn/Br catalysts (416/32 = 13 times less citations) may be because zirconium forms substantially less soluble aromatic acid–metal complexes than cobalt and manganese [34,69,80]. This makes it more difficult to remove from the product after oxidation. A recent patent claims a higher solubility toward aromatic acids for hafnium than for zirconium [69].

3.4. An illustration of the complexity of MC type autoxidation catalysts — the Co/Mn/Mo/Br catalyst

There is a complex synergy between the catalyst metals themselves and the catalyst metals in the presence of aromatic acids. Each point given below will add an increasing complexity:

(1) There is a synergy between Co and Mn in Co/Mn/Br. Both Mn/Br and Co/Br catalysts are active. However, the Co/Mn/Br catalyst is more active than the sum of activities of Mn/Br and Co/Br (see Section 3.3).

(2) There is a synergy between Mo with Co and Mn. Fig. 3.1 gives the rate of oxidation of 1,2,4-trimethylbenzene (pseudocumene) in 20% water/acetic acid in the presence of varying amounts of trimellitic acid (1,2,4-tricarboxybenzene) [79]. Fig. 3.1 illustrates that the presence of very small amounts of molybdenum (added as molybdenum(VI) oxide pentandionate) greatly enhances its activity. For example, in the absence of trimellitic acid and at a Mo/(Co+Mn) mol/mol ratio of 0.003, the rate is enhanced from 1.43 to 3.02 ml O_2 reacted/min.

(3) This synergy can become antagonistic simply by raising the Mo/(Co+Mn) ratio to 0.100 (note the break on the X axis in Fig. 3.1). The rate without Mo is 1.43 ml O_2 reacted/min and 0.0 with Mo. Molybdenum is now a catalyst poison rather than an activator.

(4) Trimellitic acid (the eventual product from the oxidation of 1,2,4-trimethylbenzene) can deactivate the Co/Mn/Br catalyst. This was discussed in Section 1.8. This is illustrated in Fig. 3.1 at a Mo/(Co+Mn) ratio of 0.00 where increasing amounts of trimellitic acid decreases the rate from 1.47 to 0.77

to 0.00 ml O_2 reacted/min. It can also be seen in the Mo containing catalysts since the rate with 71 mmol trimellitic acid present is generally lower than when 24 mmol trimellitic acid is present.

(5) But trimellitic acid can, under the appropriate experimental conditions, activate the autoxidation! The rate of oxidation is higher for a Co/Mn/Mo/Br catalyst with 24 mmol trimellitic acid present than in its absence up to a Mo/(Co + Mn) ratio of 0.020 (see Fig. 3.1). More examples of this activation are discussed in Section 3.10.

We conclude that optimization of MC type catalysts are difficult. For example, when finding a new catalyst, one would normally add roughly the same molar amounts of some substance to a Co/Mn/Br catalyst. Addition of molybdenum, however, at the same concentration as cobalt and manganese would not result in a synergistic interaction, but a strongly antagonistic one! Since activation and deactivation can occur in the presence of selected aromatic acids, both effects could be seen in a given reaction since aromatic acids are the usual products of MC oxidations and their concentration would increase during a batch reaction.

The author has been interested in relating the electronic configuration of metals to their catalytic effects. As an aside, we can note that the poisoning effect of molybdenum at high concentrations may be rationalized by assuming that the predominant oxidation state of molybdenum during oxidation is Mo(VI), a d^0 electronic configuration, and at higher concentrations, significant amounts of Mo(V), a d^1 configuration, may form. In Section 1.8, we have noted that vanadium and copper are strong poisons. Vanadium(IV) has a d^1 electronic configuration and copper(II) is related by the 'hole formalism' to vanadium, since it has a d^9 configuration. It is being suggested that Mo(V) may be forming at higher concentrations and that this is species responsible for the observed deactivation. It would be interesting to determine exactly how metals in d^1 electronic configurations interact with Co(III), Mn(III), and peroxides.

3.5. *Kinetic rationalization of Co, Co/Zr, Co/Mn/Br, and Co/Mn/Br/M (M = Mo,Zr,Hf) catalysts*

Fig. 3.2 gives the kinetically available pathways starting with a RH,ROOH, Co(II), Mn(II), Br^- mixture in 10% water/acetic acid based on extensive kinetic studies by Jones [6] and the author [2]. *It is assumed that the relative reactivity of these catalysts can be rationalized by the rate of generation of the radical, $R^{\cdot}$, starting from Co(II).*

(1) Cobalt catalysts. Using the notation of Jones, the initially formed cobalt(III) species produced from a peroxide is dubbed $[Co(III)]_a$. It is known to re-arrange to another Co(III) species of unknown structure, dubbed $[Co(III)]_s$. $[Co(III)]_a$ is much more reactive than $[Co(III)]_s$ toward bromide, Mn(II), hydrogen peroxide, and (presumably) *p*-xylene [6]. In cobalt catalysts, the reaction of Co(III) with *p*-xylene is sufficiently slow so that it is forced to react with $[Co(III)]_s$ rather than $[Co(III)]_a$ [6]. The sequence is step 1 to step 2 to step 3 (see Fig. 3.2).

(2) Co/Zr catalysts. The addition of zirconium to cobalt catalysts activates the autoxidation of *p*-xylene to terephthalic acid (enhancing yields from 40 to 90%) [81] and cyclohexane to adipic acid [82]. Chester et al. gives kinetic evidence that the equilibria between the different forms is being affected by zirconium and suggest that a Co–Zr complex is forming. Assuming a high reactivity for the latter, this may open up a new pathway, steps 4,5. The small amounts of zirconium necessary to activate these catalysts is believable since $[Co(III)]_a$ is 2–3 orders of magnitude more reactive than $[Co(III)]_s$. We are assuming that the $[Co(III)]_a$–Zr complex is also very active. Steinmetz et. al. [82] observes that hydrogen peroxide with a Co/Zr catalyst generates Co(III) while Co itself does not. He suggests that k_1 of the Haber–Weiss cycle (Eqns. 1.10 and 1.11) is being favored over k_2, hence, higher $[Co(III)]_a$ (and $[Co(III)]_s$) would be observed. Both mechanisms may be occurring simultaneously.

(3) Co/Mn/Br catalysts. The addition of Mn(II) with cobalt results in a new pathway since step 5 is 1,040 times faster than step 2 [2]. A Co/Mn/Br catalyst is now able to utilize the highly reactive $[Co(III)]_a$ which a Co catalyst cannot. Steps 6,7,8 are much faster than step 3 [2] making the MC catalyst much more reactive than a cobalt only catalyst.

(4) Co/Mn/Zr/Br catalysts. The two suggestions made for Co/Zr catalysts to explain their higher reactivity relative to Co catalysts, would not apply to Co/Mn/Br catalysts because the rate determining step, step 7, occurs after the generation of cobalt(III).

The author has observed that continuous addition of low concentration of phenols deactivates MC oxidation, but not in the presence of zirconium. This suggests that zirconium(IV) may complex with phenol and hence avoid formation of the phenoxy radical. Phenols oxidize readily to carbon dioxide under MC conditions. In the presence of zirconium(IV), we would postulate that the phenol is oxidized while bonded to the Zr. The fact that this family of activators is active at very low concentrations is consistent with this hypothesis since the steady state concentration of phenols is very low during oxidation. Hf, Zr (and Mo in its VI oxidation state) are all d^0 metals which prefer coordination to oxygen donors (rather than nitrogen donors as do the transition metals). The fact that the group I, II, III non-transition elements do not strongly activate may be due to the fact that Hf(IV), Zr(IV), and Mo(VI) have much higher polarizing power hence complex more strongly than the former.

3.6. *Other types of catalysts*

The virtue of the Ni/Mn/Zr/Br catalyst is that it is equally active as a Co/Mn/Br catalyst but uses less expensive metals (Ni and Mn) than cobalt [83]. Fig. 1.2 gives the reactivity of these and related catalysts. Addition of Ni activates a Mn/Br catalyst and zirconium addition usually provides additional activity to any metal/bromide combination. The relative reactivity is Ni/Br < Mn/Br < Ni/Mn/Br < Co/Mn/Br < Mn/Zr/Br < Ni/Mn/Zr/Br < Co/Mn/Zr/Br.

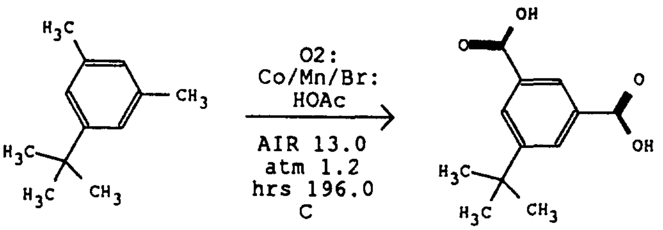
Non-transition metals, which are present in the Co/Ca/Br, Mn/Si/Br, Co/Ce/Zn/Br catalysts, may be present to change the acetate concentration (see Section 3.12). The V/Br catalyst appears to be limited in use to water as a solvent [63,84].

The addition of polysiloxane to Co/Mn/Br is claimed to activate and produce higher yields. For example terephthalic acid yields obtained with and without the polysiloxane were 59% with and 54% without. These are rather low yields however, even in the presence of the polysiloxane, since yields of 90–95% are often reported (see Table 4.2).

Addition of ruthenium in catalytic amounts allows one to overcome the deactivating effects of N- and S-containing compounds (i.e., quinoline, indole, 2-naphthylamine, thionaphthene) during the oxidation of 2,6-dimethylnaphthalene to 2,6-dicarboxynaphthalene. For example, the yield of 46% in the presence of thionaphthene was increased to 75% by addition of $RuCl_3$ to a normal Co/Mn/Br catalyst [85].

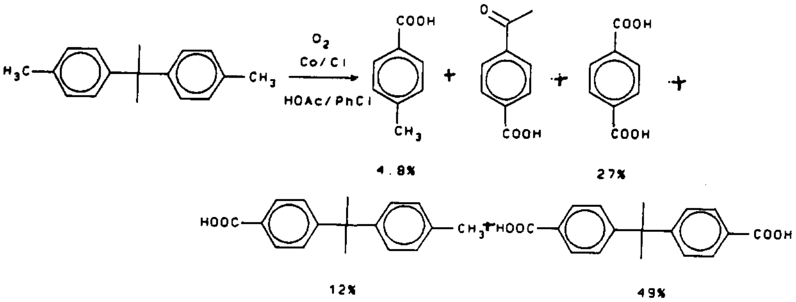
There are four reports for the use of metal/chloride/bromide catalysts [86,87,89,89]. In the oxidation of durene to pyromellitic acid, the presence of chloride increased the reaction rate, giving a lighter-colored product [88]. The cobalt(II) acetate/sodium bromide catalyzed oxidation of toluene was accelerated by added $CoCl_2$. They proposed, without experimental evidence, that the reason was due to polynuclear complex formation [87].

While metal/bromide and metal/bromide/chloride catalysts are both selective in benzylic oxidation, metal/chloride catalysts are not. For example, in the oxidation of 4-*t*-butyltoluene to 4-*t*-butylbenzoic acid, reported yields are 87% [90], 87% [91], and 96% [40] for Co/Mn/Br catalysts but only a 7.7% yield is obtained with a Co/Cl catalyst [89]:



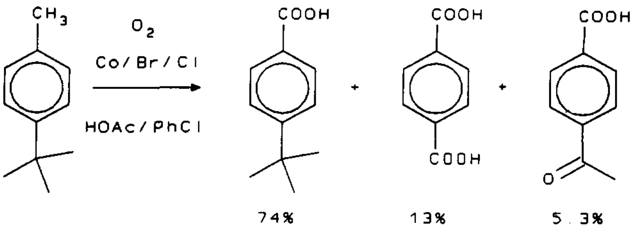
(3.1)

Extensive carbon–carbon bond cleavage is evident. Similar results are obtained with 2,2′-di-*p*-tolylpropane. A 90% yield to 2,2′-di(*p*-carboxyphenyl)propane is obtained with an MC type catalyst [40] while only a 49% yield is obtained using Co/Cl [89].



(3.2)

The selectivity in a Co/Br/Cl catalyst is similar to a Co/Br catalyst giving much higher yields of *t*-butylbenzoic acid relative to terephthalic acid [89]:



(3.3)

While a Co/Br/Cl catalyst is active and selective, a Co/Br/I catalyst has been reported not to be active toward ethylbenzene (reactivity = 0.0). These observations will be rationalized in Section 3.7.

It is claimed that Co/Ce/Br catalysts are more active than Co/Mn/Br catalysts in acetic anhydride during the oxidation of decahydronaphthalene [41].

It has been reported that triethanolamine affects the activity of Co/Br catalysts during the oxidation of 1,3,5-trimethylbenzene (mesitylene) [42,43,94]. During oxidation of *p*-xylene in acetic acid, cobalt/bromide/pyridine mixtures with the molar ratio Co:Br:Py = 1:2:1–2 have the highest catalytic activity in the first stage of the reaction [95].

3.7. Comparison of MC and non-MC catalysts in acetic acid

The MC catalyst is defined as a combination of bromide with metals. The uniqueness of bromide anion is important and hence has been documented in many of the early patents in this area. Table 3.2 illustrates the difference of metal and metal/bromide catalysts run under identical conditions as taken from these patents. Much lower rate of oxygen uptake and yields to aromatic carboxylic acids is characteristic with non-bromine containing catalysts.

Bromide is an active catalyst without the metal present. For example with oxidations of water soluble feedstocks, such as *p*-toluic acid, with no catalyst, the yield is 7% terephthalic acid, with HCl 15% yield, and with HBr 89%. The conditions necessary however are extreme — two hours at 31 atmospheres of oxygen. Substitution of the water by acetic acid allows one to obtain a 89% yield in one hour at 5.6 atmospheres oxygen [84].

3.8. Rationalization of the uniqueness of cobalt/bromide catalysts and of observations made in metal/bromide/chloride catalysts

Co/F, Co/Cl and Co/I autoxidation catalysts are much less active than Co/Br catalysts. These observations can be rationalized by assuming a simple mechanism of initiation:

$$\mathrm{Co(III)} + \mathrm{X} \rightarrow \mathrm{Co(II)} + \mathrm{X} \quad \mathrm{X} = \text{halogen anion} \qquad (3.4)$$

$$\mathrm{X}^{\cdot} + \mathrm{PhCH_3} \rightarrow \mathrm{PhCH_2^{\cdot}} + \mathrm{HX} \qquad (3.5)$$

The spontaneity of reaction 3.4 increases I > Br > Cl > I (see Table 3.3), while that of reaction 3.5 is opposite, F > Cl > Br > I. These values are only approximate since they are based on redox potentials in water and the solvation energies of $X^{\cdot}$, $PhCH_3$, and $PhCH_2$. are not considered. The most thermodynamically 'neutral' situation occurs for Br –. Bromide has the ability to do both reactions well, while the others are inhibited by either reaction 3.4 or 3.5. Perhaps more pertinent, however is the rate of these reactions. Reaction 3.4 is not observed to occur for fluoride, is quite slow for chloride, and much faster for bromide, with iodide being the fastest. Iodide does not function well because of its inability to participate in reaction 3.5

Co/Br/Cl catalysts behave similar to metal bromide catalysts because the reaction of bromide with Co(III) is much faster than its reaction with chloride hence the mechanism remains essentially the same as a metal/bromide catalyst. The author has observed that a displacement reaction occurs upon addition of sodium chloride to a metal/bromide catalyst:

$$\mathrm{X{-}Ph{-}CH_2Br} + \mathrm{NaCl} \rightarrow \mathrm{X{-}Ph{-}C{-}H_2Cl} + \mathrm{NaBr} \qquad (3.6)$$

The enhanced activity by addition of NaCl can be explained by the inactive bromide, as a benzylic bromide, becoming 'active' bromide as sodium bromide via this displacement reaction. The inactivity of the Co/Br/I catalyst can be explained by the fact that iodide reacts faster with cobalt(III) than does bromide and 'I' does not have sufficient energy to react with a methylbenzene to give its benzylic radical, reaction 3.5.

3.9. Sources of active bromide

Active sources of bromine are compounds that can easily form the bromide ion in acetic acid/water solutions under the conditions employed in the oxidation. The usual bromide sources are either hydrogen bromide or sodium bromide. In addition potassium bromate, elemental bromine, and organic compounds that are relatively easily solvolyzed to HBr such as benzyl bromide can be used. Those in the latter category are bromoform [47], acetylene tetrabromide [90], and even bromobenzene [74], the latter in high concentrations.

3.10. Activating effects of carboxylic acids

There are many puzzling observations in MC oxidations. One of the most interesting is that the presence of carboxylic acids can both activate and deactivate MC oxidations and it is this effect that is responsible for some for these puzzlements. Arthur Hay, one of the early workers in the area of MC oxidation states: "... it is believed that the cobalt, bromine and carboxylic acid constituents of the catalyst combine in some unusual manner to produce the unique catalyst of this invention" [96]. The catalyst is not just a combination of metals with bromide, but carboxylic acids are probably also contributing an important role. We have already discussed deactivation by acids such as 1,2-dicarboxy, 1,2,4-tricarboxy-, and 1,2,3-tricarboxybenzenes (see Section 1.8) and, by way of introduction, activation in Section 3.4.

With Co/Mn/Br catalysts, addition of aromatic acids to MC oxidations usually activate the oxidations at relatively low concentrations and then deactivate as the concentration is further increased. This is reported for benzoic acid, *o*-phthalic acid and 1,2,4-tricarboxybenzene (trimellitic acid) [34]. During the Co/Mn/Br catalyzed oxidation of 1,2,4-trimethylbenzene (pseudocumene), there is a 100% drop in rate when 12 wt.% of 1,2,4-tricarboxybenzene was added. Under identical circumstances except using a Co/Mn/Br/Zr catalyst, 1,2,4-tricarboxybenzene addition now exhibits a 38% increase in rate. This is similar to the Co/Mn/Mo/Br example given in Section 3.4. Maleic acid has also been reported to activate the oxidation of 2-methylnaphthalene. The average rate of oxidation with maleic acid was 0.130 mol naphthoic acid/liter/hour and without the maleic acid the rate is 0.113 mol/liter/hour. In the oxidation of 2-methylthiophene, addition of cobalt thiophene-2-carboxylate reduced the induction period [99].

It has been reported that starting with cobalt dibromide, addition of acetates of various metals eliminates the induction period [110]. This is a pH effect which will be discussed in Section 3.12.

Similarly solventless processes operated in the batch mode are often sluggish and small amounts of carboxylic acid may be initially added. Thus small amounts of benzoic acid are added in solventless *o*-xylene reactions [77] and toluene [100] which result in faster rates of initiation. In the solventless oxidation of 2,4-dichlorotoluene, addition of 2,4-dichlorobenzoic acid (the product of the reaction) enhanced the yield from 5 to 55% and eliminated the induction period [101]. Since carboxylic acids are generated from the reagent soon after the reaction is initiated, these systems are self-activating.

Both the activation and deactivation phenomena may have the same explanation differing only by degree. As discussed earlier, Section 1.8.4, there is evidence that the deactivation is caused by excessive decarboxylation (see reaction 1.13). This significantly competes with the desired catalytic cycle:

$$\mathrm{Co(III)} + \mathrm{Mn(II)} \rightarrow \mathrm{Co(II)} + \mathrm{Mn(III)} \qquad (3.7)$$

(ligands dropped for simplicity).

However, decarboxylation also generates an alkyl or aryl radical which can initiate the chain reaction and enhance the rate (see reaction 1.4). These two competing phenomena can explain the activation at low carboxylic acid concentrations and the deactivation at high concentrations.

3.11. Solventless oxidations

Quaternary ammonium and phosphonium bromide salts are effective in solventless oxidations. Water is necessary to initiate the oxidation, but excess water decreases the rate of reaction. Quaternary iodide salts are ineffective, similar to what one finds in MC oxidations. It is claimed that the usual corrosion aspects of using bromide is eliminated in this process because of the absence of an aqueous phase [102,103]. Perhaps related is the use of lipophilic quaternary ammonium or phosphonium compounds and S-alkylisothiouronium cations as phase transfer catalysts during the oxidation of *p*-xylene in water [104–106].

3.12. pH effects in MC oxidations

Many puzzling features of MC type oxidations can be rationalized by the realization that the catalyst is fairly strongly affected by the pH (negative log of the hydrogen ion concentration) in acetic acid–water mixtures. Only a brief outline to aid in the understanding of the pH effect will be given here. The solvent system definition of acids and bases is particularly helpful in this regard. The definition of an acid is a substance which produces (i.e., increases the concentration of) the cation characteristic of the solvent. The definition of a base is a substance that increases the concentration of the anion characteristic of the solvent [107]. Since in water we have the equilibrium:

$$2H_2O \leftrightarrow H_3O^+ + OH^- \qquad (3.8)$$

substances such as HBr, NaOH, and Na acetate are acids, bases, and salts respectively. In acetic acid we have:

$$2HOAc \leftrightarrow H_2OAc^+ + OAc^- \qquad (3.9)$$

HBr is known to be a strong acid in acetic acid. Sodium hydroxide will be a base because it reacts with acetic acid to produce the acetate anion and water. Sodium acetate, which was a salt in water, is now a strong base in acetic acid since it dissociates to give the acetate anion. In acetic acid/water mixtures, the hydroxide ion and protonated acetic acid (H_2OAc^+) are stronger bases and acids than the acetate anion and H_3O^+ respectfully. They will be subsequently 'leveled' to the concentration of acetate and hydronium ion. We then have:

$$HOAc + H_2O \leftrightarrow H_3O^+ + OAc^- \qquad (3.10)$$

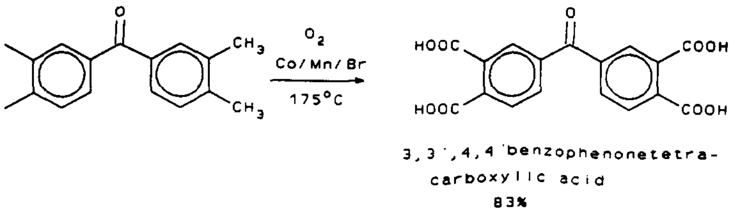
The hydronium cation is now characteristic of an acid and the acetate is characteristic of a base in acetic acid/water mixtures. There is a significant difference between water and acetic acid/water mixtures in the types of 'salts' commonly added to MC oxidations. In water, Co(II) bromide or acetate are both salts which affect the pH only slightly. This is not true in acetic acid–water mixtures however. The pH will be affected differently because cobalt(II) acetate dissociates to give the acetate anion while cobalt(II) bromide will be approximately neutral (the bromide anion is an anion of a strong acid in acetic acid just as it is in water).

The pH will affect autoxidations in two ways. The structure of the coordination compounds will vary, similarly as pH effects the coordination sphere in water. In water, a variety of different compounds of the type $M(H_2O)_n(OH)_m$, as mononuclear and polynuclear compounds, typically form. Secondly, the redox potential will be significantly changed; i.e., the oxidizing potential of the metals both in water as well as in acetic acid/water solutions vary. For example, in water cobalt(III) forms spontaneously from cobalt(II) and dioxygen at pH = 8 but does not at a pH = 1 since the redox potential of Co(II) to Co(III) changes from 0.17 V to 1.84 V. Similarly, the redox potential in 90% acetic acid/water of Mn(II)/Mn(III) changes as a function of the acetate concentration [108]. Since changes in kinetics usually accompany thermodynamic changes, a strong effect on the rates of the redox cycles in MC oxidations (see Fig. 1.1), are expected.

Both the activity and selectivity of MC oxidations are affected by changes in the acetate concentration; i.e., pH. For example with the Co/Mn/Br catalyzed oxidation of 1,2,4-trimethylbenzene (pseudocumene) at 13% water starting with the neutral salts cobalt(II) tetrafluoroborate and manganese(II) bromide [109] we have:

Acetate/metal	Rate (ml O_2/min)	Vent CO_2 (%)	CO_2/rate (%)
0.0	0.0	–	–
1.0	0.08	0.069	0.85
2.0	3.48	0.275	0.0790
3.0	2.95	0.182	0.0617
4.0	2.73	0.179	0.0655

The rate of carbon dioxide formation during the oxidation is indicated by the concentration of carbon dioxide in the gas stream being vented from the reactor and is one indicator of the selectivity of the reaction. Many more examples of this type are given in ref. [109]. This effect has been seen in different ways by many others, some who do not attribute it as a pH effect. Thus starting with cobalt(II) bromide, many people have observed an long induction period [65,66,110,111] and that addition of sodium(I), barium(II), and zinc(II) acetates eliminates this induction period [110,112]. The presence of acetate has been reported to enhance the yield of 4,4'-dicarboxybiphenyl from 4,4'-dimethylbiphenyl [113,114]. It has been reported that better yields are obtained in the reaction:



(3.11)

in the presence of monochloroacetic acid (83%) than without (26%) [115].

3.13. *Effect of the bromine/metals ratio*

There are three reports on the activity of cobalt/bromide catalysts as a function of the Br/Co ratio. In the oxidation of *o*-xylene at an initial cobalt concentration of 0.100M, the rate rapidly increases as the Br/Co ratio increases to 1.0, then the rate falls to zero at a ratio of 2.0 [47]. Similarly, during the oxidation of *p*-xylene and at a cobalt concentration of 0.050 M, the rate rapidly increased to a maximum rate at 1.0, but then the rate remains constant up to a Br/Co = 9. When the cobalt concentration was lowered to 0.020 M, the maximum rate occurred at a Br/Co = 1.7 [66]. The maximum rate of oxidation of 1,3-dimethyl-2,4-dichloropyzazole occurs at a Br/Co ratio (mol/mol) of 0.50 [116]. Subtle changes in selectivity can occur by variation of the ratio. For example, in the oxidation of 5-*t*-butyl-*m*-xylene, reaction 2.1, increasing the bromine/(Co + Mn) ratio increased the amount of undesirable trimesic acid. As the ratio was increased from 0.20 to 1.0, the trimesic yield increased from 0.70 to 6.64% [72].

3.14. *Effect of the manganese/cobalt ratio*

The variation of the Mn/Co ratio in the catalyst does affect the selectivity and yield. Thus during the oxidation of 3,3'4,4'-tetramethylphenyl sulfone, the yield was 99.0% at a Co/Mn ratio of 0.1 and 87.1% at a ratio of 0.001. The purity of the product similarly was affected as it decreased from 96.8 to 84.6% as the Mn/Co ratio was changed from 0.1 to 0.001 [117]. During the oxidation of 1,3-dimethyl-2,4-dichloropyrazole, addition of $Mn(OAc)_2$ to $Co(OAc)_2$ at a constant bromide concentration resulted in a maximum rate of reaction at a mole ratio of 0.2–0.3 [116]. The variation of this ratio affects the amount of acetic acid decomposition and overall observed losses due to carbon dioxide and carbon monoxide formation [1,118,119]. Ring degradation during the oxidation of 2,6-dimethylnaphthalene occurs to produce 1,2,4-tricarboxybenzene (trimellitic acid). This undesirable by-product was reduced from 3.1 to 2.1% by increasing the Mn/Co ratio (mol/mol) from 1:1 to 3:1 [60].

4. MC oxidation of methylbenzenes

4.1. Introduction

We now begin to discuss the scope of MC oxidation; i.e., the various classes of organic compounds that have been oxygenated.

There exists an enormous literature describing the results when hydrocarbons are subjected to MC type oxidations. These will be summarized in tables, such as Table 4.1, and figures, such as Fig. 4.1. A few comments need to be made on designations given in these tables. For catalysts designated as Co/Mn/Br or Ni/Mn/Zr/Br, the metals are nearly always added as their acetates and the bromide in an ionic form,

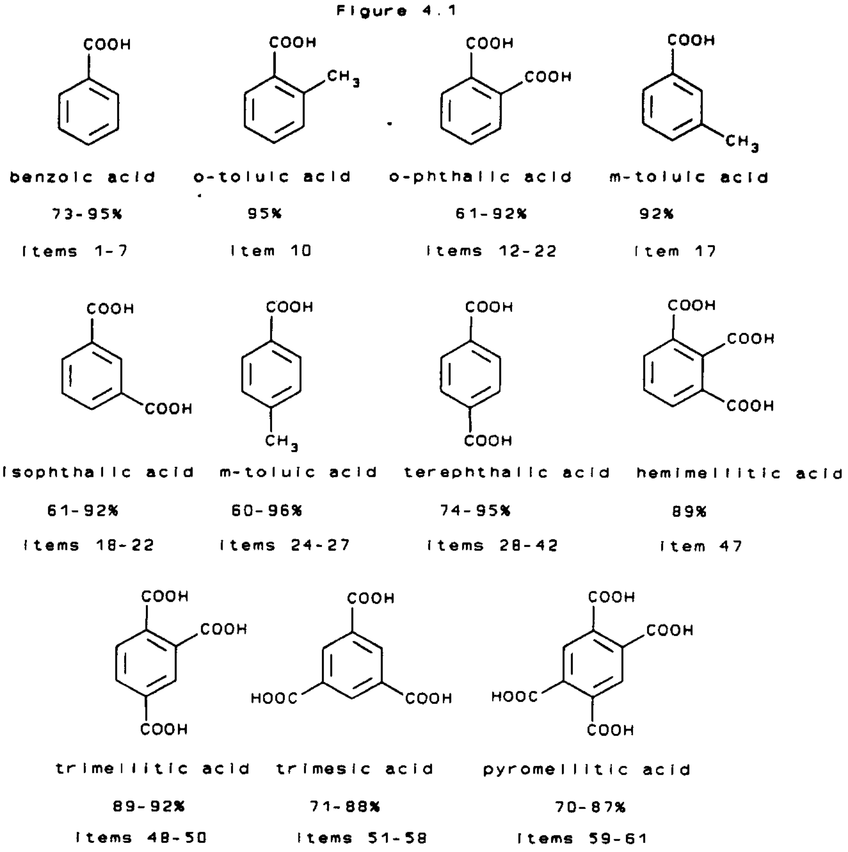


Fig. 4.1. Selected aromatic acids produced from the MC oxidation of methylbenzenes (see Table 4.2 for details).

Table 4.1
Formation of benzylic alcohols, acetates and aldehydes during the oxidation of methylbenzenes

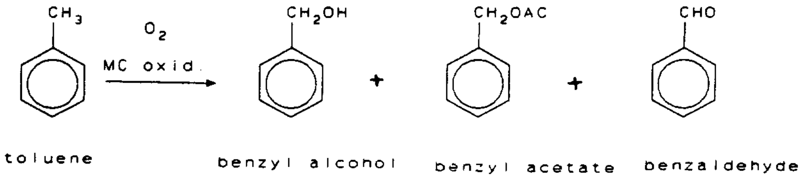
Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
To Benzylic Alcohols:									
	$-CH_3$ to $-CH_2OH$ (toluene to benzyl alcohol)								
1.	Co/Br	HOAc	78	16	–	150	–	air	[126]
	1,4-CH_3 to 1-CH_2OH-4-CH_3 (*p*-xylene to *p*-methylbenzyl alcohol)								
2.	Co/Mn/Br	–	33	9.8	0.33	82	1.0	air	[38]
	1-CH_3-4-COOH to 1-CH_2OH-4-COOH								
3.	Co/Cu/Br	HOAc	29	8.7	1.0	150	39	air	[39]
To Benzylic Acetates:									
	1-CH_3 to 1-CH_2OAc (toluene to benzyl acetate)								
4.	Co/Br,NaOAc	Ac_2O, HOAc	30	13.5	1.1	70–109	1.0	O_2	[11,96]
5.	Co/Br	HOAc	78	39	–	150	–	air	[126]
6.	Co/Cu/Br	HOAc	77	38	5.0	150	33	O_2	[54]
7.	Co/Ce/Zn/Br	Ac_2O	90	15	–	90	–	–	[53]
	1-CH_3-3-Cl to 1-CH_2OAc-3-Cl (3-chlorotoluene to 3-chlorobenzyl acetate)								
8.	Co/Cu/Br	HOAc	39	25	1.0	150	40	air	[39]
	1-CH_3-4-Cl to 1-CH_2OAc-4-Cl								
9.	Co/Cu/Br	HOAc	60	31	1.0	150	40	air	[39]
	1-CH_3-4-OCH_3 to 1-CH_2OAc-4-OCH_3								
10.	Co/Cu/Br	HOAc	94	20	1.0	150	40	air	[39]
	1,4-CH_3 to 1-CH_3-4-CH_2OAc (*p*-xylene to *p*-methylbenzyl acetate)								
11.	Co/Br,NaOAc	Ac_2O/HOAc	36	22	2.7	70–109	1.0	O_2	[11]
12.	Co/Cu/Br	HOAc	82	35	–	–	–	air	[40]
13.	Co/Cu/Br	HOAc	90	31	1.0	150	39	air	[39]
	1-CH_3-4-COOH to 1-CH_2OAc-4-COOH								
14.	Co/Cu/Br	HOAc	19	11	–	–	–	air	[40]
To Benzyl Propionate:									
	$-CH_3$ to $-CH_2OC(=O)CH_2CH_3$ (toluene to benzyl propionate)								
15.	$Co(OAc)_2$, $CoBr_2$, KOH	propionic acid	–	16	4.3	122	1.0	O_2	[96]
To Benzyl Benzoate:									
	$-CH_3$ to $-CH_2OC(=O)Ph$ (toluene to benzyl benzoate)								
16.	Co/Mn/Br	solventless	–	10	2.0	200	10	O_2	[100]
To Benzaldehydes:									
	$-CH_3$ to $-CHO$ (toluene to benzaldehyde)								
17.	Co/Br,NaOAc	Ac_2O	30	6.6	1.1	70–109	1.0	O_2	[11]
18.	Co/Cu/Br	HOAc	54	26	5.0	100	33	O_2	[54]
	1-CH_3-2-$SO_3^-Na^+$ to 1-CHO-2-$SO_3^-Na^+$								
19.	Co/Br	HOAc	48	26	1.0	70–90	1.0	–	[128]
	1-CH_3-4-*t*-butyl to 1-CHO-4-*t*-butyl								
20.	Co/Br	HOAc	50	25	–	75	1.0	–	[127]
21.	Co/Br	HOAc	40	25	0.5	60	–	–	[129]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	P (atm)	O_2 source	Ref. No.
	$1\text{-}CH_3\text{-}4\text{-}NO_2$ to $1\text{-}CHO\text{-}4\text{-}NO_2$								
22.	Co/Mn/Br	HOAc	57	8.7	29	85	–	–	[130]
	$1,4\text{-}CH_3$ to $1\text{-}CH_3\text{-}4\text{-}CHO$ (*p*-xylene to *p*-tolualdehyde)								
23.	$Co(OAc)_2$,NaBr,NaOAc	Ac_2O	36	7.9	2.7	70–109	1.0	O_2	[11]
24.	Co/Mn/Br	–	33	36	0.33	82	1.0	air	[38]
25.	Co/Cu/Br	HOAc	82	15	–	–	–	air	[40]
	$1\text{-}CH_3\text{-}4\text{-}OCH_3$ to $1\text{-}CHO\text{-}4\text{-}OCH_3$								
26.	Co/Br	HOAc	50	37	–	75	1.0	–	[127]
27.	Co/Br	HOAc	67	52	–	–	–	–	[314]
28.	Co/Br/Cu	HOAc	94	12	1.0	150	40	air	[39]
29.	$CoCl_2$,$CrCl_3$	diglyme	45	55	5	90	1.0	O_2	[131]
30.	Co	HOAc	79	58	–	115	20	–	[127]

usually hydrobromic acid or sodium bromide. The oxidation states of the acetates are in their most stable, non-oxidizing form. For the most common metals these are Co(II), Mn(II), Ni(II), Cu(II), Cr(III) Fe(III), Zr(IV) and Hf(IV). Occasionally the metal/bromide is added as cobalt(II) or manganese(II) bromide hydrates. These will also be designated by the element/slash notation; i.e., Co/Br if $CoBr_2$ was added. When a catalyst component is claimed to give special properties it is completely designated. For example, the use of alkylammonium bromide salts in item 6 in Table 4.2. Conversions are in molar percent. Yields are in molar percent based on the moles of hydrocarbon initially added. The gaseous oxidant, dioxygen, which is nearly always air, contains 20.9% oxygen, or 100% pure oxygen which is indicated by the symbol 'O_2.' For proprietary reasons, only the conversion and yields are reported for the reactions characterized at the Amoco Research and Development laboratories [40]. The MC method is often contrasted with other autoxidation methods in these tables. Information on the non-MC methods is given as the last entries under a given feedstock (for example see items 29 and 30 in Table 4.1).

4.2. Oxidation to intermediates (see Table 4.1)

Reaction intermediates are defined as oxygenated compounds that form before the carboxylic acid does. The MC oxidation of methyl groups proceeds to carboxylic acids through the formation of peroxides (rarely reported), alcohols, acetates, and aldehydes. Using toluene as an example:



(4.1)

We do not know whether the benzylic alcohol or the acetate is the primary product from the reaction. There is evidence that the benzaldehyde proceeds both from the methyl group as well as from the alcohol and acetate [124,125]. Any preparative use of this method must recognize that the reaction products will consist of mixtures of the benzylic alcohols, acetates, aldehydes and carboxylic acid and probably some unreacted reagent. All of these products often are not reported however and the reader may therefore be left with the impression that only those reported were indeed present. To obtain a maximum yield of a given intermediate, the conversion is generally < 100%.

Table 4.2
Oxidation of the polymethylbenzenes to polycarboxylic acids

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Reference No.
	–CH_3 to –COOH (toluene to benzoic acid)								
1.	Co/Br	HOAc	–	86	–	90–112	0	O_2	[11]
2.	Co/Mn/Br, polysiloxane	HOAc	–	73	0.58	200	–	air	[199]
3.	Co/Mn/Br	benzoic acid	–	96	0.50	190–200	26	–	[120]
4.	MC catalyst	HOAc	–	88	–	–	–	–	[90]
5.	Co/Mn/Br	solventless	–	94	2.0	200	10	O_2	[100][a]
6.	$CoCl_2$/didecyl$(CH_3)_2N^+Br^-$	solventless	–	92	3.0	160	12	air	[102]
7.	$CrCl_3$/didecyl$(CH_3)_2N^+Br^-$	solventless	–	80	3.00	160	12	air	[102]
8.	Co/MEK	HOAc	–	89	26	90	1.0	O_2	[28][b]
9.	Co, Mn, MEK	HOAc	46	40	3.3	185–200	50	air	[19]
	1-CH_3 to 1-CH_3-2-COOH (*o*-xylene to *o*-toluic acid)								
10.	$CoCl_2$/(ocyl)$_4N^+Br$	solventless	–	95	3.0	170	10	air	[103]
11.	Co/MEK	HOAc	–	68	24	90	1.0	O_2	[28]
	1,2-CH_3 to 1,2-COOH (*o*-xylene to *o*-phthalic acid)								
12.	Co/Mn/Br	solventless	–	85–92	1.2	227	28	air	[77]
13.	Co/Br	HOAc	–	83	7.0	110	1.0	O_2	[47]
14.	Co/Mn/Br	benzoic acid	–	82	115	150	1.0	O_2	[97]
15.	Co/Mn/Br	propionic acid	–	82	48	130	1.0	O_2	[134]
16.	Co/Mn/Br	propionic acid	–	83	8.0	130	1.0	O_2	[84]
	1,3-CH_3 to 1-CH_3-3-COOH (*m*-xylene to *m*-toluic acid)								
17.	$CoCl_2$/(ocyl)$_4N^+Br$	solventless	–	92	3.0	170	10.0	air	[103]
	1,3-CH_3 to 1,3-COOH (*m*-xylene to isophthalic acid)								
18.	Co/Mn/Br,polysiloxane	HOAc	–	61	0.45	230	–	air	[199]
19.	Co/Mn/Br	HOAc, ODB	–	91	4.0	200	25	air	[74][c]
20.	Co/Mn/Br	propionic acid	–	62	20	130	1.0	O_2	[134]
21.	Co/Mn/Br	propionic acid	–	80	15	130	1.0	O_2	[84]
22.	Co/Mn/Br	benzoic acid/benzene	–	90	4.0	200	30	air	[74]
23.	Co/MEK	HOAc	–	93	24	90	1.0	O_2	[28]
	1,4-CH_3 to 1-CH_3-4-COOH (*p*-xylene to *p*-toluic acid)								
24.	$CoCl_2$/(ocyl)$_4N^+Br$	solventless	–	96	3.0	170	10.0	air	[103]
25.	Co/Mn/Br	HOAc	93	63	–	–	–	–	[37]
26.	Co/Br	HOAc	–	78	4.0	105	1.0	air	[132]
27.	Co/Mn/Br	HOAc	100	60	2.0	82	1.0	air	[38]
	1,4-CH_3 to 1,4-COOH (*p*-xylene to terephthalic acid)								
28.	Co/Mn/Br	HOAc	–	93	0.60	193–216	22	air	[67]
29.	MC catalyst	HOAc	–	90	–	–	–	–	[90]
30.	Co/Br	HOAc	–	78	1.8	110	1.0	O_2	[47]
31.	Mn/Br	HOAc	–	75	2.0	195	1427	air	[22]
32.	Ce/Br	HOAc	–	74	1.5	205	27	air	[135]
33.	Co/Mn/Br, polysiloxane	HOAc	–	59	0.50	200	24	air	[199]
34.	Co/Br	HOAc/acetophenone	–	89	3.7	133	1.0	O_2	[47]
35.	Mn/Br	octanoic acid	–	80	–	194	13–27	air	[136]
36.	Co/Mn/Br	propionic acid	–	91	20	130	1.0	O_2	[134]
37.	Co/Mn/Br	propionic acid	–	92	20	130	1.0	O_2	[84]
38.	Co/Mn/Br	benzoic acid	–	75	–	150	1.0	O_2	[97]
39.	Co/Mn/Br	benzoic acid	–	78	20	150	1.0	O_2	[134]
40.	Co/Mn/Br	benzoic acid	–	80	20	150	1.0	O_2	[84]
41.	Co/Mn/Br	solventless	–	43	20	137	1.0	O_2	[134]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Reference No.
	1,4-CH_3 to 1,4-COOH (*p*-xylene to terephthalic acid) (continued)								
42.	Co/Mn/Br	H_2O	–	–	1.0	221	29	air	[33]
43.	HBr	H_2O	–	37	16.5	200	26	air	[84][d]
44.	Co/Mn	propionic acid	–	93	5.0	110	1.0	O_2	[47]
45.	$Co(OAc)_2$, paraldehyde	HOAc	100	91	–	120	15	air	[27]
46.	$Co(OAc)_2$, MEK	HOAc	–	93	24	90	1.0	O_2	[28]
	1,2,3-CH_3 to 1,2,3-COOH (hemimellitene to hemimellitic acid)								
47.	Co/Mn/Br	HOAc	–	89	–	–	–	–	[40]
	1,2,4-CH_3 to 1,2,4-COOH (pseudocumene to trimellitic acid)								
48.	Co/Mn/Br/Zr	HOAc	–	90	1.0	160–210	10–27	air	[83]
49.	Ni/Mn/Br/Zr	HOAc	–	90	1.0	160–210	10–27	air	[83]
50.	Co/Mn/Ti/Ce/Br	HOAc	–	92	7.3	–	–	air	[137]
	1,3,5-CH_3 to 1,3,5-COOH								
51.	Co/Mn/Br	HOAc	–	85	–	202–226	13–28	air	[136]
52.	Co/Mn/Br	HOAc	–	77	3.0	196	27	air	[22]
53.	Co/Mn/Br	HOAc	–	80–83	–	140	10	–	[42]
54.	Co/Mn/Br	HOAc	–	78	5.0	140	–	–	[43]
55.	Co/Mn/Br	HOAc	–	71	1.3	223	22	air	[67]
56.	Co/Mn/Br	HOAc	–	88	–	220	20	air	[138]
57.	Co/Mn/Br	propionic acid	–	80	48	130	1.0	O_2	[134]
58.	Co/Br/triethanolamine	HOAc	–	80	–	–	–	–	[94]
	1,2,4,5-CH_3 to 1,2,4,5-COOH (durene to pyromellitic acid)								
59.	Co/Mn/Br	HOAc,Ac_2O	–	87	0.41	130	–	–	[315]
60.	Co/Mn/Br/Cl	HOAc	–	70	2.0	140–210	–	–	[88]
61.	Co/Mn/Br/Zr	H_2O,HOAc	–	84	2.4	171–227	10–31	air	[49]

[a] Initial 'solvent' was 94.5% toluene and 5.5% benzoic acid.

[b] MEK is methyl ethyl ketone.

[c] ODB is *o*-dichlorobenzene.

[d] Also 29% yield to *p*-toluic acid.

Reported yields to benzylic alcohols are 12, 9.8, and 8.7% where the substituent on the ring is X = H, X = 4-CH_3, and X = 4-COOH respectively (items 1–3). These alcohols react with the acetic acid solvent to form acetate esters. Benzylic acetate yields from 11 to 39% have been reported where X = H, 3-Cl, 4-Cl, 4-OCH_3, 4-CH_3, and 4-COOH (see items 4–14). There is no correlation with the Hammett substituent constants, which vary from -0.78 to $+0.42$, with the yields. The Co/Cu/Br catalyzed reactions have been thoroughly studied as a function of temperature, pressure, and Co/Cu/Br ratios [54,39]. The author is unaware of any study which relates intermediate yields with the ring electron density or with type of catalyst used.

As expected, when the acetic acid solvent is replaced by another carboxylic acid solvent, the benzylic acetates are replaced by their respective benzylic carboxylates. Thus the propionate is obtained when the acetic acid solvent was replaced by propionic acid, and a benzoate is obtained during the solventless oxidation of toluene (see items 15 and 16). In the solventless oxidation to toluene, the benzoate was formed because of the high concentration of benzoic acid that forms near the end of the reaction.

Table 4.3
Oxidation of intermediates of methylbenzenes

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Oxidation of Benzylic Chlorides:									
	1,2,5-CH_3-4-CH_2Cl to 1,2,4,5-COOH (pyromellitic acid)								
1.	Mn/Br	HOAc	n –	54	2.0	250	50–60	air	[139]
	1,4-CH_2Cl to 1,4-COOH								
2.	Co/Mn/Br	HOAc	–	99	22	110	1.0	O_2	[84]
Oxidation of Benzylic Acetates:									
	1-$CH_2OC(=O)CH_3$ to 1-$CH(OC(=O)CH_3))_2$ (benzyl acetate to benzaldiacetate)								
3.	Co/Ce/Zn/Br	HOAc	90	45	–	90	–	–	[140]
Oxidation of Benzyl Alcohols:									
	1-CH_2OH-4-CH_3 to 1,4-COOH (*p*-methylbenzyl alcohol to terephthalic acid)								
4.	Co/Br/polysiloxane	HOAc	–	59	0.63	210	–	air	[199]
Oxidation of Benzaldehydes:									
	1-CH_3-4-CHO to 1,4-COOH (*p*-tolualdehyde to terephthalic acid)								
5.	Co/Mn/Br	propionic acid	–	90	20	130	1.0	O_2	[84]
6.	HBr	H_2O	97	96	2.0	180	27	O_2	[84]
	1,2-CH_3-4-CHO to 1,2,4-COOH (trimellitic acid)								
7.	Co/Mn/Br/Zr	HOAc	–	94	–	–	–	–	[40]
	1,3-CH_3-4-CHO to 1,2,4-(COOH) (2,4-dimethylbenzaldehyde to trimellitic acid)								
8.	Co/Mn/Br/Zr	HOAc	–	94	–	–	–	–	[40]
9.	Mn/Br	H_2O	100	90	–	200–220	20–30	air	[141]
10.	Co/Mn/Br	HOAc	–	79	2.1	220	22	air	[143]
	1,2,4-CH_3-5-CHO to 1,2,4,5-COOH (pyromellitic acid)								
11.	Mn/Fe/Br	H_2O	–	89	–	180–280	–	–	[142]
12.	Mn/Br	H_2O	100	85	–	200–220	20–30	air	[141]

Reported yields to benzaldehydes are 7, 8, 9, 15, 25, 25, 26, 26, 36, 37% for various catalysts and reagents (see items 17–30 in Table 4.1). Substituents on the ring range from X = H, 4-OCH_3, 4-*t*-butyl, 4-NO_2, 4-CH_3. Higher yields of 55 and 58% from non-MC type catalysts are reported using Co/Cl and Co catalysts (see items 29 and 30).

4.3. *Oxidation of the polymethylbenzenes to polycarboxylic acids (see Table 4.2)*

Excellent yields to the polycarboxylic geometrical isomers of monomethyl-, dimethyl-, and trimethyl-derivatives are known (see Table 4.2 and Fig. 4.1). For the tetramethyl derivatives, results for only the 1,2,4,5-geometrical isomer (durene) have been reported. The author was unable to convert 1,2,3,4-tetramethylbenzene to 1,2,3,4-tetracarboxybenzene. There is no known successful MC oxidation of penta- or hexamethyl benzene to their corresponding pentacarboxy- and hexacarboxy-derivatives. Presumably the ring becomes sufficiently deactivated so that the high temperatures necessary to completely oxidize them would result in extensive decarboxylation (see discussion in Section 1.8.4). For example, an intermediate during the oxidation of pentamethylbenzene would be 2,3,5-tricarboxy-*p*-xylene whose sum of Hammett substitute constants would be similar to 2,5-dichloro-3-nitro-*p*-xylene. Extensive decarboxylation has been reported for the latter [52] (see Section 1.8.4). Staged pressure, temperature, and catalyst regimes are used in the oxidation of pseudocumene, hemimellitene and durene for reasons delineated in Section 1.7.

The yields to benzoic acid, *o*-phthalic acid, terephthalic acid, isophthalic acid, and trimellitic acid are probably understated in the tables since these are commercialized processes (or have been in the past) and the highest yields are trade secrets. The patent literature, describing numerous improvements to these industrial processes, is beyond the scope of the review.

The MC oxidation of *o*-xylene to phthalic acid has been studied extensively because it poses a threat to the established gas phase industrial process. The reactions can be performed in the solventless mode. Yields as high as 85–92% are reported when addition of trace amounts of aromatic acids are initially added, by maintaining a 2–7 wt.% water concentration in the reactor, and by using trace amounts of zirconium with the usual Co/Mn/Br catalyst (see item 12). Selectivity of the gas phase process is 78% [20].

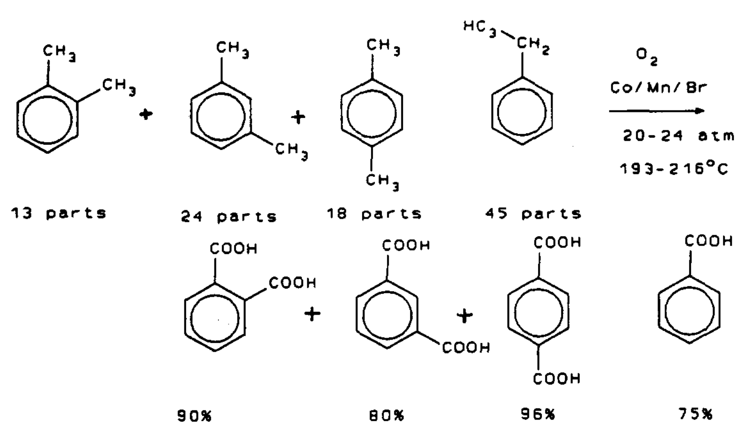
MC type systems can easily oxidize adjacent methyl groups on a ring to *o*-phthalic acids as can be seen in the case of *o*-xylene, pseudocumene, hemimellitene, and durene. In systems which use only cobalt as a catalyst, the *o*-methyl groups react very sluggishly (see Section 1.6). Thus *o*-xylene goes to *o*-toluic acid and not *o*-phthalic acid (see item 11).

The oxidation of just the first methyl group is possible using the MC system. The oxidation of *p*-xylene to *p*-toluic acid has been studied as a function of cobalt concentration, Co/Br ratios, and *p*-xylene concentration at temperatures from 63 to 105°C giving a maximum reported yield of 78% (see item 26). (See Section 1.6 for a further discussion.)

The use of phase transfer reagents (quaternary ammonium and phosphonium bromides) are effective in solventless oxidations. The use of $CoCl_2$ with didecyldimethylammonium bromide gives quite unusual results however. Only the first methyl group becomes oxidized to carboxylic acid groups (see items 10, 17, 24).

Efforts to avoid the inevitable loss of acetic acid by combustion to carbon oxides, has led to efforts to use water as a solvent rather than acetic acid. Results with comparable yields to those attained in acetic acid have been reported by using a two stage, continuous process in which the first stage is conducted at 185°C and the second stage at 221°C. Two disadvantages however are that 35 times more catalyst metals and twice as long a residence time is required in water as compared to acetic acid (see item 42).

The simultaneous oxygenation of a *o*-xylene/*m*-xylene/*p*-xylene/ethylbenzene mixture has been studied since it is one that is produced by crude oil refineries. These can be oxidized in good yields to their corresponding acids:



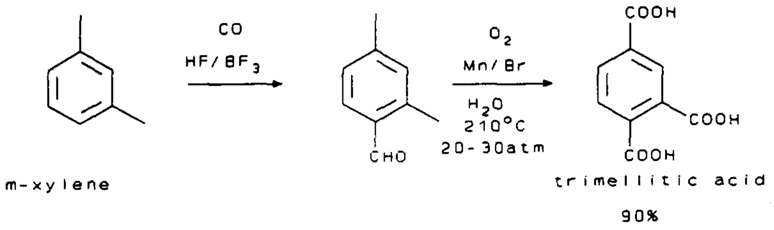
(4.2)

Separation is accomplished by cooling the reactor slurry to about 110°C and filtering. The solids are comprised mostly of the terephthalic acid and isophthalic acid. The filtrate is distilled to first remove water and acetic acid, then benzoic acid, and finally *o*-phthalic acid as its anhydride [136].

4.4. Oxidation of intermediates of methylbenzenes (see Table 4.3)

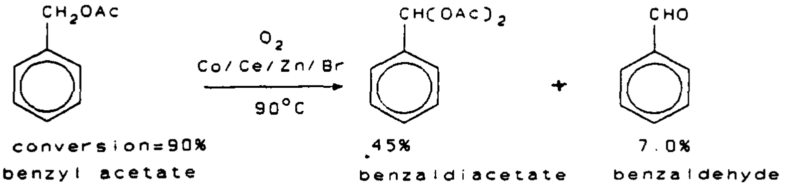
The initial rate of reaction will be high since the intermediate alcohols, acetates, and aldehydes are more easily oxidized than the methyl group (see Section 1.6). The oxidation of benzylic chlorides are placed in this category since they may be present in Co/Mn/Br/Cl catalysts. They solvolyze to benzylic alcohols just as benzylic bromides do.

An important commercial development is the conversion of *m*-xylene to trimellitic acid and pseudocumene (1,2,4-trimethylbenzene) to pyromellitic acid by Mitsubishi Gas Kagaku (items 9 and 12). Taking *m*-xylene as an example, the first step is the carbonylation of the xylene using a HF/BF$_3$ catalyst. The HF/BF$_3$ is first complexed with *m*-xylene, then carbon monoxide is reacted with the complex to form a HF/BF$_3$ complex of the 2,4-dimethylbenzaldehyde. This complex is then thermally degraded in the gas phase. 2,5-Dimethylbenzaldehyde is then oxidized to the triacid in water:



(4.3)

It has been reported that the benzylic acetate can be oxidized to the benzaldiacetate in 41% yield (see item 3):

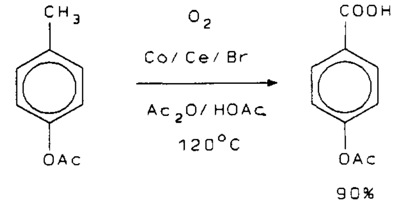


(4.4)

4.5. Oxidation of derivatives of methylbenzenes (see Table 4.4)

Acetoxy-, acetyl-, bromo-, chloro-, carboxy-, flouro-, methoxy-, nitrile-, nitro-, toluidines (as acetyl derivatives), and sulfonyl carboxylic acids have been prepared. Noticeably absent are any iodo-derivatives, which may be simply because of lack of incentive, and phenols and primary amines which are strong autoxidation inhibitors. The derivatives have been placed in alphabetical order in Table 4.4. We shall now discuss these derivatives in the same order as they appear on the table, with some exceptions where it makes chemical sense to do so.

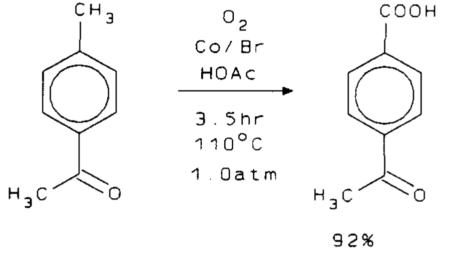
The solvolysis of the acetoxy group to phenols can be avoided by performing the reaction in an acetic anhydride/acetic acid mixture, items 1, 2 in Table 4.4 (see also item 36 in Table 5.1):



p-cresyl acetate 4-acetoxybenzoic acid

(4.5)

Apparently a methyl group is more reactive than an acetyl group since the latter is unaffected during the reaction (see item 3):

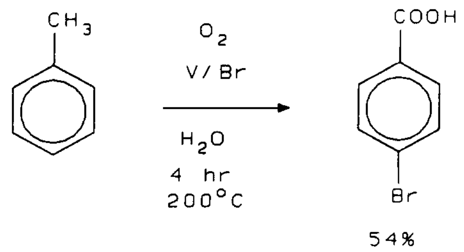


p-methyl acetophenone p-acetobenzoic acid

(4.6)

A wide variety of bromo-, and chloro-aromatic acids have been prepared. Rings with both chloro- and fluoro- present, as well as chloro- and methoxy, and chloro-, nitro-, chloro- have also been prepared (see Fig. 4.2). A very small amount of the ring bromine is released into solution since bromide was not added with the cobalt and manganese in these oxidations but they still occurred readily (see items 10, 13, 14, 16). Consistent with ring bromine loss is the presence of 1–2% benzoic acid during the oxidation of 4-bromotoluene (see item 8).

Rather unique MC reactions are the simultaneous bromination and oxidation of toluene and *p*-xylene using a V/Br catalyst in water (items 7, 19):



toluene p-bromobenzoic acid

(4.7)

Table 4.4
Oxidation of derivatives of methylbenzenes

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Acetoxy Derivatives:									
	1-CH_3-3-acetoxy to 1-COOH-3-acetoxy								
1.	Co/Mn/Br	HOAc/Ac_2O	—	82	—	—	—	—	[40]
2.	Co/Ce/Br	HOAc/Ac_2O	—	90	—	120	—	—	[144]
Acetyl Derivatives:									
	1-CH_3-4-acetyl to 1-COOH-4-acetyl								
3.	Co/Br	HOAc,benzene	—	92	3.5	110	1.0	O_2	[47]
Benzofuran Derivatives:									
	2,7-dimethylbenzofuran to 2,7-dicarboxybenzofuran								
4.	Co/Mn/Br	HOAc	—	93	2.0	180	50	—	[145]
Bromo Derivatives:									
	1-CH_3-2-Br to 1-COOH-2-Br								
5.	Co/Mn/Br	HOAc	—	80	—	—	—	—	[40]
6.	Co/Br	HOAc	—	91	2.0	90–112	1.0	O_2	[11]
	1-CH_3 to 1-COOH-2-Br (toluene to 2-bromobenzoic acid)								
7.	V/Br	H_2O	—	54	4.0	200	—	O_2	[63]
	1-CH_3-4-Br to 1-COOH-4-Br								
8.	Co/Mn/Br	HOAc	—	82	—	—	—	—	[40]
9.	Co/Cl/(hexyl)$_4P^+Br$	solventless	—	100	6.0	17	170	air	[103]
	1,2-CH_3-4-Br to 1,2-COOH-4-Br								
10.	Co/Mn	HOAC	—	69	—	—	—	—	[40]
	1,3-CH_3-4-Br to 1-COOH-3-CH_3-4-Br								
11.	Co/Br	HOAc	—	87	5.0	140	25	air	[146]
	1,3-CH_3-4-Br to 1,3-COOH-4-Br								
12.	Co/Mn/Br	HOAc	—	65	—	—	—	—	[40][a]
	1,3-CH_3-4,6-Br to 1,3-COOH-4,6-Br								
13.	Co/Mn	HOAc	—	84–95	—	—	—	—	[40][b]
	1,4-CH_3-2-Br to 1,4-COOH-2-Br								
14.	Co/Mn	HOAc	—	72–86	—	—	—	—	[40]
15.	Co/Mn/Br	HOAc	—	—	3.0	170	10	air	[147]
	1,4-CH_3-2,5-Br to 1,4-COOH-2,5-Br								
16.	Co/Mn	HOAc	—	80	—	—	—	—	[40]
17.	Co/Mn/Br	HOAc	—	70	1.0	210	28	air	[148]
	1,2,4-CH_3-3,5,6-Br to 1,2,4-CH_3-3,5,6-Br								
18.	Co/Mn/Br	HOAc	—	70–75	1.0	210	—	air	[148]
	1,4-CH_3 to 2,6-Br-1,4-COOH								
19.	V/Br	H_2O	—	36	4.0	200	—	O_2	[63]
Carboxyl Derivatives:									
	1-CH_3-2-COOH to 1,2-COOH (*p*-toluic acid to terephthalic acid)								
20.	Co/Mn/Br	HOAc	41	21	—	—	—	—	[40]
21.	Co/Mn	HOAc	0	0	—	—	—	—	[40]
22.	HBr	H_2O	88	82	2.0	180	27	O_2	[84,63]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
	1-CH_3-3-COOH to 1,3-COOH (*m*-toluic acid to isophthalic acid)								
23.	Co/Mn/Br	HOAc	89	79	—	—	—	—	[40]
24.	Co/Mn	HOAc	17	12	—	—	—	—	[40]
25.	HBr	H_2O	—	97	2.0	180	30–50	O_2	[84,63]
	1-CH_3-4-COOH to 1,4-COOH (*p*-toluic acid to terephthalic acid)								
26.	Co/Mn/Br,polysiloxane	HOAc	—	85	0.40	200	—	air	[199]
27.	Co/Mn/Br	HOAc	90	89	—	—	—	—	[40]
28.	Co/Br	HOAc	—	80	1.3	110	1.0	O_2	[47]
29.	Co/Mn/Br	propionic acid	—	91	20	130	1.0	O_2	[134]
30.	Co/MEK	HOAc	—	92	31	90	1.0	O_2	[28]
31.	Co/Mn	HOAc	3.5	95	—	—	—	—	[40]
32.	HCl	H_2O	33	15	2.0	200	31	O_2	[84][c]
33.	HBr	H_2O	93	89	2.0	200	31	O_2	[84,63]
34.	No catalyst	H_2O	41	7	2.0	200	31	O_2	[84]
	1,2-CH_3-4-COOH to 1,2,4-COOH								
35.	Co/Mn/Br/Zr	HOAc	—	95	—	—	—	—	[40]
	1,4-CH_3-5-COOH to 1,2,4-COOH (trimellitic acid)								
36.	Co/Mn/Br/Zr	HOAc	—	97	—	—	—	—	[40]
Chloro Derivatives:									
	1-CH_3-2-Cl to 1-COOH-2-Cl								
37.	Co/Br	HOAc	—	86	—	90–112	1.0	O_2	[11]
38.	Co/Br	—	100	97–98	2.0	95	1.0	—	[55]
	1-CH_3-3-Cl to 1-COOH-3-Cl								
39.	Co/Br	HOAc	—	96	—	90	—	—	[149]
40.	Co/Br	HOAc	—	96	7.0	130	3.0	—	[150]
	1-CH_3-4-Cl to 1-COOH-4-Cl								
41.	Co/Br	HOAc	—	88	—	90–112	1.0	O_2	[11]
42.	Co/Br	HOAc	—	96	2.0	145	9.0	—	[151]
43.	Co/Br	HOAc	—	96	—	—	8.0	—	[152]
44.	Co/Mn/Br	HOAc	—	99	22	110	1.0	O_2	[84]
45.	$CoCl_2/(hexyl)_4N^+Br$	solventless	—	99	5.0	170	7.5	O_2	[103]
	1-CH_3-2,4-Cl to 1-COOH-2,4-Cl								
46.	Co/Br	HOAc	—	97	1.8	130	—	—	[153]
47.	Co/Mn/Br	HOAc	100	98	—	160	16	air	[154]
48.	Co(II)stearate	solventless	—	55–60	6.0	150	—	O_2	[155]
	1,3-CH_3-4,6-Cl to mixture								
50.	Co/Br	—	—	—	—	—	—	—	[156]
	1,4-CH_3-2-Cl to 1,4-COOH-2-Cl								
51.	Co/Mn/Br	HOAc	—	81	—	—	—	—	[40]
52.	Co/MEK	HOAc	—	59	28	90	1.0	O_2	[28]
	1,4-CH_3-2,5-Cl to 1,4-COOH-2,5-Cl (2,5-dichloroterephthalic acid)								
53.	Co/Mn/Br	—	—	—	—	150–300	6.8–68	—	[157]
54.	Mn/Ni/Br	HOAc	—	—	—	190–210	15–24	—	[158]
2,2-*Dichlorocyclopropane Derivatives*:									
	1-CH_3-3-(2,2-dichlorocyclopropane) to 1-COOH-3-(2,2-dichlorocyclopropane)								
55.	Mn/Br	HOAc	—	—	4.0–5.0	177	27	air	[159]
	1-CH_3-4-(2,2-dichlorocyclopropane) to 1-COOH-4-(2,2-dichlorocyclopropane)								
56.	Co/Mn/Br	HOAc	—	—	4.0–5.0	177	27	air	[159]

Table 4.4 (continued)

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
	1-CH_3-4-(1-CH_3-dichlorocyclopropane) to 1-COOH-4-(1-CH_3-dichlorocyclopropane)								
57.	Co/Mn/Br	HOAc	—	—	4.0–5.0	177	27	air	[159]
Diphenylmaleic Anhydride Derivatives:									
	3,3′-dimethyldiphenylmaleic anhydride to 3,3′-dicarboxydiphenylmaleic anhydride								
58.	Co/Mn/Br	HOAc	—	76	1.0	175–210	24–31	air	[160]
Hexachlorobicyclohepteneyl Derivatives:									
	1-CH_3-2-hexachlorochlorobicycloheptenyl to 1-COOH-2-hexachlorobicycloheptenyl								
59.	Co/Mn/Br	HOAc	—	70	—	204	27	air	[161]
	1-CH(CH_3)-2-2-hexachlorobicycloheptenyl to 1-COOH-2-hexachlorobicycloheptenyl								
60.	Co/Mn/Br	HOAc	—	68	—	204	27	air	[161]
Methoxy Derivatives:									
	1-CH_3-3-OCH_3 to 1-COOH-3-OCH_3								
61.	Co/Br	HOAc	—	—	—	—	—	—	[61]
	1-CH_3-4-OCH_3 to 1-COOH-4-OCH_3								
62.	Co/Mn/Br	HOAc,H_2O	—	85	0.5	121–162	10–17	air	[162]
63.	Co/Cl/n-hexylamine$_4^+$Br	solventless	—	98	6.0	160	16	air	[103]
	1,4-CH_3-2-OCH_3 to 1,4-COOH-2-OCH_3								
64.	Co/Mn/Br	HOAc	—	42	—	—	—	—	[40]
Miscellaneous Derivatives:									
	1-CH_3-2-CH(CH_3)$_2$C(=O)OCH_3 to 1-COOH-2-CH(CH_3)$_2$C(=O)OCH_3								
65.	Co/Mn/Br	HOAc	—	51	0.5	202	20	air	[163]
	1,2-CH_3-4-CH(CH_3)$_2$C(=O)OCH_3 to 1,2-COOH-4-CH(CH_3)$_2$C(=O)OCH_3								
66.	Co/Mn/Br	HOAc	—	67	0.5	202	20	—	[163]
	1-CH_3-2-Cl-4-F to 1-COOH-2-Cl-4-F								
67.	Co/Mn/Br	HOAc	—	90	7.5	90–100	—	—	[164]
	1-CH_3-3,5-Cl-6-OCH_3 to 1-$COOH_3$-3,5-Cl-6-OCH_3								
68.	Co/Br	—	—	93–97	—	—	—	—	[165]
	1,4-CH_3-2,5-Cl-3-NO_2 to 1-COOH-2,5-Cl-3-NO_3								
69.	Co/Mn/Br	HOAc	—	38	42	200	20	O_2	[52]
Nitrile Derivatives:									
	1-CH_3-4-CN to 1,4-COOH (*p*-tolunitrile to terephthalic acid)								
70.	Co/Mn/Br	propionic acid	—	52	5.0	130	1.0	—	[84]
	1-CH_3-4-CN to 1-COOH-4-CN (*p*-tolunitrile to 4-cyanobenzoic acid)								
71.	Co/Mn/Br	Ac_2O	—	96	8–12	100	—	—	[284]
	1-CH_3-3-CN to 1-COOH-3-CN (*m*-tolunitrile to 3-cyanobenzoic acid)								
72.	Co/Mn/Br	Ac_2O	—	91	8–12	100	—	—	[284]
	1,3,5-CH_3-2-CN to 1,3,5-COOH-2-CN								
73.	Co/Mn/Br	Ac_2O	—	—	8–12	100	—	—	[284]
Nitro Derivatives:									
	1-CH_3-3-NO_2 to 1-COOH-3-NO_2								
74.	Co/Mn/Br	HOAc	80	64	—	—	—	—	[40]
75.	Co/Mn/Br	HOAc	—	100	1.4	105	27	air	[167]
76.	Co/Mn/Br	HOAc	—	90	7.5	115–140	14	air	[168]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
	$1\text{-}CH_3\text{-}4\text{-}NO_2$ to $1\text{-}COOH\text{-}4\text{-}NO_2$								
77.	Co/Mn/Br	HOAc	—	86	1.2	204	27	air	[167]
78.	Co/Mn/Br	HOAc	—	82	1.1	213	27	air	[169]
79.	Co/Br	HOAc	—	99	—	80–150	—	—	[170]
80.	Co/Ce/Zr/Br	HOAc	—	78	4.0	155	14	air	[171]
81.	Co/Br	HOAc	—	94	3.0	140	25	—	[172]
82.	HBr	H_2O	—	88	2.0	200	—	H_2O_2	[84,63]
83.	HBr	H_2O	—	84	2.0	200	—	O_2	[63]
85.	Co/Cl/(hexyl)$_4^+$Br	solventless	46	46	4.0	20	170	air	[103]
	$1\text{-}CH_3\text{-}2\text{-}NO_2$ to $1\text{-}COOH\text{-}2\text{-}NO_2$ (*o*-nitrotoluene to 2-nitrobenzoic acid)								
86.	Co/Mn/Br	HOAc	17	<1	0.50	164–208	17–27	air	[173]
87.	Co/Mn/Br	HOAc/Ac_2O	20	6	0.50	160–205	20–27	air	[173]
	$1\text{-}CH_3\text{-}2\text{-}NO_2 + 1\text{-}CH_3\text{-}4\text{-}NO_2$ to $1\text{-}COOH\text{-}2\text{-}NO_2 + 1\text{-}COOH\text{-}4\text{-}NO_2$								
88.	Co/Mn/Br	HOAc	12+68	0+51	1.05	213	27	air	[169]
89.	Co/Mn/Br	HOAc	55+81	38+72	1.2	149–194	17–31	air	[173]
90.	Co/Mn/Br	HOAc	31+53	13+38	1.2	196–217	24–31	air	[173]
91.	Co/Mn/Zr/Br	HOAc	—	83+93	—	146–199	17–20	air	[173]
	$1\text{-}CH_3\text{-}2\text{-}NO_2 + 1,4\text{-}CH_3$ to $1\text{-}COOH\text{-}2\text{-}NO_2 + 1,4\text{-}COOH$								
92.	Co/Mn/Zr/Br	HOAc	100+100	96+96	—	121–210	17–27	air	[173]
	$1,4\text{-}CH_3\text{-}2\text{-}NO_2$ to $1,4\text{-}COOH\text{-}2\text{-}NO_2$								
93.	Co/Mn/Br	HOAc	—	80	2	—	180–233 20–34	air	[173]
	$1,4\text{-}CH_3\text{-}2\text{-}NO_2 + 1\text{-}CH_3$ to $1,4\text{-}COOH\text{-}2\text{-}NO_2 + 1\text{-}COOH$ (benzoic acid)								
94.	Co/Mn/Br/Zr	HOAc	100+100	74+91	—	162–213	17–24	air	[173]
	$1,3,5\text{-}CH_3\text{-}2\text{-}NO_2$ to $3,5\text{-}CH_3\text{-}2\text{-}NO_2\text{-}1\text{-}COOH$								
95.	Co/Mn/Br	HOAc	58	13.4	168	121	1.0	air	[173]
Sulfonic Acid Derivatives:									
	$1\text{-}CH_3\text{-}4\text{-}S(=O)_2(NH_2)$ to $1\text{-}COOH\text{-}4\text{-}S(=O)_2(NH_2)$								
96.	Co/Br	HOAc	—	—	1.8	130	—	air	[174]
	$1\text{-}CH_3\text{-}2\text{-}S(=O)_2(NH_2)$ to saccharin								
97.	Co/Mn/Br/Zr	Ac_2O	—	83	4.9	112–122	—	—	[175]
98.	Co/Mn/Br	HOAc	—	51	3.0	140	14	air	[176]
99.	Co/Mn/Br	HOAc	—	74	0.1	190	—	—	[177]
	$1\text{-}CH_3\text{-}2\text{-}S(=O)_2(NH_2)$ to 3-hydroxy-2,3-dihydrobenzisothiazole-1,1-dioxide								
100.	Co/Mn/Br	HOAc	94	81	0.1	120–190	6.0	O_2	[178]
	$1\text{-}CH_3\text{-}2\text{-}Cl\text{-}4\text{-}SO_3CH_3$ to $1\text{-}COOH\text{-}2\text{-}Cl\text{-}4\text{-}SO_3CH_3$								
101.	Co/Ca/Br	HOAc	—	87	—	150–160	—	—	[179]
	$1,4\text{-}CH_3\text{-}2\text{-}SO_3\text{-}Na+$ to $1,4\text{-}COOH\text{-}2\text{-}CO_2\text{-}Na+$								
102.	Co/Mn/Br	HOAc	—	83	—	100	—	—	[180]
Tertiary-butyl Derivatives:									
	1-*t*-butyl to 1-COOH								
103.	Co/Mn/Br	propionic acid	—	11	20	130	1.0	O_2	[134]
	$1\text{-}CH_3\text{-}4\text{-}$*t*-butyl to 1-COOH-4-*t*-butyl								
104.	MC catalyst	HOAc	—	87	—	—	—	air	[90]
105.	Mn/Br	HOAc	—	59	2.0	204–216	27	air	[22]
106.	Co/Mn/Br	propionic acid	—	65	20	130	1.0	O_2	[134]
107.	Co/Br	HOAc	—	87	5.0	130	—	O_2	[91]
108.	Co/Br	HOAc	—	96	—	120	25	air	[92]
109.	Mn/Br	HOAc	—	86	2.0	205	27	air	[181]
110.	Co/Cl/Br	HOAc,PhCl	—	73	2.0	182	14	—	[89]
111.	Co/2-butanone	HOAc	—	96	1.0	138	—	—	[89]

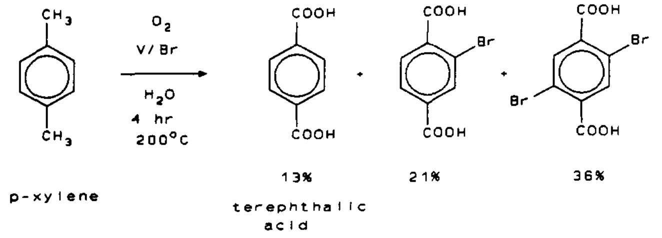
Table 4.4 (continued)

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
	1,2-CH_3-4-*t*-butyl to 1,2-COOH-4-*t*-butyl								
112.	Co/Mn/Br	HOAc	—	92	—	110	—	—	[182]
	1,3-CH_3-5-*t*-butyl to 1,3-COOH-5-*t*-butyl								
113.	MC catalyst	HOAc	—	82	—	—	—	—	[90]
114.	Co/Br	HOAc	—	85	5.0	130	—	O_2	[91]
115.	Co/Mn/Br	HOAc	—	87–94	—	200	20	air	[72]
Tertiary Octyl Derivatives:									
	1-CH_3-4-$C(CH_3)_2CH_2C(CH_3)_3$ to 1-COOH-4-$C(CH_3)_2CH_2C(CH_3)_3$								
116.	Co/Mn/Br	HOAc	—	40	1.67	160–180	19–26	air	[181]
Toluidines (via Acetyl Derivatives):									
	1-CH_3-4-NHC(=O)CH_3 to 1-COOH-4-NHC(=O)CH_3								
117.	Co/Br	HOAc	—	95	—	100	1.0	air	[184]
	1-CH_3-3-Cl-4-NHC(=O)CH_3 to 1-COOH-4-Cl-4-NHC(=O)CH_3								
118.	Co/Br	HOAc	—	95	—	100	1.0	air	[183,184]
	1-CH_3-3-Br-4-NHC(=O)CH_3 to 1-COOH-3-Br-4-NHC(=O)CH_3								
119.	Co/Br	HOAc	—	95	—	100	1.0	air	[183,184]
	1-CH_3-2-Cl-4-NHC(=O)CH_3 to 1-COOH-2-Cl-4-NHC(=O)CH_3								
120.	Co/Br	HOAc	—	95	—	100	1.0	air	[183,184]
	1-CH_3-2-Br-4-NHC(=O)CH_3 to 1-COOH-2-Br-4-NHC(=O)CH_3								
121.	Co/Br	HOAc	—	95	—	100	1.0	air	[183,184]
Toluate:									
	1-CH_3-4-C(=O)OCH_3 (methyl *p*-toluate) to 1-COOH-4-C(=O)OCH_3								
122.	Co/Mn/Br	HOAc	97	94	—	—	—	—	[40]
123.	Co/Br	HOAc	—	80	0.5	150	—	—	[185]
Trifluoroethyl Derivatives:									
	3,3′,4,4′-$(CH_3Ph)_3CCF_3$ to 3,3′,4,4′-$(CH_3Ph)_3CCF_3$								
124.	Co/Mn/Br	HOAc	—	97	2.4	100–176	7.4	O_2	[186]

[a] Reagent was 92% pure.

[b] Reagent was 79% pure and contained other dibrominated xylenes.

[c] Hydrogen peroxide is first decomposed to dioxygen in a glass tube and then heated.



(4.8)

Part of the reason may be because much higher temperatures and pressures are required to oxygenate in water as compared to acetic acid.

In contrast to the MC method, *o*-chloro groups do not oxidize readily using Co/MEK type systems [28] (see items 51, 52). Long reaction times (28 h) are required to obtain a 59% yield in contrast to the MC method which gives a 81% yield in less than an hour:

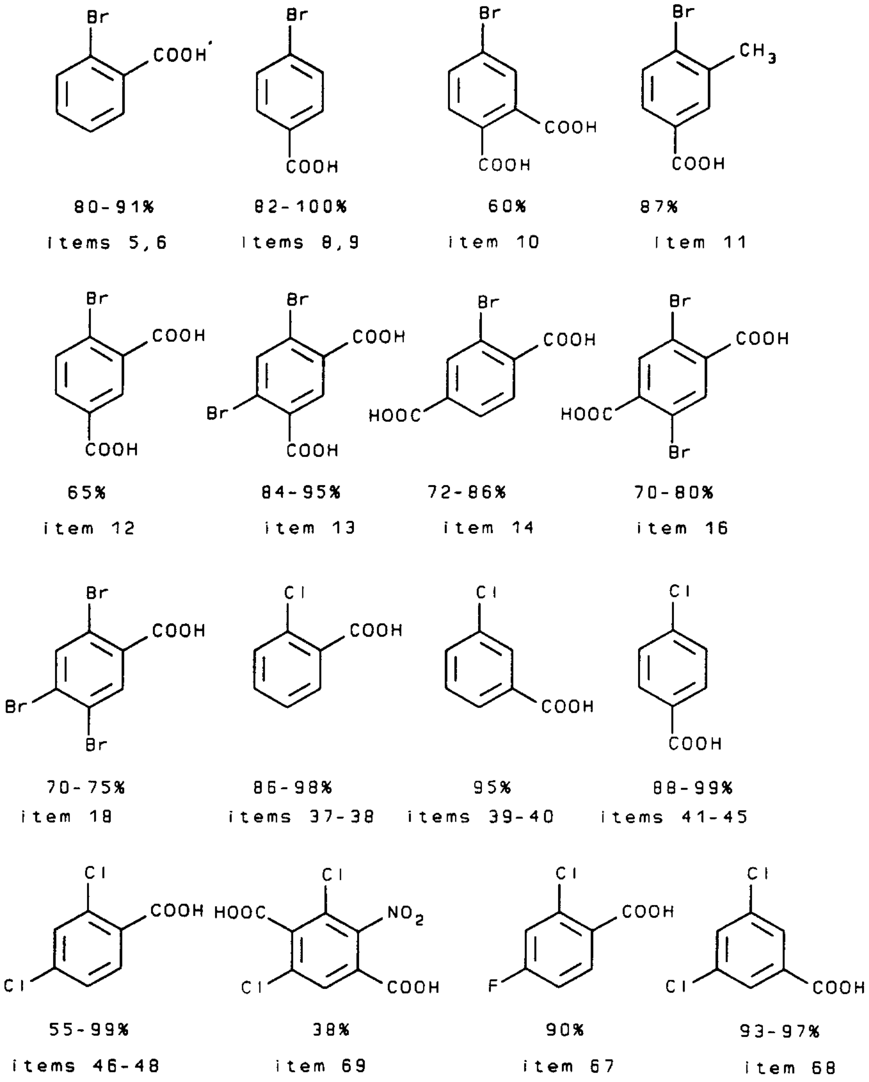
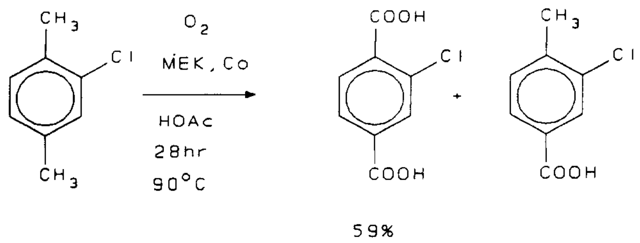
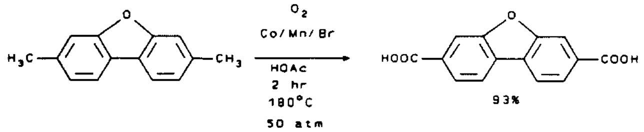


Fig. 4.2. Ring halogenated aromatic acids produced from MC oxidation (see Table 4.4 for details).



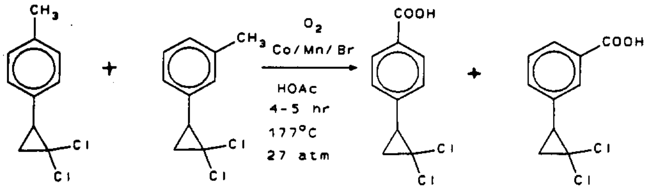
(4.9)

2,7-Dimethylbenzofuran has been oxidized to the dicarboxy-derivative in 93% yield (item 4):



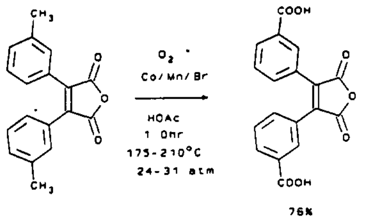
(4.10)

A mixture of the *meta*- and *para*-isomers of 2,2-dichlorocyclopropyltoluenes have been oxidized. The corresponding acid of the *para*-isomer was isolated from the precipitated reactor solids. The meta isomer remained in the filtrate and was subsequently isolated from it (items 55–57):



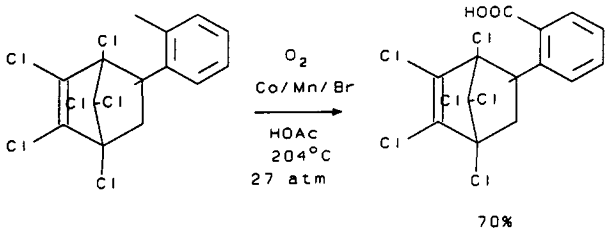
(4.11)

3,3′-Dicarboxy-diphenylmaleic anhydride has also been prepared (item 58):



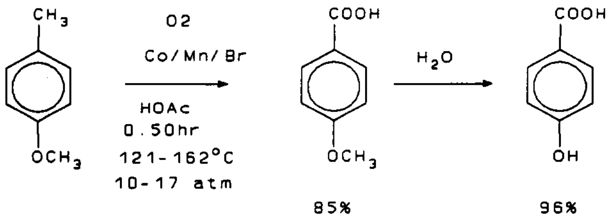
(4.12)

Hexachlorobicycloheptenyl derivatives have been prepared (items 59 and 60):



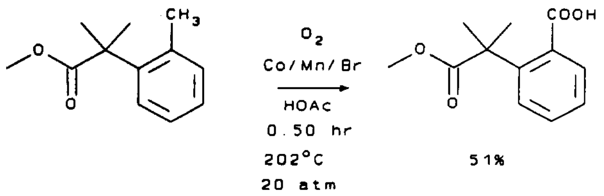
(4.13)

p-Hydroxybenzoic acid has been prepared by oxidation of *p*-methoxytoluene (item 62), which then was hydrolyzed to the phenol in 96% yield:



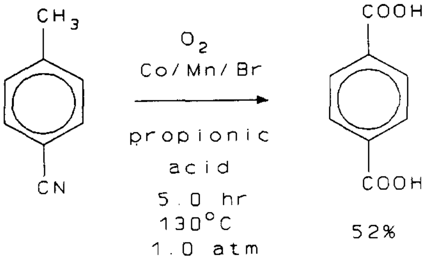
(4.14)

The benzylic methyl group is oxidized preferentially to an alkyl chain (items 65 and 66):



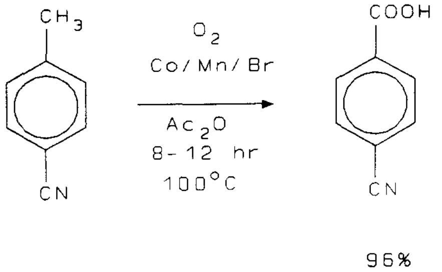
(4.15)

The nitrile group becomes solvolyzed to the carboxylic acid during the oxidation of 4-tolunitrile, presumably by the water generated by the oxidation of the methyl group (item 70):



(4.16)

The solvolysis of the nitrile group can be avoided by using acetic anhydride as the solvent, which immediately reacts with the water generated during the reaction (item 71):

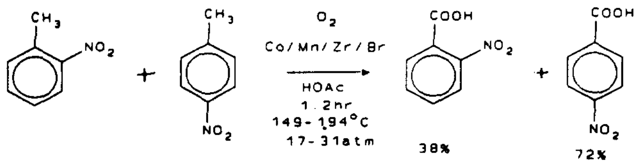


(4.17)

The low temperatures employed are probably necessary since acetic anhydride is autoxidized much more readily than acetic acid. The 3-methyl and 1,3,5-trimethyl derivatives have also been prepared (see items 72–73). An ethyl derivative has been oxidized to the carboxylic acid (item 29 of Table 5.1).

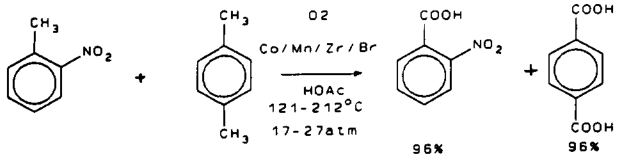
Nitro derivatives of polymethylbenzenes are difficult to oxidize. 3-Nitrotoluene and 4-nitrotoluene are 4.3 and 5.6 times less reactive than toluene (based on Hammett constants) and therefore high temperatures and/or pressures are necessary to achieve high yields in reasonable reaction times (items 74–85). *o*-Nitrotoluene is very reluctant to react. No detectable *o*-nitrobenzoic acid was found after reaction at 164–208°C under 17–27 atm pressure of air. Use of an acetic acid/acetic anhydride mixture as a solvent did result in a 20% conversion and 6% yield to nitrobenzoic acid under similar conditions. Whether this is a result of the different solvent or because acetic anhydride extensively decomposes (presumably to produce various radical products) with a resultant co-oxidation, is uncertain (see items 86, 87).

Excellent yields to *o*-nitrobenzoic acid, and other *o*-nitro derivatives, can be achieved by co-oxidation with another methylaromatic compound and by the knowledge that *o*-nitrobenzoic acid apparently extensively decarboxylates above 176°C. The initial report that no *o*-nitrobenzoic acid resulted from MC oxidation of a mixture of *o*- and *p*-nitrotoluenes may be because of the high temperature employed (213°C) (item 88). In another, later report these experiments were repeated, although not identically. Much lower yields to *o*-nitrobenzoic acid yields were reported when going to ***higher temperatures*** (see item 90), presumably due to decarboxylation of the *o*-nitrobenzoic acid:



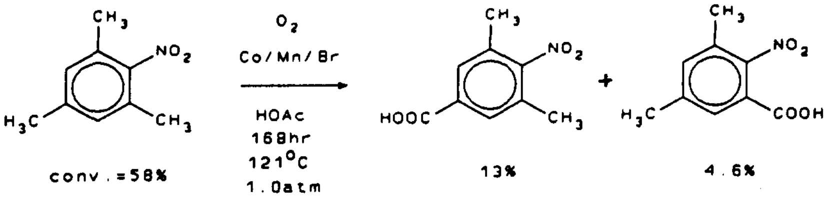
(4.18)

Very high yields of both *o*- and *p*-nitrobenzoic acid can be achieved by starting the reaction with all of the *o*-nitrotoluene initially present (batch mode of oxidation) and continuous addition of *p*-nitrotoluene (semi-continuous mode). Yields of 83% and 93% yield, respectively, were then obtained (see item 91). Similarly, *o*-nitrobenzoic and terephthalic acid can be co-produced both in 96% yields (see item 92):



(4.19)

2-Nitro-*p*-xylene, which gives only a 2% yield alone, can be co-oxidized with toluene to give 74% and 91% yields, respectively (see item 93–94). The original idea of co-producing *o*-nitrotoluene with another methylaromatic compound came from the results of oxidizing nitro-mesitylene (item 95):

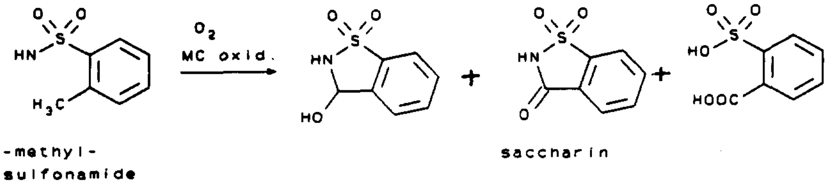


(4.20)

It was observed that both the *o*- and *p*-methyl groups were converted to acids under mild conditions. The interpretation was that the *p*-methyl group were co-oxidizing the *o*-methyl group to its carboxylic acid.

The acidity of sulfonic acid prevents the oxidation of 4-methylbenzenesulfonic acid under MC conditions (see Section 3.12). However, their methyl esters, sodium salts and sulfonamides have been successfully oxidized (see items 101 and 102).

2-Methylsulfonamide becomes oxidized to a mixture of products including saccharin:

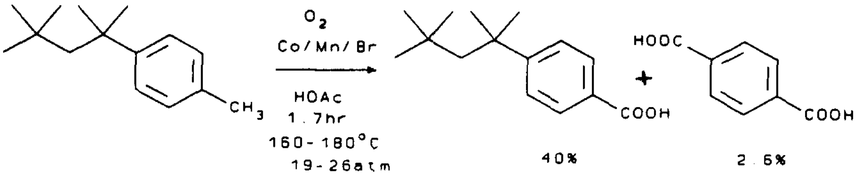


(4.21)

Saccharin can be obtained in 51–83 yields (see items 96–100). The intermediate 3-hydroxy-2,3-dihydrobenzisothiazole-1,1-dioxide can also be obtained in good yield (item 100).

The *t*-butyl group autooxidizes much more slowly than a benzylic methyl group as expected since primary, aliphatic C–H bonds have significantly higher bond strengths. Thus only a 11% benzoic acid is obtained from the oxidation of *t*-butylbenzene (item 103) while, under the same experimental conditions, a 91% yield of terephthalic acid is obtained from *p*-xylene or *p*-toluic acid [134]. Under the same experimental conditions, 4-*t*-butyltoluene is oxidized to 4-*t*-butylbenzoic acid in 65% yield (see item 106). The oxidation of the *t*-butyl group can be minimized by decreasing the Br/metals ratio and minimizing reaction temperature [72]. Yields in the 90–95% range have been reported for 4-*t*-butylbenzoic acid, 4-*t*-butyl-*o*-phthalic acid, and 5-*t*-butyl-1,3-isophthalic acid (items 104–115).

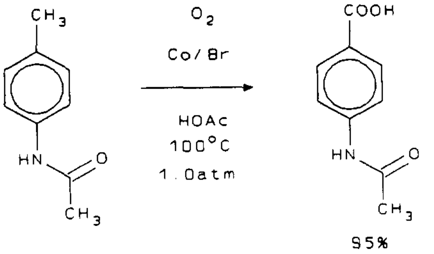
The benzylic methyl group becomes oxidized prior to the methylenic alkyl group since *p*-*t*-octylbenzoic acid can be obtained in 40% yield (item 116):



(4.22)

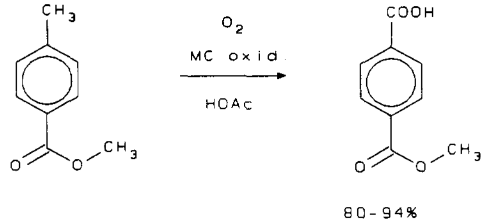
A 2.6% yield to terephthalic acid was also formed.

Primary amines are antioxidants and hence cannot be oxidized directly. *p*-Aminobenzoic acid can be prepared however, by first acylating the *p*-toluidine, performing an MC oxidation (see items 117–121), and then hydrolyzing the product:



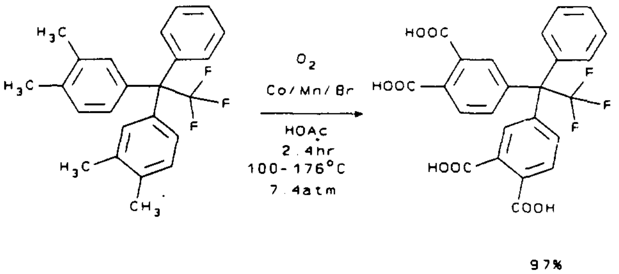
(4.23)

Methyl esters of aromatic carboxylic acids are stable during an MC oxidation (items 122 and 123):



(4.24)

A trifluoroethyl derivative has been prepared (item 124):



(4.25)

5. Oxidation of ethylbenzenes (see Table 5.1)

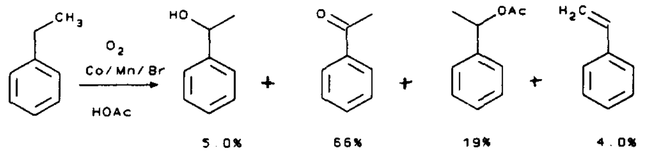
Similar to the methylbenzenes, ethylbenzenes can be oxidized using the MC method to a mixture of α-methyl alcohols, α-methyl acetates, ketones (i.e., acetophenones), and styrene (see item 1):

Table 5.1
Products and intermediates formed during the oxidation of ethylbenzenes and oxidation of ethylbenzene intermediates

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
To Alcohols:									
	$-CH_2CH_3$ to 1-$CH_2(OH)CH_3$ (ethylbenzene to α-methylbenzyl alcohol)								
1.	Co/Mn/Br	HOAc	95	5.0	–	–	–	–	[40]
2.	Co/Br	HOAc	87	8.4	7.0	90	1.0	O_2	[187]
	1-CH_2CH_3-4-OCH_3 to 1-$(CH_2OH)CH_3$-4-OCH_3								
3.	Co/Mn/Br	HOAc	77	5.0	–	–	–	–	[40]
To Acetates:									
	$-CH_2CH_3$ to 1-$CH_2(OAc)CH_3$ (ethylbenzene to α-methylbenzyl acetate)								
4.	Co/Mn/Br	HOAc	95	25	–	–	–	–	[40]
5.	Co/Br	HOAc,Ac_2O	97	29	25	90	1.0	O_2	[187]
6.	Co/Br,NaOAc	HOAc/Ac_2O	78	10	–	–	1.0	O_2	[96]
To Ketones:									
	$-CH_2CH_3$ to $-C(=O)CH_3$ (ethylbenzene to acetophenone)								
7.	Co on RS(1),NH_4Br^a	HOAc,Ac_2O	100	98	50	75	1.0	O_2	[187]
8.	Co/Br	HOAc,Ac_2O	94	66	50	75	1.0	O_2	[187]
9.	Co/Br	HOAc	–	82	1.5	87–110	1.0	O_2	[47]
10.	Co/Br,NaOAc	HOAc,Ac_2O	78	19	–	–	1.0	O_2	[96]
11.	Co/Mn/Br	HOAc	95	42	–	–	–	–	[40]
12.	Co/MEK	HOAc	–	25	48	90	1.0	O_2	[28]
13.	Co	HOAc	71	11	1.8	168–178	50	air	[19]
14.	Co/Cl	diglyme,MEK	–	45	40	60	–	–	[131]
15.	Zn,Fe$(OAc)_2^b$	HOAc,py	–	7.0	16	25	–	–	[188]
	1-CH_2CH_3-4-OCH_3 to 1-$C(=O)CH_3$-4-OCH_3								
16.	Co/Mn/Br	HOAc	77	20	–	–	–	–	[40]
	1-CH_2CH_3-4-$S(=O)_2(NH_2)$ to 1-$C(=O)CH_3$-4-$S(=O)_2(NH_2)$ (*p*-ethylbenzenesulfonamide to *p*-acetylbenzenesulfonamide)								
17.	Co/Mn/Br	HOAc	–	76	–	65	–	air	[189]
	1,3-CH_2CH_3 to 1-CH_2CH_3-3-$C(=O)CH_3$								
18.	Co/Mn/Br/MEK	HOAc,Ac_2O	–	74	3.0	70	–	–	[190]
	1-CH_3-4-CH_2CH_3 to 1-COOH-4-$C(=O)CH_3$								
19.	Co/Br	HOAc	–	78	0.75	90–112	1.0	O_2	[11,47]
To Styrenes:									
	1-CH_2CH_3 TO 1-$CH{=}CH_3$								
20.	Co/Br	HOAc,Ac_2O	94	4.0	50	75	1.0	O_2	[187]
To Acids:									
	1-CH_2CH_3 to 1-COOH (ethylbenzene to benzoic acid)								
21.	MC catalyst	HOAc	–	79	–	–	–	–	[90]
22.	Mn/Br	HOAc	–	79	2.0	204–216	27	air	[22]
23.	Mn/Br	HOAc	–	87	3.0	196	27	air	[191]
24.	Co/Mn/Br	benzoic/benzene	–	90	4.0	200	30	air	[74]
25.	Co/Mn/Br	benzoic acid	–	96	0.5	190–200	26	air	[120]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
	1,2-CH_2CH_3 to 1,2-COOH								
26.	MC catalyst	HOAc	–	–	2.0	195	14–28	air	[22]
	1,3-CH_2CH_3 to 1,3-COOH								
27.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[22]
	1,4-CH_2CH_3 to 1,4-COOH								
28.	Mn/Br	HOAc	–	45	2.0	180	20–27	air	[192]
	1-CH_2CH_3-4-CN to 1-COOH-4-CN								
29.	Co/Mn/Br	Ac_2O	–	73	8–12	100	–	–	[294]
	1-CH_2CH_3-4-OCH_3 to 1-COOH-4-OCH_3								
30.	Co/Mn/Br	HOAc	77	48	–	–	–	air	[40]
Oxidation of Intermediates:									
	1-C(=O)CH_3 to 1-COOH								
31.	Co/Mn/Br	propionic acid	–	93	20	130	1.0	O_2	[134]
32.	Mn/Br	propionic acid	–	90	20	130	1.0	O_2	[84]
33.	HBr	H_2O	–	74	20	200	26	air	[84]
34.	V,HBr	H_2O	–	58	4.0	200	–	O_2	[63]
	1-CH_2CH_3-4-C(=O)CH_3 to 1-4-COOH								
35.	Co/Br	HOAc	–	71	2.2	30–65	1.0	O_2	[47]
	1-C(=O)CH_3-4-acetoxy to 1-COOH-4-acetoxy								
36.	Co/Mn/Br	HOAc,Ac_2O	96	86	0.40	149	20	air	[73]
	1,4-C(=O)CH_3 to 1,4-COOH								
37.	Mn/Cu/Br	H_2O	–	62	3.0	200	30	O_2	[84]

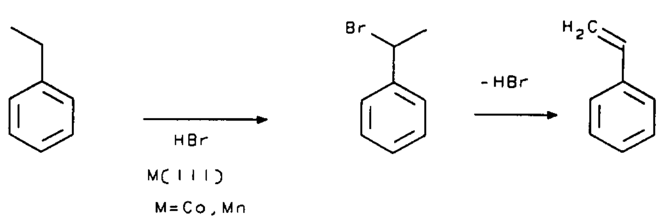
[a] RS = cross-linked polystyrene sulfonic acid ion-exchange resin
[b] This is not an autoxidation.



(5.1)

It is not known whether there is a direct route from the ethyl group to the ketone without alcohol formation. Reported yields to the alcohols under standard MC conditions are low — 5 to 8% (see items 1–3). Acetates form in 13–29% yields (items 4–6). Good yields of acetophenone, 25, 42, 66 and 82%, can be obtained from ethylbenzene (items 7–19). The yields are similar to non-MC cobalt catalysts (i.e., 11, 25, 48% (items 12–14)). 'GIF' systems are inferior (see item 15). Ketones of methoxy- (item 16), sulfonamide (item 17), and polyethyl (item 18) derivatives are also reported. A supported cobalt cross-linked polystyrene sulfonic acid catalyst with soluble ammonium bromide is claimed to give a much better selectivity to acetophenone (98% yield) than a mixture of cobalt acetate/ammonium bromide (60%) (item 7).

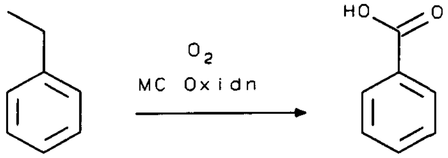
Styrene probably comes from bromination followed by dehydrohalogenation as has been proposed during the oxidation of tetralins [11]:



(5.2)

Bromination is a common occurrence in MC oxidations as previously discussed for benzylic bromides (see Section 1.8.5).

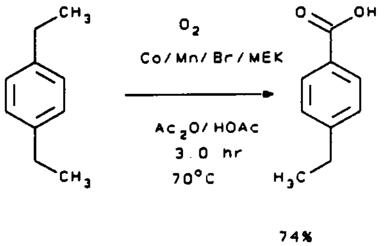
The ethyl group or any of the above intermediates can be further reacted to the carboxylic acid with a loss of a carbon atom (items 21–37). For example:



(5.3)

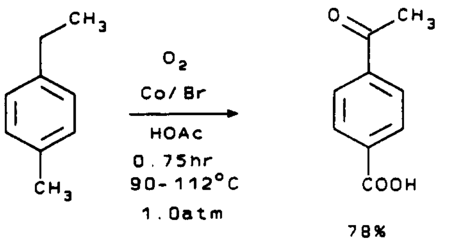
The fate of the lost carbon atom, as methanol, methyl acetate, or carbon dioxide is unknown. Oxidation of ethylbenzene to benzoic acid occurs under relatively mild conditions in reported yields from 79–90% (items 21–25). The 4-methoxy and 4-nitrile benzoic acids have been prepared starting from the ethyl-derivatives (items 29–30). Various acetophenones (items 31–37) have been oxidized to their carboxylic acids in good yields.

The initial oxidation of an ethyl group apparently deactivates the ring since a 74% yield to 4-ethylacetophenone is obtained (item 18):



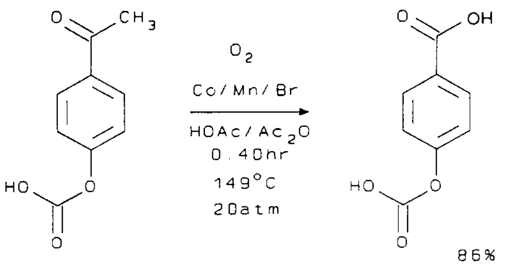
(5.4)

1-Methyl-4-ethylbenzene gives 1-carboxy-4-acetophenone in 78% yield (item 19): probably via the initial formation of 1-methyl-4-acetophenone followed by oxidation of the methyl group.



(5.5)

Phenols, although they are strong autoxidation poisons, can be masked by formation of their acetoxy derivatives (see item 36). For the oxidation of *p*-acetoxyacetophenone to *p*-acetoxybenzoic acid:

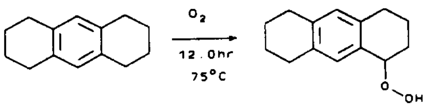


(5.6)

Continuous addition of acetic anhydride was used, presumably to limit the water concentration in the reactor and lessen the solvolysis of the acetate to the phenol. The yields were very sensitive to the amount of acetic anhydride addition. Small amounts of the phenols (approximately 1%) were present in the reaction mixture upon completion of the reaction (item 36).

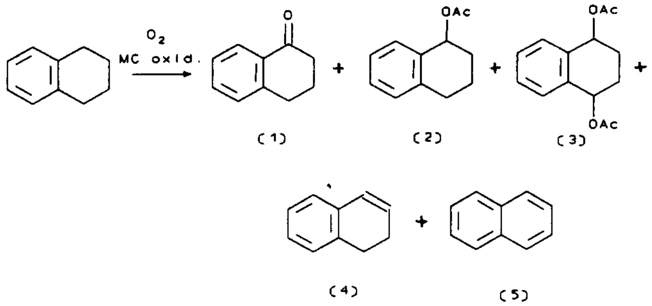
6. Oxidation of tetralins (see Table 6.1)

Peroxides are the primary product in autoxidations but is rarely isolated [133]. The peroxide of a tetrahydronaphthalene (tetralin) can be made directly from dioxygen [193]:



(6.1)

The chemistry of tetrahydronaphthalene is similar to that of the ethylbenzene derivatives discussed in Section 5. The oxidation of tetrahydronaphthalene (tetralin) yields a mixture of products associated with the oxidation of the benzylic methylene group:



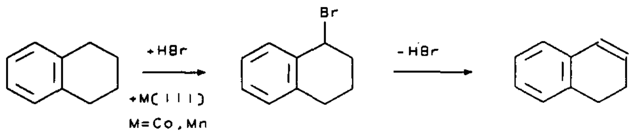
(6.2)

Table 6.1 gives the reported conversion and yields to the products given in reaction 6.2. The tetralone, product 1 in reaction 6.2, can be optimized by reactions close to room temperature and having an excess of dioxygen present [194] while the 1,2-dehydronaphthalene (product 4) formation is maximized by operating with a minimum concentration of dioxygen [111]. A number of methyl-tetrahydronaphthalenes have also been reported [111,194]. Acetic anhydride and a cerium containing catalyst apparently favors acetate formation [195].

The 1,2-dihydronaphthalene and naphthalene probably comes from bromination, analogous to the formation of benzylic bromides for the methyl benzenes, followed by dehydrohalogenation [11]:

Table 6.1
Reported products from the MC oxidation of tetrahydronaphthalene

	Product from reaction 6.2						
	Conv.	(1)	(2)	(3)	(4)	(5)	Ref. No.
Co/Br HOAc	82	46	–	–	15	–	[194]
Co/Br HOAc	–	46	–	–	10	0.5	[11]
Co/Br propionic acid	33	5.0	–	–	21	5.0	[11]
Co/Ce/Br Ac_2O	76	–	69	12	–	18	[195]
Co/Mn/Br HOAc	52	5.0	2.6	–	–	37	[40]



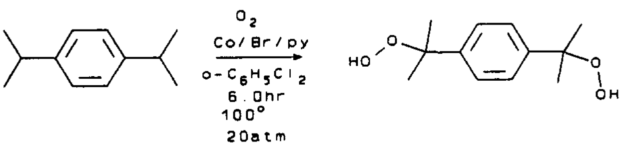
(6.3)

A repeat of this sequence would yield naphthalene. The MC oxidation of tetralin or tetralin derivatives to *o*-phthalic acid similar to ethylbenzene being oxidized to benzoic acids, has not been reported. Although it probably could be accomplished, the formation of olefinic derivatives would make it more difficult.

7. Oxidation of isopropylbenzenes (see Table 7.1)

The interest in isopropylbenzenes stems from their relatively easy preparation via alkylation with propylene. Isopropylbenzenes have been used to prepare benzoic acid, items 3–8, *o*-phthalic acid (item 9), isophthalic acid (item 10), and terephthalic acid (items 11–15). Yields to aromatic acids from isopropylbenzenes, run under identical conditions, appear to be lower than from methyl and ethylbenzenes. Thus the yields to benzoic acid, from toluene, ethylbenzene, and isopropylbenzene (cumene) are 88, 79, and 57% respectively [90]. For *p*-xylene and di-isopropylbenzene to terephthalic acid yields of 75 and 59% have been reported [97].

The reaction mechanism of the isopropylbenzenes to the aromatic carboxyl derivatives has been studied in some detail [14]. Fig. 7.1 combines the information from Kooyman et al. with the well-established acid-catalyzed re-arrangement of the peroxide to phenol and acetone. The formation of free radicals during the MC oxidation of cumene has been observed via esr [29]. The peroxide is relatively easily formed (item 1):



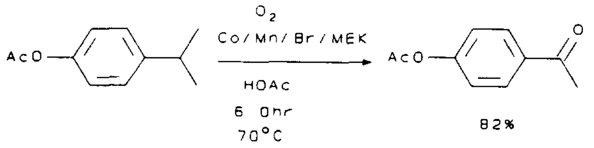
(7.1)

Acetic acid is known to catalyze its re-arrangement to phenol and acetone. The formation of phenol both inhibits the reaction and constitutes a yield loss. The alkoxy radical either loses a methyl radical to give

Table 7.1
Products from the MC oxidation of isopropylbenzenes

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
To Intermediates:									
	1,4-diisopropyl to 1,4-diisopropyl peroxide								
1.	Co/Br/Py *o*-$C6H_4Cl_2$	–	98	78	6.0	100	20	–	[196
	1-iPr-4-OC(=O)CH_3 to 1-C(=O)CH_3-4-OC(=O)CH_3 (*p*-isopropylphenyl acetate to acetoxyacetophenone)								
2.	Co/Mn/Br/MEK	HOAc	–	82	6.0	70	–	–	[197
To Carboxylic Acids:									
	1-iPr to 1-COOH (isopropylbenzene(cumene) to benzoic acid)								
3.	MC catalyst	HOAc	–	80	–	–	–	–	[90]
4.	Mn/Br	HOAc	–	56	2.0	204–216	27	air	[22]
5.	Mn/Br,polysiloxane	HOAc	–	89	0.70	190	–	air	[199]
6.	Co/Mn/Br	propionic acid	–	81	20.0	130	1.0	O_2	[198]
7.	Co/Mn/Br	benzoic acid	–	90	10.0	–	1.0	O_2	[198]
8.	V/Br	H_2O	–	59	4.0	200	–	O_2	[63]
	1,2-iPr to 1,2-COOH								
9.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[22]
	1,3-iPr to 1,3-COOH								
10.	Mn/Br	HOAc	–	–	–	195	14–27	air	[22]
	1,4-iPr to 1,4-COOH								
11.	Mn/Br polysiloxane	HOAc	–	73	0.75	210	–	air	[199]
12.	Co/Mn/Br	propionic acid	–	43	8.0	130	1.0	O_2	[84]
13.	V/Br	propionic acid	–	55	5.0	200	15	O_2	[84]
14.	Mn/Cu/Br	H_2O	–	60	3.0	200	30	O_2	[84]
15.	HBr	H_2O	–	40	20	200	26	O_2	[84]
Derivatives of Isopropylbenzenes:									
	1-iPr-4-COOH to 1,4-COOH								
16.	Mn/Cu/Br	H_2O	–	81	3.0	200	30	O_2	[84]
17.	V/Br	H_2O	–	82	4.0	200	–	O_2	[63]
18.	Co/Mn	buteric acid	–	85	1.5	150	–	O_2	[14]
Oxidation of Intermediates:									
	1,4-C(OH)$(CH_3)_2$ to 1,4-COOH								
19.	Mn/Cu/Br	H_2O	–	52	3.0	200	30	O_2	[84]

acetophenone (the desired pathway) or abstracts a hydrogen atom to give the alcohol. Dehydration of the alcohol to α-methylstyrene is undesirable because of a slower reaction to the glycol which eventually goes to the carboxylic acid [14].



(7.2)

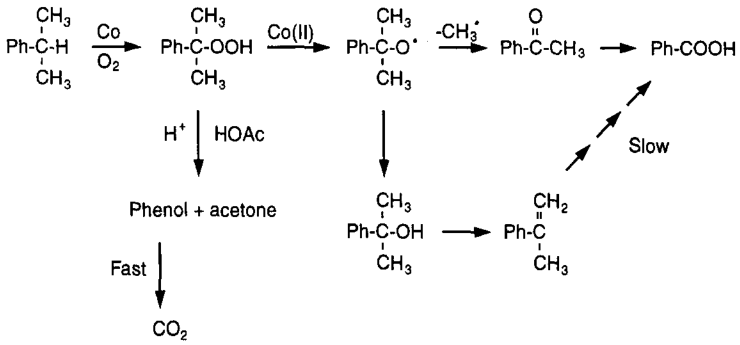
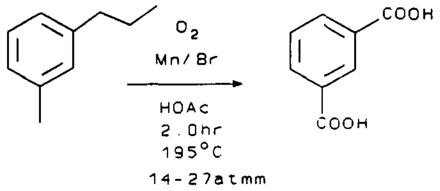


Fig. 7.1. Suggested mechanism for the oxidation of isopropylbenzenes to aromatic acids.

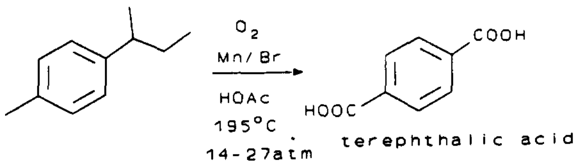
The type of bromine source as well as the mode of addition of bromine was different since benzylic bromide was added every hour for up to six hours.

8. Results from the MC oxidation of other alkylbenzenes (see Table 8.1)

At high temperatures and pressures (above 190°C and above 14 atm air), alkyl groups can be ozidized with a carboxyl group, as expected from the discussion in Section 14. Benzene derivatives with methyl-, n- and iso-propyl, n- and sec-butyl groups on the ring can be ozidized to their corresponding carboxylic acids (see items 1–13 in Table 8.1). Examples are (items 2 and 12):

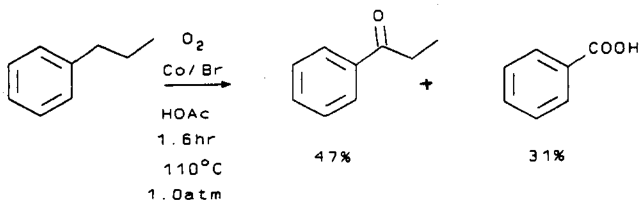


(8.1)



(8.2)

At lower temperatures and pressures, one can obtain reasonable yields of the benzylic intermediates. The oxidation of the n-propyl group goes through the propionphenone, as expected (item 14):

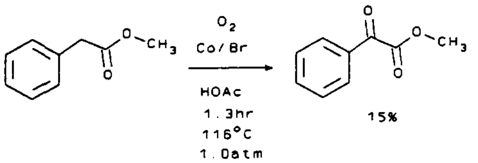


(8.3)

Benzylic oxidation occurs in methyl phenyl acetate (item 15):

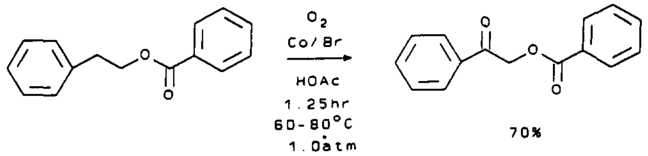
Table 8.1
Oxidation of miscellaneous alkylbenzenes

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
	1-n-propyl to 1-COOH (benzoic acid)								
1.	Co/Mn/Br	HOAc	–	79	–	–	–	–	[40]
	1-CH_3-2-n-propyl to 1,2-COOH								
2.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[192,22]
	1-CH_3-3-n-propyl to 1,3-COOH (isophthalic acid)								
3.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[192,22]
	1-CH_3-4-n-propyl to 1,4-COOH (terephthalic acid)								
4.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[192,22]
	1-CH_3-4-iPr to 1,4-COOH (*p*-cymene to terephthalic acid)								
5.	Co/Mn/Br	–	–	70	–	150	20	air	[307]
6.	Co/Mn/Br	propionic acid	–	67	30	130	1.0	O_2	[84]
7.	Mn/Br	HOAc	–	55	2.0	180	20–27	air	[192]
8.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[22]
	1-CH_3-2-n-butyl to 1,2-COOH (to *o*-phthalic acid)								
9.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[192,22]
	1-CH_3-3-n-butyl to 1,3-COOH (to isophthalic acid)								
10.	Mn/Br	HOAc	–	–	2.0	195	14–27	air	[192,22]
	1-CH_3-4-n-butyl to 1,4-COOH (2-(4-tolyl)-butane to terephthalic acid)								
11.	Mn/Br	HOAc	–	–	–	195	14–27	air	[22]
	1-CH_3-2-(-$CH_2(CH_3)(CH_2CH_3)$) to 1,2-COOH								
12.	Mn/Br	HOAc	–	–	–	195	14–27	air	[22]
	1-CH_3-4-(-$CH_2(CH_3)(CH_2CH_3)$) to 1,4-COOH								
13.	Mn/Br	HOAc	–	–	–	195	14–27	air	[22]
Partial Oxidations of Alkyl Groups:									
	1-n-propyl to -C(=O)CH_2CH_3 (n-propylbenzene to propionphenone)								
14.	Co/Br	HOAc	–	47	1.6	110	1.0	O_2	[47]
	1-CH_2C(=O)OCH_3 to 1-C(=O)C(=O)OCH_3 (methyl phenylacetate to methyl benzoylformate)								
15.	Co/Br	HOAc	38	15	1.3	116	1.0	O_2	[11]
	1-CH_2CH_2O(C=O)Ph to 1-C(=O)CH_2O(C=O)Ph (b-phenylethyl benzoate to phenaceylbenzoate)								
16.	Co/Br	HOAc	–	70	1.3	60–80	1.0	O_2	[11]
	Benzyl-n-butyl ether to n-butylbenzoate								
17.	Co/Br	HOAc	–	60	1.0	100	1.0	O_2	[11]
Oxidation of Styrenes:									
	Styrene to styrene oxide								
18.	MC catalyst	HOAc	–	–	–	110	–	–	[200]
	α-Methylstyrene to acetophenone								
19.	Co(OAc)$_2$,NaBr,NaOAc	HOAc,Ac_2O	45	30	–	–	1.0	–	[11]



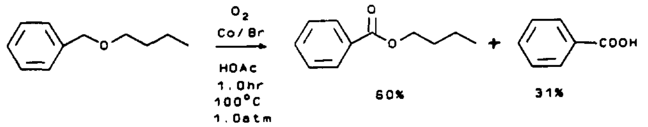
(8.4)

in phenyethyl benzoate (item 16):



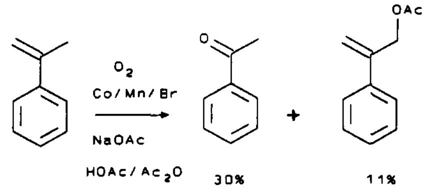
(8.5)

as well as in benzyl-n-butyl ether (item 17):



(8.6)

There is a report that styrene can form styrene oxide (item 18), presumably by the preacids formed during the oxidation of styrene to acetophenone, but without a stated yield. Styrene gives a 30% yield to acetophenone and 11% yield to α-acetoxysztyrene (item 19):



(8.7)

9. Oxidation of alkylnaphthalenes

9.1 Introduction

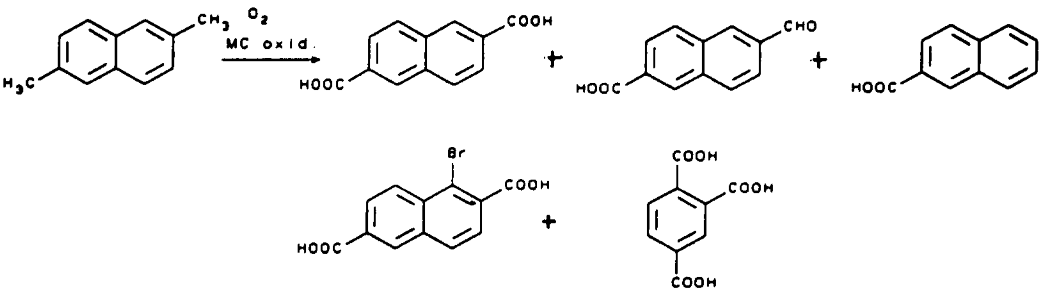
The chemistry of naphthalene derivatives is similar to benzene derivatives, except that: (1) the ring is easily brominated and (2) the ring is more easily oxidized. Since the most favorable bromination site is in the 1-position [201], one should expect to see this as a by-product. The C–H bond strength of the methyl group on naphthalene (86 kcal/mol) is weaker than the corresponding benzene derivatives (88–89 kcal/mol) hence the naphthalene derivatives should be more easily oxidized than benzene derivatives. In practice, one finds them significantly less reactive because the reactions are self-inhibiting by peroxy radical attack of the ring. This also results in a kinetic chain length of about 12 [15]. In addition, naphthoquinones form during the oxidation which also auto-retard the reaction [15]. This probably is the reason why quite high catalyst concentrations are required to successfully complete these reactions. This self-inhibiting reaction apparently accounts for the stability of naphthalenes as lubricating oils [202] and why the conversion of naphthalene substrate during oxidation decreases as the substrate concentration increases [62]. After initial ring attack by a peroxyradical, one of the naphthalene rings is ultimately destroyed giving a phnyl carboxylic acid as a by-product.

Thus typical products from the MC oxidation of 2,6-dimethylnaphthalene are significant amounts of a 1-bromo-2,6-dicarboxynaphthalene and trimellitic acid along with small amounts of an aldehyde and mono-decarboxylated product:

Table 9.1
MC oxidation of methylnaphthalenes

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Oxidation of Methyl Naphthalenes to Intermediates:									
	2,6-CH_3 to 2-CHO-6-CH_2OAc								
1.	Co/Mn/Br	HOAc,Ac_2O	–	10	2.5	120	25	–	[207]
	2-CH_3 to 2-CHO								
2.	Co	HOAc	70	49	–	90	1.0	–	[127]
	2-CH_3-7-OC(=O)CH_2CH_3 to 2-CHO-7-OC(=O)CH_2CH_3 (2-methyl-7-propionyloxonaphthalene to 2-formyl-7-propionyloxonaphthalene)								
3.	Co/Mn/Br	HOAc/Ac_2O	100	19	2.0	180	8.0	air	[208]
	2-CH_3-6-OC(=O)CH_3 to 2-CHO-6-OC(=O)CH_3 (2-methyl-6-acetoxynaphthalene to 2-formyl-6-acetoxynaphthalene)								
4.	Co/Mn/Br	HOAc/Ac_2O	55	40	2.4	120	25	air	[208]
	2-CH_3-6-OC(=O)C$(CH_3)_3$ to 2-CHO-6-OC(=O)C$(CH_3)_3$ (2-methyl-6-isobutyrylnaphthalene)								
5.	Co/Mn/Br	HOAc/Ac_2O	100	21	2.4	150	10	air	[208]
Oxidation of Polymethylnaphthalenes to Carboxylic Acids:									
	1-CH_3 to 1-COOH								
6.	Co/Mn/Br	HOAc	–	75	–	204	27	air	[122]
	2-CH_3 to 2-COOH								
7.	Co/Mn/Br	HOAc	–	83	–	204	27	air	[122]
8.	Co/Mn/Br	HOAc	–	88–89	0.35	120	20	air	[209]
9.	Co/Br	HOAc	–	87	–	120–150	20	–	[210]
	1,4-CH_3 to 1,4-COOH								
10.	Co/Mn/Br	HOAc	–	86	1.0	115	30	–	[211]
11.	Co/Mn/Br	HOAc	93	72	1.8	–	–	–	[212]
	2,3-CH_3 to 2,3-COOH								
12.	Co/Mn/Br	HOAc	–	78	–	120	10	air	[213]
13.	Co/Ce/Br	HOAc	–	76	0.75	–	8.0	–	[214]
14.	Co/Mn/Zr/Br	HOAc	–	73	0.75	140	–	air	[215]
	2,6-CH_3 to 2,6-COOH								
15.	Co/Mn/Br	HOAc	–	93	1.5	196	16	air	[60]
16.	Co/Mn/Br	HOAc	–	85	–	150	10	–	[62]
17.	Co/Mn/Br	HOAc	–	95	0.50	200	30	–	[216]
18.	Co/Mn/Br	propionic acid	–	30	20	130	1.0	O_2	[84]
19.	Co/Mn/Ru/Br	HOAc	100	69	2.0	150	10	air	[85]
20.	Co/Mn/Br	HOAc,Ac_2O	–	44	2.5	120	25	–	[207]
	2,7-CH_3 to 2,7-COOH								
21.	Co/Mn/Br	HOAc	–	79	–	–	–	–	[40]
	1,2,5,6-CH_3 to 1,2,5,6-COOH								
22.	Co/Mn/Br	HOAc	–	68	0.50	175	50	air	[217]
Oxidation of Derivatives of Methylnaphthalenes:									
	1-CH_3-4-CN to 1-COOH-4-CN								
23.	Co/Mn/Br	Ac_2O	–	66	8–12	100	–	–	[284]
	2-CH_3-1-Br to 2-COOH-1-Br								
24.	Co/Mn/Br	HOAc	–	77	3.0	160	8.0	–	[218]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
	2-CH_3-7-OC(=O)CH_2CH_3 to 2-COOH-6-OC(=O)CH_2CH_3 (2-methyl-6-propionyloxo)								
25.	Co/Mn/Br	HOAc/Ac_2O	100	51	2.0	180	8.0	air	[208]
	2-CH_3-6-OC(=O)CH_3 to 2-COOH-6-OC(=O)CH_3								
26.	Co/Mn/Br	HOAc	100	85	2.0	90	–	–	[219]
27.	Co/Mn/Br	HOAc/Ac_2O	100	88	2.0	115	2	air	[208]
	2-CH_3-6-C(=O)C$(CH_3)_3$ to 2,6-COOH								
28.	Co/Mn/Br	HOAc	–	82	8.0	180–220	–	air	[220]
Oxidation of Intermediates of Methylnaphthalenes:									
	1-CH_2OH-4-CH_3 to 1-CH_2OH-4-COOH (1-hydromethyl-4-methylnaphthalene to 1-hydroxymethyl-4-carboxynaphthalene)								
29.	Co/Mn/Br	HOAc	–	65	–	70	1.0	air	[206]
	1-CH_2OH-4-CH_3 to 1,4-COOH (1-hydromethyl-4-methylnaphthalene to 1,4-dicarboxynaphthalene)								
30.	Co/Mn/Br	HOAc	–	71	4.0	100	1.0	air	[206]



(9.1)

Despite these problems, high yields to 2,6-dicarboxybenzene can be obtained by optimization of the hydrocarbon throughput, Co/Mn ratio, temperature, and catalyst concentration during continuous operation. The trimellitic acid formed does deactivate the catalyst (see Section 1.8). Addition of trimellitic acid so that the trimellitic acid/catalyst metals, mol/mol, ratio = 1.0 resulted in a decrease in yield from 91 to 48% during semi-continuous operation (item 15).

9.2. *Oxidation of methylnaphthalenes (see Table 9.1)*

The intermediates from the MC oxidation of the methyl group are similar in kind and yields to the benzene derivatives (see Section 4.2). Thus items 1–5 report a 10% yield to an acetate and 19–49% yields to aldehydes. The formyl acetoxy-, propionyloxy-, and isobutyryloxo- have been prepared as mixtures of the aldehyde and acid (items 3–5, 25, 27):

Table 9.2
Results from the MC oxidation of ethylnaphthalenes

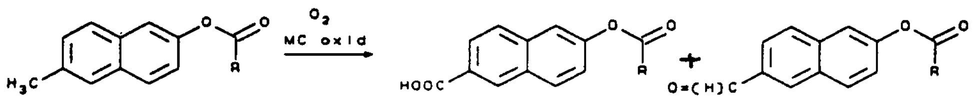
Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Oxidation of Ethyl Derivatives to Intermediates:									
	2-Et to 2-C(=O)CH_3								
1.	Co/Mn/Br	HOAc	87	28	–	–	–	–	[40]
Oxidation of Ethyl Derivatives to Naphthoic Acids:									
	2,6-Et to 2,6-COOH								
2.	Co/Mn/Ce/Br	HOAc	–	90	–	193–197	27	air	[222]
3.	Co/Mn/Ni/Br	HOAc	–	94	–	180	25	air	[223]
4.	Co/Mn/Br	HOAc	93	84	3.0	200	30	air	[224]
	2-Et-6-OC(=O)CH_3 to 2-COOH-6-OC(=O)CH_3O								
5.	Co/Mn/Br	HOAc	100	76	2.5	120	25	air	[208]
Oxidation of Intermediates:									
	2-acetyl-6-CH_3 to 2,6-COOH								
6.	Co/Mn/Br	HOAc	–	92	–	200	20	–	[225]
7.	Co/Mn/Br	HOAc	–	94	1.0	210	20	air	[226]
8.	Co/Mn/Br	HOAc	–	79	0.60	180	57	air	[227]
9.	Co/Mn/Br	HOAc,H_2O	–	81	–	140–190	25	–	[228]
	2-acetyl to 2-COOH								
10.	Co/Mn/Br	HOAc	97	96	–	–	–	–	[40]

Table 9.3
MC oxidation of isopropylnaphthalene derivatives

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
To Intermediates:									
	2,6-iPr to 2,6-diisoperoxide								
1.	$CoBr_2Py_2$	*o*-$C_6H_4Cl_2$	98	76	6.0	100	20	–	[196]
To Carboxylic Acids:									
	2,6-iPr to 2,6-COOH								
2.	Co/Mn/Br	HOAc	–	82	2.0	200	30	air	[229]
3.	Co/Mn/Br	HOAc	–	83	4.0	200	30	–	[230]
4.	Co/Mn/Br	HOAc	–	84	–	200	30	–	[231]
5.	Co/Mn/Br/AcONa	HOAc	–	85	–	–	–	–	[232]
6.	Co/Mn	propionic acid	79	63	12	160	10	air	[233]
7.	Co/Mn/Ce/KOAc/Br	HOAc	–	92	4.0	200	30	air	[234]
8.	Co/Mn/Ce/Br	HOAc	–	74	–	193	27	air	[205]
9.	Co/Mn/Br/AcONa	HOAc	–	84	–	170	–	–	[235]
10.	Co/Mn/Br	HOAc	–	82	5.0	180–190	20	air	[236]
11.	Cu/Mn/Br	HOAc	–	80	–	190	30	–	[204]

Table 9.4
Results from the MC oxidation of miscellaneous naphthalene derivatives

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Oxidation of Alkylnaphthalenes to Naphthoic Acids:									
	1-$CH_2CH_2CH(CH_3)_2$ to 1-COOH (1-isoamylnaphthalene to 1-naphthoic acid)								
1.	Co/Mn/Br	HOAc	–	50	–	204	27	air	[122]
Oxidation of Miscelleneous Naphthalene Derivatives:									
	2-methyl-6-($C(=O)CH_2CH_2CH_3$) to 2,6-COOH								
2.	Co/Mn/Fe/HBr	HOAc	–	90	–	210	20	air	[237]
	1,8-ethane to 1,8-COOH								
3.	Co/Mn/Br	HOAc	–	72	2.0	204	27	air	[238]
4.	Co/Mn/Br	HOAc,PhCl	–	93	2.0	200	20	air	[239]
	1,8-ethanenaphthalene to acenaphthenone								
5.	Co/Mn/Br	HOAc	100	85	5.0	30	–	–	[240]
	acenaphthequinone to 1,8-naphthalic anhydride								
6.	Co/Mn/Br	$PrCO_2H$	–	–	–	–	–	–	[241]
	anthracene to anthraquinone								
7.	Co/Mn/Br	HOAc	–	82	–	121–149	28	air	[242]
	phenanthrene to 2,2′-diphenic acid								
8.	Co/Mn/Br	propionic acid	–	28	16	130	1.0	O_2	[84]



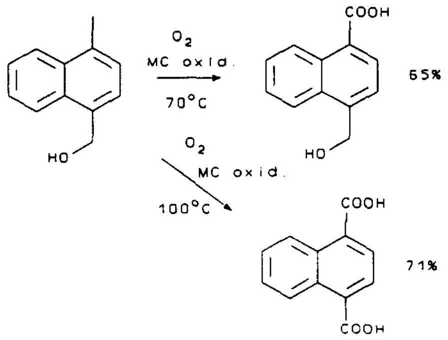
(9.2)

Changing from a Co/Br catalyst to a more active Co/Mn/Br resulted in a higher yield to the acid (79%).

There is an extensive patent literature for the preparation and oxidation of 2,6-dimethyl-, diethyl- and diisopropyl-derivatives because they can be oxidized to 2,6 dicarboxynaphthalene. The large scale commercial production of this acid has been announced by Amoco Chemical for start-up in 1995. It is used to make a polyester with ethylene glycol similar to terephthalic acid [203]. All 2,6-derivatives, dimethyl-, diethyl-, di-isoproyl-, etc. form 1,2,4-tricarboxybenzene (trimellitic acid) as a by-product in significant yields. Trimellitic yields of 11% [204] and 16% [205,204] have been reported as a result of ring oxidation during the oxidation of 2,6-diisopropylnaphthalene.

High yields of naphthalene carboxylic acids of the 1; 2; 1,4; 2,3; 2,6; 2,7, and 1,2,5,6 isomers have been prepared (see items 6–22). Bromo- and cyano-derivatives, the latter without solvolysis of the cyano bond, have been prepared (see items 23 and 24).

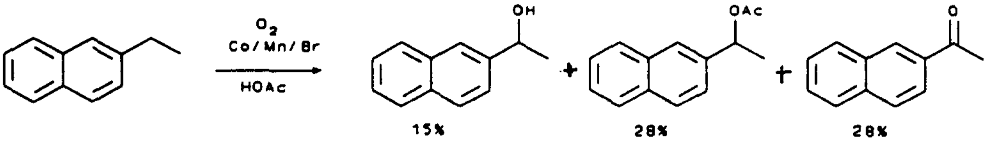
1-Hydroxymethyl-ethylnaphthalene was prepared from 1-methylnaphthalene by chloromethylation with *para*-formaldehyde and hydrochloric acid followed by hydrolysis with sodium hydroxide. The alcohol–acid, reaction 9.3, could be achieved in 65% yield by keeping a reaction temperature of 70°C and the di-acid could be obtained by raising the temperature to 100°C (items 29 and 30):



(9.3)

9.3. *Oxidation of ethylnaphthalenes (see Table 9.2)*

As in the case of ethylbenzenes (see Section 5), mixtures of the acetophenones, alcohols and acetates can be obtained (see item 1):



(9.4)

The 2- and 2,6-dicarboxynaphthalenes have been prepared from ethyl- and aceto-derivatives (see items 2–10).

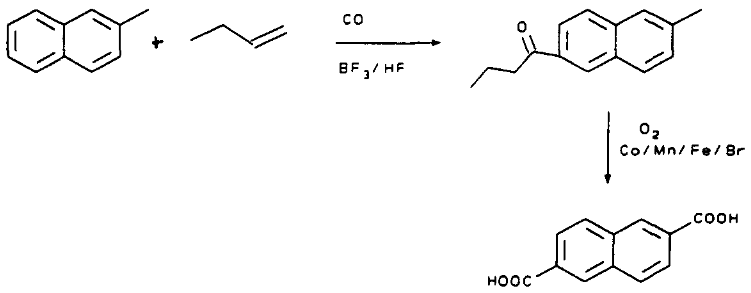
9.4. *Oxidation of isopropylnaphthalenes (see Table 9.3)*

A peroxide of 2,6-di-isopropylnaphthalene has been isolated, similar as that reported for the benzene derivative (Section 7), (see item 1).

As discussed with the benzene derivatives, the isopropyl derivatives should give much lower yields than the methyl derivatives and this is found. Since naphthalene derivatives are self-inhibited by ring attack (Section 9.1), the yields will be depressed even lower. Under comparable conditions, the yields to 2,6-dicarboxynaphthalene using the dimethyl reagent (93%, [60]) is much higher than with the di-isopropyl reagent (74%, [205]) with 6.3 times more trimellitic acid formation in the latter.

9.5. *Oxidation of miscellaneous alkylnaphthalenes (see Table 9.4)*

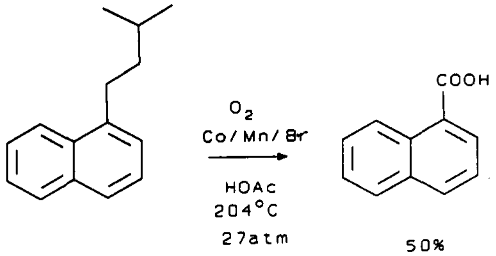
The preparation of 2,6-dicarboxynaphthalene has been prepared starting with the carbonylation of 2-methylnaphthalene with propylene (see item 2):



(9.5)

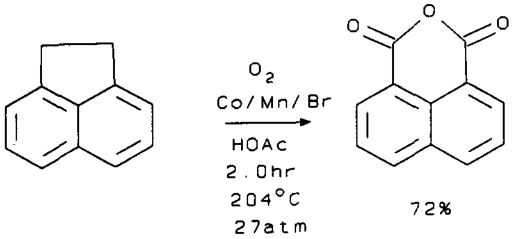
1000 tons of the diacid were produced in 1990 by Mitsubishi Gas Chemicals [237].

As we found for the long-chained alkyl derivatives of benzene (Section 8), 1-isoamylnaphthalene can be used to prepare 1-naphthoic acid (see item 1):



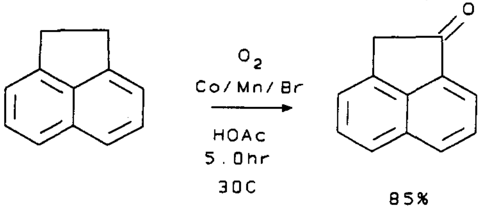
(9.6)

As expected, 1,8-ethanenaphthalene can be oxidized to the 1,8-dicarboxynaphthalene in 72–85% yields (see items 3 and 4):



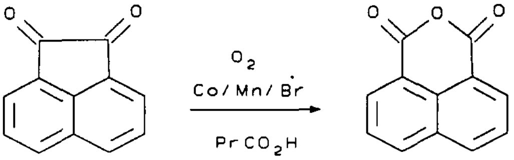
(9.7)

Related reactions are the oxidation of 1,8-ethanenaphthalene to the mono-ketone (item 5):



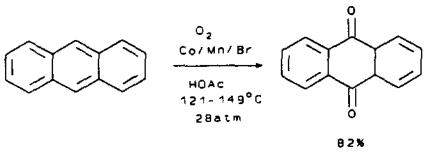
(9.8)

and the quinone to the anhydride (item 6):



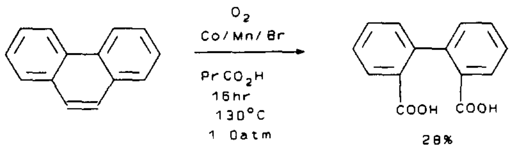
(9.9)

Anthracene is easily oxidized anthraquinone in 82% yield (item 7):



(9.10)

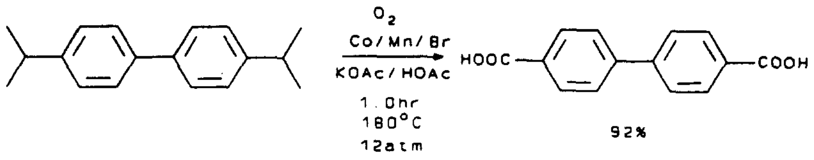
Similarly phenanthrene is oxidized to 2,2′-diphenic acid (item 8):



(9.11)

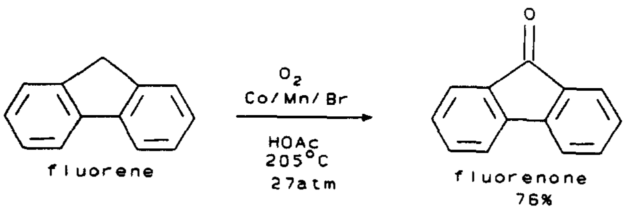
10. Oxidation of biphenyls (see Table 10.1)

Alkyl groups (methyl, ethyl, acetyl and isopropyl) in the 2; 2,2′-; 3,5-; 2,5-; 3,4′-; 4,4′-; 3,4,4′-; 2,5,4′-, and 3,3′,4,4′-positions have been autoxidized. For example, the oxidation of 4,4′-diisopropylbiphenyl (item 14):



(10.1)

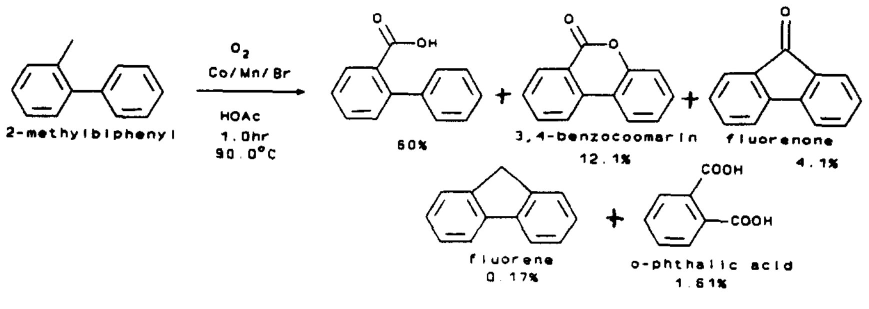
Under high temperatures (> 200°C) and pressures methylenic groups can be converted to ketones in high yield without substantial cleavage of the methylenic bond (item 1).



(10.2)

More examples will be given in Section 11.

The oxidation of 2-methylbiphenyl gives the expected acid, but also a 12% yield to 3,4-benzocoumarine and a 4.1% yield to fluorenone (item 3):



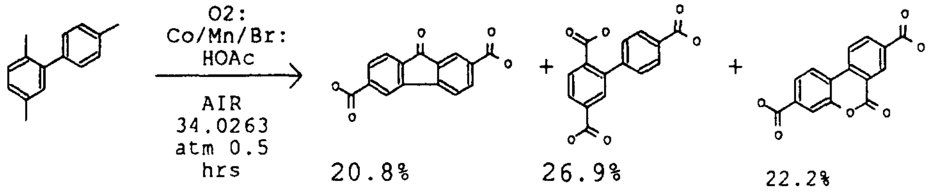
(10.3)

Table 10.1
MC reactions of alkylbiphenyl compounds

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp (°C)	*P* (atm)	O_2 source	Ref. No.
	2,2′-CH2– to 2,2′-C(=O)– (fluorene to fluorenone)								
1.	Co/Mn/Br	HOAc	–	76	–	205	27	air	[123]
	2-CH_3 to 2-COOH								
2.	$CoCl_2$/ (didecyl)$_2NH_2^+$Br	solventless	–	89	4.0	160	20	air	[103]
3.	Co/Mn/Br	HOAc	–	60	7.0	100	1.0	air	[40]
	4-CH_3 to 4-COOH								
4.	$CoCl_2$/ (decyl)$_2H_2N^+$Br	solventless	–	92	3.0	165	10	air	[103]
	4-acetyl to 4-COOH								
5.	Co/Mn/Br	HOAc	–	99	1.0	170–180	20	air	[245]
6.	Co/Mn/Br	HOAc	–	98	0.67	150–180	20	air	[246]
	3,5-CH_3 to 3,5-COOH (3,5-dimethylbiphenyl to 5-phenyl isophthalic acid)								
7.	Co/Mn/Br	HOAc	–	85	–	–	–	–	[40]
	2,5-CH_3 to 2,5-COOH								
8.	Co/Mn/Br	HOAc	–	34	–	–	–	–	[40]
	3,4′-CH_3 to 3,4′-COOH								
9.	MC oxidation	HOAc	–	79	–	–	–	–	[40]
	4,4′-CH_3 to 4,4′-COOH								
10.	Co/Ce/Br	HOAc	–	98	2.0	–	10	air	[86]
11.	Co/Mn/Br	HOAc	–	91	–	–	–	–	[40]
	R = 4-Et-4′-acetyl to 4,4′-COOH								
12.	Co/Mn/Br	HOAc	–	73	–	160	9.0	air	[166]
	4,4′-Et to 4,4′-COOH								
13.	Co/Mn/Br	HOAc	–	85	1.0	180	15	air	[248]
	4,4′-iPr to 4,4′-COOH								
14.	Co/Mn/Br/KOAc	HOAc	–	92	1.0	180	12	air	[113]
15.	Co/Mn/Br	HOAc	–	36	5.7	180	–	air	[249]
16.	Co/Mn/Br/KOAc	HOAc	–	97	–	200	30	–	[114]
17.	Co/Mn/Cl	HOAc,PhCl	100	75	4.0	170	68	air	[250]
18.	Co/Mn	propionic acid	100	93	4.0	175	7.9	air	[251]
	3,3′,4-CH_3 to 3,3′,4-COOH								
19.	MC oxidation	HOAc	–	71	–	–	–	–	[40]
	3,4,4′-CH_3 to 3,4,4′-COOH								
20.	MC oxidation	HOAc	–	76	–	–	–	–	[40]
	2,5,4′-CH_3 to 2,5,4′-COOH								
21.	Co/Mn/Br	HOAc	–	27	0.50	224	34	air	[244]
	R = 3,3′,4,4′-CH_3 to 3,3′,4,4′-COOH								
22.	MC oxidation	HOAc	–	64	–	–	–	–	[40]
23.	Co/Mn/Br/Zr	HOAc	–	76	–	–	–	–	[40]

The benzocoumarine could form by initial formation of the peracid, Ph–Ph–C(=O)OOH, followed by homolytic dissociation of the peroxide bond to Ph–Ph(=O)O˙ and then intramolecular radical attack to the adjacent ring carbon atom. Evidence for the formation of the peracid is that the aldehyde, Ph–Ph–CHO, the precursor to the peracid, was observed in 0.17% yield. This is similar to that reported from thermal and copper catalyzed rearrangement of the *o*-phenylbenzoyloxy radical [243] to 3,4-benzocoumarine. The fluorenone can form by the initial formation of the Ph–Ph–CH_2 radical, intramolecular attack on the 2′-position on the adjacent ring to form fluorene (found in 0.17% yield), followed by oxidation to fluorenone (see reaction 10.1 above). Some cleavage of the biphenyl moiety can occur since a 1.6% yield to *o*-phthalic acid was found.

Similar products are obtained starting with 2,5,4′-dimethylbiphenyl (item 21):



(10.4)

11. Oxidation of oligomeric compounds (see Table 11.1)

These are defined as compounds of the type $(HOOC)_nPh\text{–}X\text{–}Ph(COOH)_n$ which are most often prepared by oxidation of the corresponding methyl derivatives $(H_3C)_nPh\text{–}X\text{–}Ph(CH_3)_n$. An amazing array of these compounds have been prepared.

X remains unchanged during the reaction for the following:

		Items
X = CO	benzophenones	17–23,62
$X = C(CH_3)(CH_2CH_3)$	2,2-butane derivatives	7,8
$X = C(CH_3)_2$	2,2-propane derivatives	9,10,53
$X = CHCCl_3$	1,1-trichloroethane derivatives	13
$X = C(Ph)(CF_3)$	1,1-phenyl(trifluoromethyl) derivatives	14
$X = C(CF_3)_2$	2,2-hexafluoropropyl derivatives	15,16,59–61
X = oxygen	diphenylethers	26–42,60–62,64
X = –C(=O)O–	phenylbenzoates	43–46
X = S	diphenylsulfides	47
$X = S(=O)_2$	diphenylsulfones	48–52,64

The following X groups change during MC oxidation:

Methylenic groups to ketones:
$-CH_2-$ to –C(=O)– see items 1–3,62

1,1-*Ethyl derivatives to ketones*
$-CH(CH_3)$ to –C(=O)– see items 4–6
$-CH_2-C(=O)$ to –C(=O)C(=O)– see items 24,54

Benzils to aromatic acids:

$$(H_3C)_nPh-C(=O)C(=O)-Ph(CH_3)_n \rightarrow (COOH)_nPh-COOH$$

Table 11.1
MC oxidation of oligomeric compounds

Item	Catalyst	Solvent	Conv., (%)	Yield, (%)	Time, (h)	Temp, (°C)	*P* (atm)	O_2 source	Ref. No.
Reagent is $(R)_nPh\text{-}X\text{-}Ph(R)_n$:									
	$X = -CH_2-$ to $-C(=O)$ R = H (diphenylmethane to benzophenone)								
1.	Co/Mn/Br	HOAc	—	80	—	205	27	air	[123]
	$X = -CH_2-$ to $-C(=O)$ R = 2-CH_3 to 2-COOH (*o*-methyldiphenylmethane to 2-benzoylbenzoic acid)								
2.	Co/Mn/Br	HOAc	—	52	168	90	1.0	air	[244]
	$X = -CH_2-$ to $-C(=O)$ R = 4,4′-*t*-butyl (remains unchanged)								
3.	Co/Mn/Br	HOAc	—	77	—	205	27	air	[123]
	$X = CHCH_3$ to $X = C(=O)$ R = 3,3′-CH_3 to 3,3′-COOH (1,1-bis(3-methylphenyl)ethane to benzophenone-3,3′-dicarboxylic acid)								
4.	Co/Mn/Ce/Br	HOAc	—	98	2.0	—	—	air	[86]
	$X = CHCH_3$ (1,1-ethane) to $X = C(=O)$ R = 4,4′-CH_3 to 4,4′-COOH (1,1-bis(4-methylphenyl)ethane to benzophenone-4,4′-dicarboxylic acid)								
5.	Co/Ni/Br	HOAc	—	96	2.0	—	—	air	[86]
	$X = CHCH_3$ to $X = C(=O)$ R = 3,3′,4,4′-CH_3 to 3,3′,4,4′-COOH (1,1-bis(3,4-methylphenyl)ethane to benzophenone-3,3′,4,4′-dicarboxylic acid)								
6.	Co/Mn/Zr/Br	HOAc	—	65	—	—	—	air	[40]
	$X = C(CH_3)(CH_2CH_3)$ (2,2-butane, remains unchanged) R = 4,4′-CH_3 to 4,4′-COOH (2,2-di-*p*-tolylbutane to 2,2-di(*p*-carboxyphenyl)butane)								
7.	Co/Mn	HOAc	—	90	—	204	27	air	[252,253]
8.	Co/Mn/Br	HOAc	—	—	—	204	27	air	[252,253]
	$X = C(CH_3)_2$ (remains unchanged) R = 4,4′-CH_3 to 4,4′-COOH (2,2-di-*p*-tolylpropane to 2,2-di(*p*-carboxyphenyl)propane)								
9.	MC oxidation	HOAc	—	90	—	—	—	air	[40]
	$X = C(CH_3)_2$ (remains unchanged) R = 3,3′,4,4′-CH_3 to 3,3′,4,4′-COOH (2,2-di(*o*-xylyl)propane to isopropylidenebis(phthalic acid))								
10.	Co/Mn/Br/Zr	HOAc	—	90	—	—	—	—	[40]
	$X = -CH{=}CH-$ (stilbene) to 1,4-dicarboxybenzene (terephthalic acid)								
11.	Co/Mn/Br	HOAc	—	79	0.25	175	24	O_2	[254]
12.	Co,MEK	HOAc	—	68	24	130	17	O_2	[254]
	$X = CHCCl_3$ R = 4,4′-CH_3 to 4,4′-COOH								
13.	Co/Br	HOAc	—	—	—	110–120	—	—	[255]
	$X = C(Ph)(CF_3)$ R = 3,3′,4,4′-CH_3 to 3,3′,4,4′-COOH								
14.	Co/Mn/Br	HOAc	—	97	2.4	100–176	7.4	air	[186]
	$X = C(CF_3)_2$ R = 3,3′,4,4′-CH_3 to 3,3′,4,4′-COOH								
15.	Co/Mn/Br	HOAc	—	88	7.0	170–175	7.5	air	[186]
16.	Co/Mn/Br	HOAc	—	71–87	0.75–1.02	168–193	12–18	air	[256]
	$X = C{=}O$ (benzophenones) R = 4-CH_3 to 4-COOH								
17.	Co/Mn/Br	HOAc	—	91	—	204	27	air	[257]
	$X = C{=}O$ (benzophenones) 2-CH_3-5-Cl + 5-CH_3-2-Cl to 2-COOH-5-Cl + 5-COOH-2-Cl								
18.	Co/Mn/Br	HOAc	—	89	—	204	27	air	[257]
	$X = C{=}O$ (benzophenones) R = 2,5-CH_3 to 2,5-COOH								
19.	MC catalyst	HOAc	—	75	—	204	27	air	[257]
	$X = C{=}O$ (benzophenones) R = 4,4′-CH_3 to 4,4′-COOH								
20.	Co/Br HOAc	—	—	72	1.1	110	1.0	O_2	[47,11]
	$X = C{=}O$ (benzophenones) R = 3,3′4,4′-CH_3 to 3,3′,4,4′-COOH								
21.	Mn/Br	HOAc	—	—	6.0	225	—	—	[258]
22.	Co/Mn/Br	HOAc/$ClCH_2CO_2H$	—	83	—	175	—	air	[115]
	$X = C{=}O$ (benzophenones) R = 3,3′,4,4′-CH_3-6,6′-Cl to 3,3′,4,4′-COOH-6,6′-Cl								
23.	Co/Mn/Br	HOAc	92	43	0.25	—	34	air	[40]

Item	Catalyst	Solvent	Conv., (%)	Yield, (%)	Time, (h)	Temp, (°C)	*P* (atm)	O_2 source	Ref. No.
	X = $-CH_2C(=O)-$ to X = $-C(=O)C(=O)-$ (deoxybenzoin to benzil) R = H								
24.	Co/Mn/Br	HOAc	—	—	—	—	—	—	[259]
	X = $-C(=O)C(=O)-$ (benzil) R = 2,2′,4,4′-CH_3 to 1,2,4-tricarboxybenzene								
25.	Co/Mn/Br	HOAc	—	81	6.0	180	10	air	[260]
	X = O (diphenylethers) R = 3-CH_3 to 3-CH_2OAc								
26.	Co/Cl/Br	HOAc	20	9.6	1.5	124	—	air	[261]
	X = O (diphenylethers) R = 3-CH_3 to 3-CHO								
27.	Co/Br	HOAc	35	21	0.30	125	—	—	[262]
28.	Co/Br/MeCHO	HOAc	35	21	0.30	125	—	—	[57]
29.	Co/Br	HOAc	41	19	5.0	119–120	—	air	[263]
	X = O (diphenylethers) 3-CH_3 to 3-COOH								
30.	Co/Br	HOAc	—	88–95	—	—	—	—	[264]
	X = O (diphenylethers) 1,4-CH_3 to 1,4-COOH (2-phenoxy-*p*-xylene to 2-phenoxyterephthalic acid)								
31.	Co/Mn/Br	HOAc	—	52	—	—	—	air	[40]
	X = O (diphenylether) R = 3,3′-CH_3 to 3,3′-COOH								
32.	Co/Mn/Br	HOAc	—	80	—	149	—	air	[68]
	X = O (diphenylether) R = 2-*t*-butyl-5,4′-CH_3 to R = 2-*t*-butyl-5,4′-COOH (2-*t*-butyl-5,4′-dimethyldiphenyl ether to 2-*t*-butyl-5,4′-dicarboxydiphenylether)								
33.	Co/Mn/Br	HOAc,Ac_2O	—	83	—	—	—	—	[40]
	X = O (diphenylether) R = 3,4′-CH_3 to 3,4′-COOH (3,4′-dimethyldiphenylether to 3,4′-oxybis(benzoic acid))								
34.	Co/Mn/Br	HOAc	—	81	—	149	—	air	[68]
	X = O (diphenylether) 4,4′-CH_3 to 4,4′-COOH (to 4,4′-oxybis(benzoic acid)								
35.	Co/Mn/Br	HOAc	—	93	1.5	150	—	air	[86]
36.	Co/Br	HOAc	—	87	1.0	90–112	1.0	O_2	[11,47]
37.	Co/Br	HOAc,AC_2O	—	80	1.0	100	1.0	O_2	[47]
38.	Co/Mn/Br	HOAc,H_2O	—	82	1.2	149	—	air	[68]
39.	Co/Br	HOAc	—	90	6.0	110	—	—	[265]
	X = O (diphenylether) R = 3,3′,4,4′-CH_3 to 3,3′,4,4′-COOH								
40.	Co/Mn/Br	HOAc	—	70	—	163	—	air	[68]
	X = O (diphenylether) R = 4-CH_3-4′-NO_2 to 4-COOH-4′-NO_2								
41.	Co/Mn/Br	HOAc	—	86	—	—	—	—	[40]
	X = O (diphenylether) R = 4-acetyl-4′-NO_2 to 4-COOH-4′-NO_2								
42.	Co/Mn/Br	HOAc	—	78	—	—	—	—	[40]
	X = $-C(=O)O-$ (benzoate, remains unchanged) R = 4,4′-CH_3 to 4,4′-COOH (*p*-cresyl-*p*-toluate to 4,4′-dicarboxyphenylbenzoate)								
43.	Co/Mn/Br	HOAc	—	88	0.45	173	27	air	[266]
	X = $-C(=O)O-$ (benzoate) R = 4,4′-CH_3-2′-Br to 4,4′-COOH-2′-Br								
44.	Co/Mn/Br	HOAc	—	80	0.23	164	27	air	[266]
	X = $-C(=O)O-$ (benzoate) R = 3′-4,4′-CH_3 to 3′-4,4′-COOH								
45.	Co/Mn/Br	HOAc	—	62	0.23	164	27	air	[266]
	X = $-C(=O)O-$ (benzoate) R = 3,3′,4,4′-CH_3 to 3,3′,4,4′-COOH (3,4-dimethylphenyl-3,4-dimethybenzoate to 3,4-dicarboxyphenyl-3,4-dicarboxybenzoate)								
46.	Co/Mn/Br	HOAc	—	66	0.23	164	27	air	[266]
	X = S (sulfide, remains unchanged) R = 4,4′-CH_3 to 4,4′-COOH								
47.	Co/Br	HOAc	—	97	2.0	116	1.0	O_2	[308]
	X = $S(=O)_2$ (sulfone,remains unchanged) R = 4,4′-CH_3 to 4,4′-COOH								
48.	Co/Mn/Br	HOAc	—	95	1.5	150	20	air	[309]
49.	Co/Mn/Br	HOAc	—	96	1.5	150	10	air	[86]
50.	Co/Br	HOAc	—	37	6.5	116	1.0	O_2	[308]
51.	Co/Br	HOAc	—	92	4.0	105–112	—	—	[313]

Table 11.1 (continued)

Item	Catalyst	Solvent	Conv., (%)	Yield, (%)	Time, (h)	Temp, (°C)	*P* (atm)	O_2 source	Ref. No.
	$X=S(=O)_2$ (sulfone) $R=3,3',4,4'$-CH_3 to 3,3′,4,4′-COOH								
52.	Co/Mn/Br	HOAc	—	99	—	170–180	—	air	[117]
Reagent is $(R)_n$Ph-X-Ph-X-Ph$(R)_n$:									
	$X=C(CH_3)_2$ $R=4,4'$-CH_3 to 4,4′-COOH								
53.	Co/Br,paraldehyde	HOAc	—	39	5.0	160—66	—	air	[310]
Reagent is Ph-Y-Ph-X-Ph-Y-Ph:									
	$Y=C(=O)CH_2$ $X=C(=O)C(=O)$ to $Y=X=C(=O)C(=O)$								
54.	Co/Mn/Br	HOAc	—	—	—	—	—	—	[31]
Reagent is $(R)_n$*Ph-Ph-X-Ph-Ph*$(R)_n$:									
	$X=C(=O)C(=O)$ (benzil) $R=4,4'$-CH_3 to 4,4′-dicarboxybiphenyl								
55.	Co/Mn/Br	HOAc	—	82	6.0	180	10	air	[260]
	$X=C(=O)C(=O)$ (benzil) 4,4′-CH_3 to 4-CH_3-4′-carboxybiphenyl								
56.	Co/Mn/Br	HOAc	—	80	6.0	—	5.0	air	[260]
	$X=C(=O)C(=O)$ (benzil) $R=4,4'$-Et to 4,4′dicarboxybiphenyl								
57.	Co/Mn/Br	HOAc	—	82	6.0	180	10	air	[260]
	$X=C(=O)C(=O)$ (benzil) $R=4,4'$-iPr to 4,4′dicarboxybiphenyl								
58.	Co/Mn/Br	HOAc	—	82	6.0	180	15	air	[260]
Reagent is $(R)_n$*Ph-X-Ph-Ph-X-Ph*$(R)_n$:									
	$X=C(CF_3)_2$ (remains unchanged) $R=4,4'$-CH_3 to 4,4-COOH								
59.	Co/Mn/Br	HOAc	—	92	—	—	—	—	[312]
Reagent is (R_n)*Ph-X-Ph-Y-Ph-X-Ph*(R_n):									
	$X=C(CF_3)_2$ $Y=O$ $R=4,4'$-CH_3 to 4,4′-COOH								
60.	Co/Mn/Br	HOAc	—	99	1.7	130–175	7.5	—	[186]
	$X=C(CF_3)_2$ $Y=O$ $R=3,3'4,4'$-CH_3 to $R=3,3'4,4'$-COOH								
61.	Co/Mn/Br	HOAc	—	96	2.3	100–188	7.5	—	[186]
	$X=Y=CH_2$ to $X=Y=C(=O)$ $R=H$								
62.	Co/Mn/Br	HOAc	—	—	—	205	27	air	[123]
	$X=C=O$ $Y=O$ $R=4,4'$-CH_3 to 4,4′-COOH								
63.	Co/Br	benzoic acid	—	95	8.0	130	—	—	[93]
	$X=S(=O)$ $Y=O$ $R=3,3'4,4'$-CH_3 to 3,3′4,4′-COOH								
64.	Co/Mn/Br	HOAc	—	85	—	—	—	air	[98]

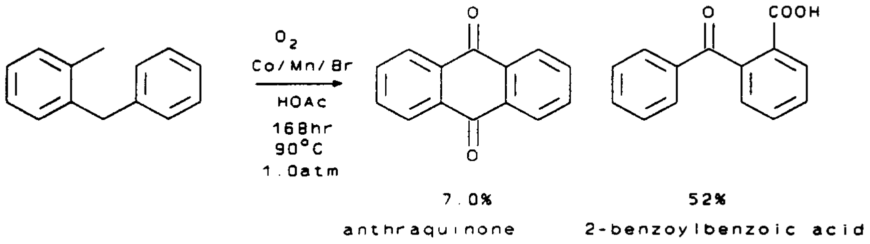
see items 25,54 – 58

Table 1 is organized with the following types of reagents, where X and Y are used interchangeably:

$(R)_n$Ph-X-Ph$(R)_n$	see items 1–52
$(R)_n$Ph-X-Ph-X-Ph$(R)_n$	see item 53
Ph-Y-Ph-X-Ph-Y-Ph	see item 54
$(R)_n$Ph-Ph-X-Ph-Ph$(R)_n$	see items 55–58
$(R)_n$Ph-X-Ph-Ph-X-Ph$(R)_n$	see item 59
(Rn)Ph-X-Ph-Y-Ph-X-Ph(Rn)	see item 60–64

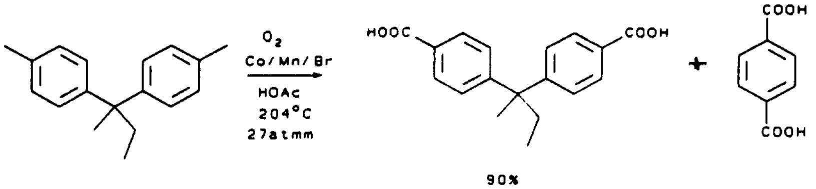
Various representative samples of products obtained in good yields are given in Fig. 11.1. *X and Y are always para to each other.*

Oxidation of *o*-methyldiphenylmethane yields the expected 2-benzoylbenzoic acid, but also the product from the *ortho* attack of the $PhCH_2^{\cdot}$ radical and subsequent oxidation to yield anthraquinone (item 2):



(11.1)

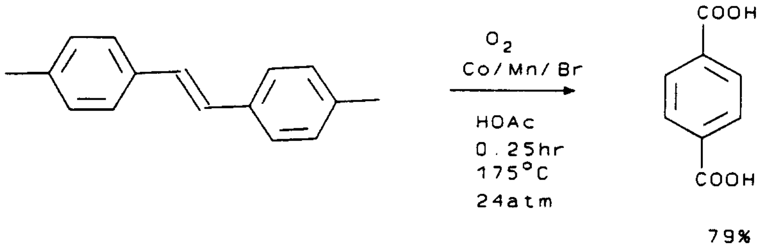
2,2-Butane derivatives are oxidized to mixtures of 2,2-di(*p*-carboxyphenyl)butane and terephthalic acid (items 7,8):



(11.2)

The acids can be easily separated since the former is very soluble in ethanol while terephthalic acid is not.

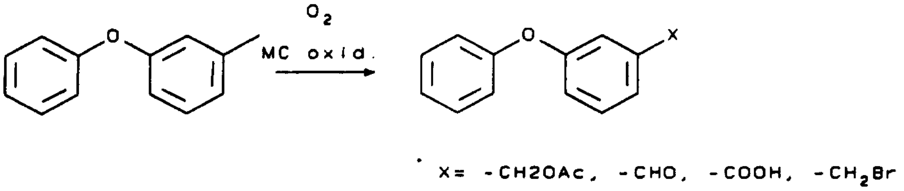
Methylstilbenes are converted to terephthalic acid in high yield (item 11):



(11.3)

using either a Co/MEK catalyzed or Co/Mn/Br catalyzed system.

Methylphenylethers are easily oxidized substances since the ether moiety imparts a high degree of reactivity to the methyl groups. 4-Methoxytoluene is 5.5 times more reactive than toluene (see Table 1.3). The benzylic acetate, aldehyde, and acid have been reported for 3-methyldiphenylether (see items 25–30):



(11.4)

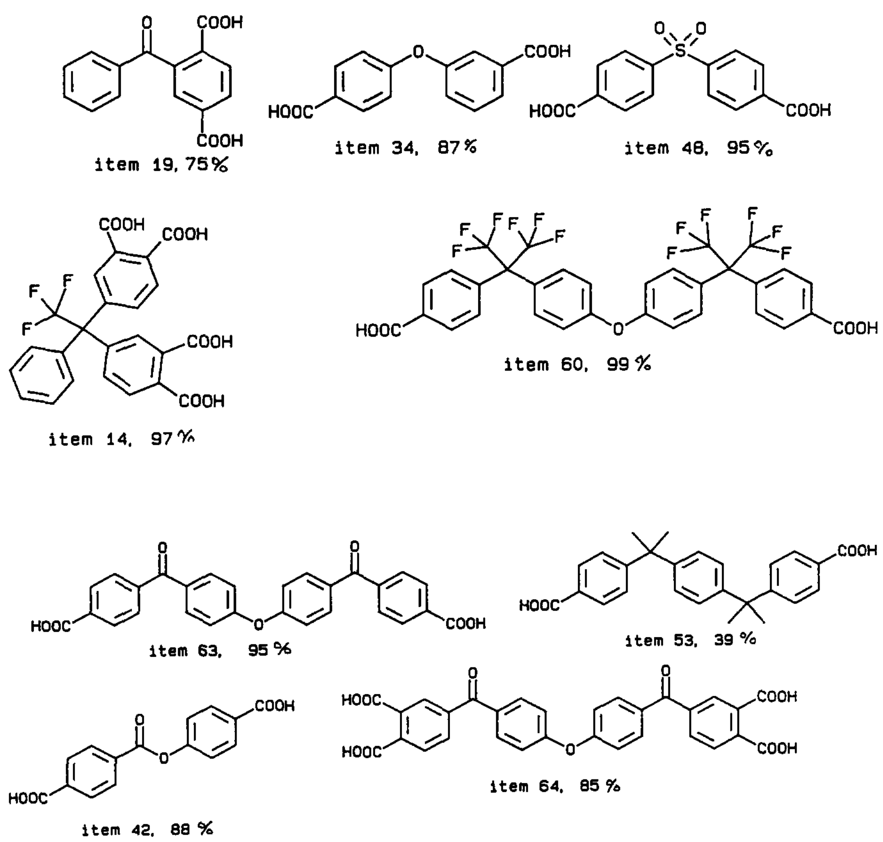
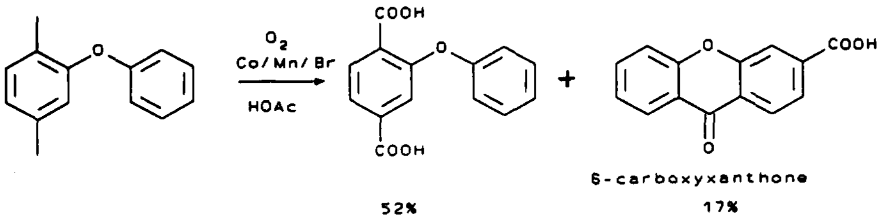


Fig. 11.1. Selected products from the MC oxidation of oligomeric compounds (see Table 11.1 for details).

A *ortho*-methyl group in a diphenylether will attack the adjacent ring to give a 17% yield to 6-carboxyxanthone (item 31):



(11.5)

12. Oxidation of heterocyclic compounds (see Table 12.1)

Alkyl substituted heterocyclic compounds with aromatic character can be autoxidized using the MC system similar to the benzene and naphthalene systems. The MC oxidation of pyridine, pyrazole, thiophene and furan derivatives have been reported. Representative products are given in Fig. 12.1.

The pyridine and pyrazole derivatives are more slowly oxidized than methylbenzenes. They apparently have the same type of response to substituents on the ring as benzene derivatives; i.e., electron withdrawing substituents slow down the rate.

Table 12.1
Summary of MC oxidations of heterocyclic compounds

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	P (atm)	O_2 source	Ref. No.
Pyridine Derivatives:									
	2-CH_3 to 2-COOH (2-picoline to 2-carboxypyridine)								
1.	Co/Mn/Br	HOAc	3	0.0	–	–	–	–	[40]
	3-CH_3 to 3-COOH (3-picoline to 3-carboxypyridine)								
2.	Co/Mn/Br	HOAc	–	72	2.0	196	27	air	[268]
3.	Co/Mn/Zr/Br	HOAc	–	80	2.0	200	20	air	[269]
4.	HBr	H_2O	57	48	5.0	200	31	O_2	[84]
	4-CH_3 to 4-COOH								
5.	Mn/Br	HOAc	–	31	2.0	204	27	air	[268]
6.	HBr	H_2O	–	84	5.0	180	30–50	O_2	[63]
	3,5-CH_3 to 3,5-COOH								
7.	MC catalyst	HOAc	–	79	–	–	–	–	[40]
	3,5-CH_3 to 3-CH_3-5-COOH								
8.	Co/Mn/Br	HOAc	–	72	–	–	–	–	[40]
	3-ethyl to 3-COOH								
9.	Co/Mn/Br	HOAc	–	–	–	200	20	air	[270]
	2-CH_2Ph to 2-C(=O)Ph (2-benzylpyridine to phenyl-2-pyridylketone)								
10.	MC catalyst	HOAc	–	60	–	–	–	–	[40]
	4-CH_2Ph to 4-C(=O)Ph (4-benzylpyridine to phenyl-4-pyridylketone)								
11.	MC catalyst	HOAc	–	92	–	–	–	–	[40]
Pyrazole Derivatives:									
	1,4-CH_3 to 1-CH_3-4-COOH								
12.	Co/Mn/Br	HOAc	99	94	1.0	130	70	air	[116]
	1,4-CH_3-5-Cl to 1-CH_3-4-COOH-5-Cl								
13.	Co/Mn/Br	HOAc	–	93	2.0	130	70	air	[116]
	1,4-CH_3-3,5-Cl to 1-CH_3-4-COOH-3,5-Cl								
14.	Co/Mn/Br	HOAc	–	95	–	–	–	–	[271]
15.	Co/Mn/Br	HOAc	–	96	1.0	130	70	air	[116]
	1,4-CH_3-3,5-Br to 1-CH_3-4-COOH-3,5-Br								
16.	Co/Mn/Br	HOAc	53	42	1.0	130	70	air	[116]
	4-CH_3-3,5-Cl to 4-COOH-3,5-Cl								
17.	Co/Mn/Br	HOAc	94	83	4.0	130	70	air	[116]
	4-CH_3-3-Cl to 4-COOH-3-Cl								
18.	Co/Mn/Br	HOAc	94	91	1.0	130	70	air	[116]
Thiophenes Derivatives:									
	2-CH_3 to 2-COOH + 2-CHO								
19.	Co/Br	HOAc	–	–	–	–	–	–	[99]
	2-CH_3-3-Cl to 2-COOH-3-Cl								
20.	Co/Mn/Br	HOAC	100	94	2.0	140	20	air	[272]
	2-Et to 2-C(=O)CH_3 + 2-CH(OAc)CH_3								
21.	Co/Br	HOAc	–	–	–	–	–	–	[273]
	2-Et-4-CH_3 to 2-CH_2(OH)CH_3-4-CH_3								
22.	Co/Br	HOAc	–	–	–	–	–	–	[274]
	2-CH_2OAc to 2-COOH								
23.	Co/Br	HOAc	–	90	–	–	–	–	[275]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Thiophenes Derivatives: (*continued*)									
	2-CH_2Ph to 2-C(=O)Ph								
24.	Co/Br	HOAc	–	–	–	–	–	–	[276]
Furan Derivatives:									
	2-CH_3-5-CHO to 2-CHO-5-CHO + 2-CHO-5-COOH + 2,5-COOH								
25.	Co/Mn/Br	–	–	36	–	–	–	–	[277]

Under identical conditions, the reactivity of 3-methylpyridine, as determined by the rate of oxygen uptake is 10 times less than for toluene [65]. 3-Methylpyridine can be oxygenated to the 3-carboxy derivative in reported 72–80% yields, but only in a 57% yield using HBr in water (items 2–6). 4-carboxypyridine has been prepared in rather low yields of 31% from 4-methylpyridine and a 84% yield using a HBr catalyst in water (items 5, 6). The methyl groups of 3,5-dimethylpyridine react consecutively and, under the proper conditions, 3-methyl-5-carboxypyridine can be obtained in a 72% yield and 3,5-dicarboxypyridine in 79% yield.

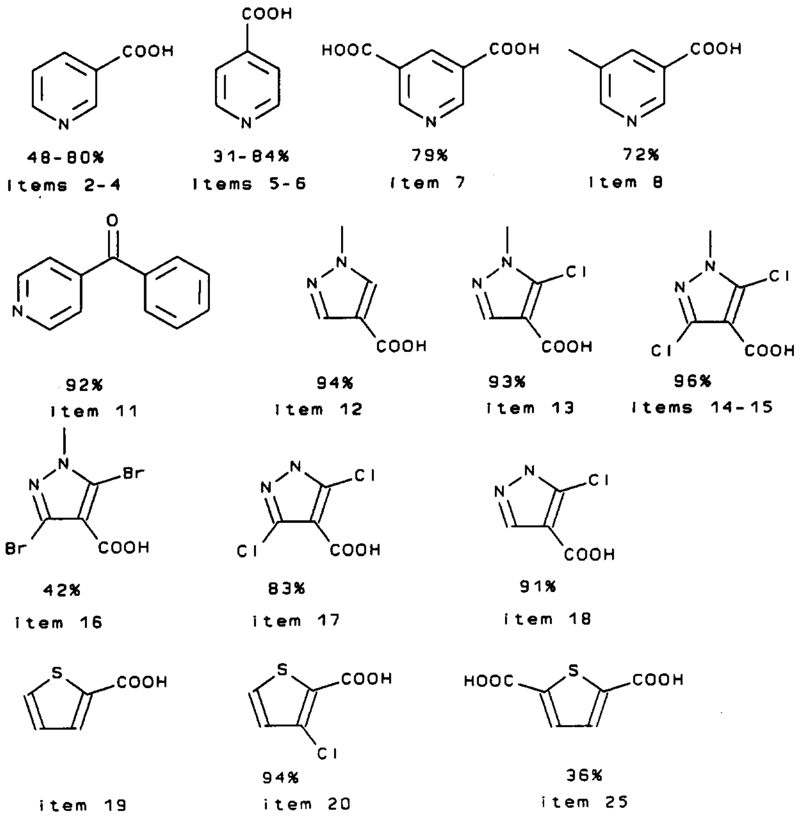
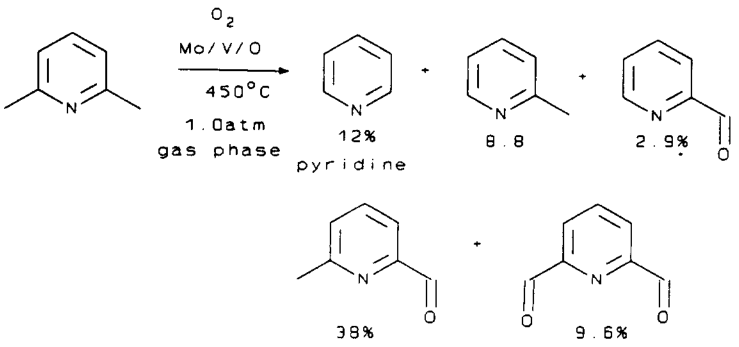


Fig. 12.1. Selected products from the MC oxidation of oligomeric compounds (see Table 12.1 for details).

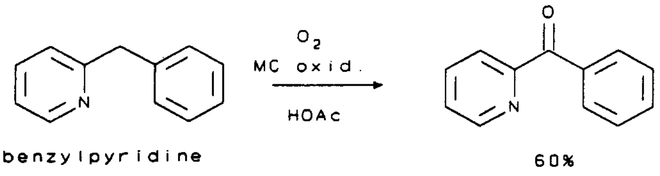
2-Methylpyridine does not react under MC autoxidation conditions [40]. Gas phase, heterogeneously catalyzed, autoxidations can activate the *ortho*-methyl group of pyridines however [267]. Aldehydes, not carboxylic acid derivatives, are the major product however. An example is:



(12.1)

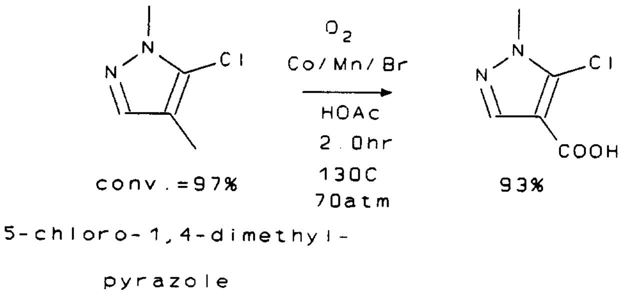
which typifies the mixtures that one can obtain. Gas phase oxidation of 3- and 4-methyl derivatives have also been reported as well as alkyl pyridine n-oxide derivatives [267].

The methylene bridge of benzylpyridines can be oxidized in good yields to ketones (items 10–11):



(12.2)

A series of 4-methylpyrazoles have been oxidized to the corresponding carboxylic acids in 42–96% yields (items 12–18). The 4-methylpyrazoles are less reactive than methylbenzenes. In a series of 1,4-dimethylpyrazoles, only the methyl group attached to the carbon atom reacts, for example:

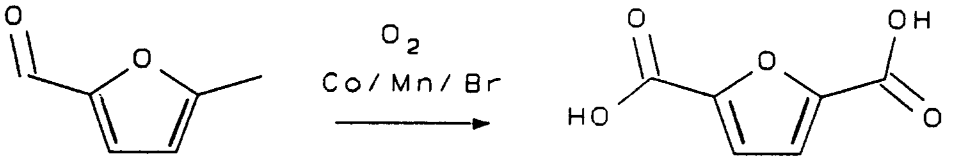


(12.3)

Chloro-substitution in the 3 or 5 positions decreased the rate of oxidation. The activity of the catalyst changed as the Co/Mn and bromine/metals ratios were varied.

There are a number of scattered reports of alkylthiophenes being oxidized to the usual oxygenated intermediates (see items 19–24). Under high pressure but moderate temperature, 2-methyl-3-chlorothiophene was successfully oxidized to 2-carboxy-3-chlorothiophene in 94% yield (item 20). Since this is probably a compound with low electron density, high yields to other thiophene derivatives are expected.

There is only one report on the oxidation of a furan derivative giving the expected products (item 25):



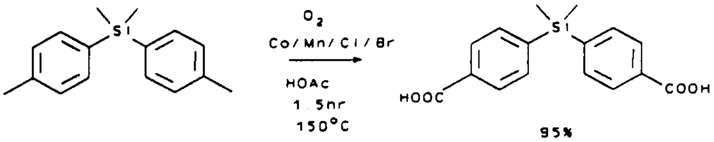
(12.4)

The ability to oxidize pyridines, pyrazoles, thiophenes, and furans suggests that carboxy derivatives of other aromatic heterocyclics such as oxazoles, thiazoles, and carbazoles is feasible. Alkyl pyrroles and imidazoles may not be autoxidizable since they contain N–H bonds that may deactivate the system similar to phenols. Masking the N–H bonds by acetylation may be feasible (see Section 1.8).

13. Oxidation of organometallic compounds (see Table 13.1)

A very limited number of organometallic compounds have been subjected to MC type oxidations. Organometallic compounds of P(III), P(V), Si(IV) and Sn(IV) are given in Table 13.1.

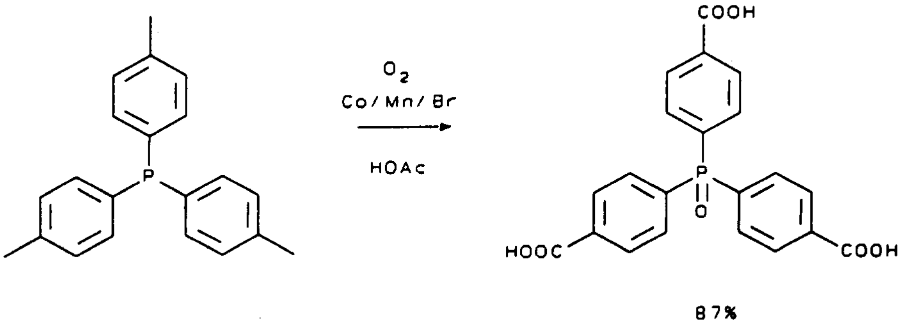
Compounds of the type $(H_3C)_nPhMX_m$ can be oxidized to compounds of the type $(HOOC)_nPhMX_m$, where M = Si, Sn and X = CH_3 (items 1–9). Only the benzylic methyl groups are oxidized. The methyl groups attached to the metal remain inert. Using item 1 as an example:



(13.1)

Solvolysis of the Si–C bond would be expected since water is one of the products of the reaction and because of the acidic acetic acid medium. Benzoic acid and hexamethylcyclotrioxane have been reported as by-products from reaction 13.1 above and water control was practiced to minimize their formation [278]. Bis(*p*-tolyl)dimethylsilane reacts much more slowly than toluene at 100°C; hence, the Si–$(CH_3)_2$ moiety significantly deactivates the benzylic methyl group [278]. Temperatures above 200°C however do result in reduced yields hence a balance of maximizing rate and selectivity must be achieved. These organosilicon carboxylic acids can be incorporated into polyesters and polyamides to produce a class of engineering thermoplastics with good heat resistance and excellent mechanical properties [278].

Methylphenylphosphine(III) compounds become oxidized to the carboxyphenylphosphine(V) oxides (items 10 and 11). For example:

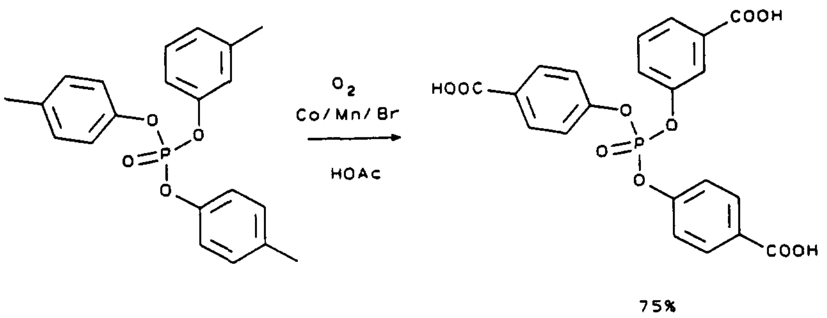


(13.2)

Trimethylbenzenephosphates have been oxidized to the expected tricarboxy derivatives, using both MC and Co/acetaldehyde methods (items 12 and 13):

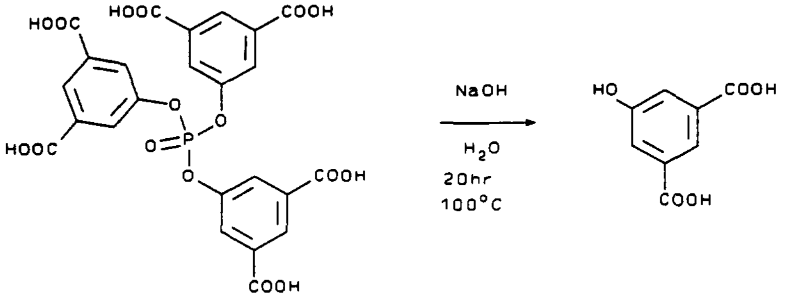
Table 13.1
MC oxidations of organometallic compounds

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Silicon Derivatives:									
	$(4\text{-}CH_3Ph)_2\text{-}Si\text{-}(CH_3)_2$ to $(4\text{-}COOH)Ph)_2\text{-}Si\text{-}(CH_3)_2$								
1.	Co,Mn,Br,Cl	HOAc	–	95	1.5	150	–	air	[86]
2.	Co/Mn/Br/Zr	HOAc	–	92	0.50	204	34	air	[278]
	$(2,5\text{-}(CH_3)_2Ph)\text{-}Si\text{-}(CH_3)_3$ to $(2,5\text{-}(COOH)_2Ph)\text{-}Si\text{-}(CH_3)_3$								
3.	Co/Mn/Br	HOAc	–	81	0.70	149–163	34	air	[281]
	$(3,5\text{-}(CH_3)_2Ph)\text{-}Si\text{-}(CH_3)_3$ to $(3,5\text{-}(COOH)_2Ph)\text{-}Si\text{-}(CH_3)_3$								
4.	Co/Mn/Br	HOAc	–	92	0.70	149–163	34	air	[281]
	$(2,4,5\text{-}(CH_3)_3Ph)\text{-}Si\text{-}(CH_3)_3$ to $(2,4,5\text{-}(COOH)_3Ph)\text{-}Si\text{-}(CH_3)_3$								
5.	Co/Mn/Br	HOAc	–	14	0.50	149–162	34	air	[281]
	$1,4\text{-}CH_3\text{-}2,5\text{-}[(Si(CH_3)_3]_2Ph$ to $1,4\text{-}COOH\text{-}2,5\text{-}[(Si(CH_3)_3]_2Ph$								
6.	Co/Mn/Br	HOAc	–	41	0.50	149–162	34	air	[281]
	$[(3,4\text{-}(CH_3)_2Ph)Si\text{-}(CH_3)2]\text{-}O\text{-}[(3,4\text{-}(CH_3)_2Ph)Si\text{-}(CH_3)_2]$ to $[(3,4\text{-}(COOH)_2Ph)Si\text{-}(CH_3)_2]\text{-}O\text{-}[(3,4\text{-}(COOH)_2Ph)Si\text{-}(CH_3)_2]$								
7.	Co/Mn/Br	HOAc	–	72	0.50	149–160	34	air	[281]
Tin Derivatives:									
	$4,4'\text{-}(CH_3Ph)_2\text{-}Sn\text{-}(CH_3)_2$ to $4,4'\text{-}(HOOCPh)_2\text{-}Sn\text{-}(CH_3)_2$								
8.	Co/Mn/Br	HOAc	–	55	–	204	27	air	[282]
	$4,4'\text{-}(i\text{-}PropylPh)\text{-}Sn\text{-}(CH_3)_2$ to $4,4'\text{-}(HOOCPh)_2\text{-}Sn\text{-}(CH_3)_2$								
9.	Co/Mn/Br	HOAc	–	–	–	204	27	air	[282]
Phosphorus Derivatives:									
	$Ph_2(4\text{-}CH_3Ph)P$ to $Ph_2(4\text{-}HOOCPh)P{=}O$								
10.	Co/Mn/Br	HOAc	–	100	–	–	–	–	[40]
	$(4\text{-}CH_3Ph)_3P$ to $(4\text{-}(HOOC)Ph)_3P{=}O$								
11.	Co/Mn/Br	HOAc	–	87	–	–	–	–	[40]
	$(3\text{-}CH_3Ph\text{-}O)_3P{=}O$ to $(3\text{-}CH_3Ph\text{-}O)_3P{=}O$								
12.	Co/Mn/Br	HOAc	–	75	–	–	–	air	[280]
13.	Co,HAc	HOAc	–	74	9.0	70–75	1.0	O_2	[279]
	$(2,5\text{-}(CH_3)_2Ph)_2P(OH)({=}O)$ to $((2\text{-}CH_3,5\text{-}HOOC)Ph)_2P(OH)({=}O)$								
14.	Co/Mn/Br	HOAc	–	65	–	205	28	air	[283]
	$2,2',5,5'\text{-}((CH_3)_2Ph)_2P(OH)({=}O)$ to $((2\text{-}CH_3,5\text{-}HOOC)Ph)((2,5\text{-}HOOC)Ph)P(OH)({=}O)$								
15.	Co/Mn/Br	HOAc	–	65	–	205	28	air	[283]
	$(2,5\text{-}CH_3Ph)P(OH)_2({=}O)$ to $(2\text{-}CH_3\text{-}5\text{-}HOOC\text{-}Ph)(P(OH)_2({=}O)$								
16.	Co/Mn/Br	HOAc	–	84	–	204	27	air	[283]



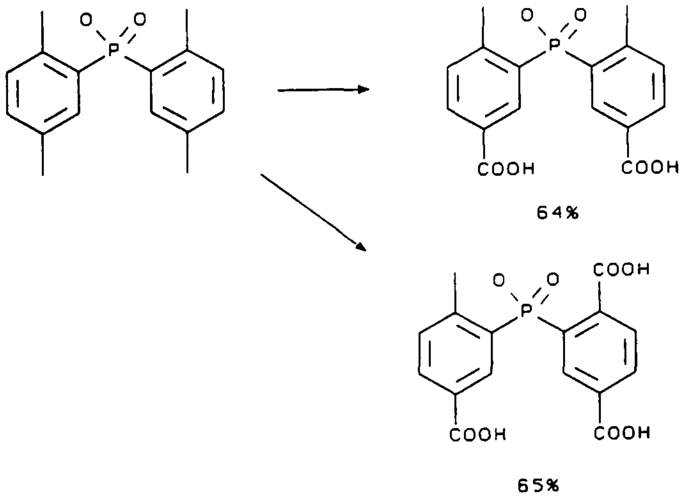
(13.3)

A number of other polycarboxybenzenephosphates have been prepared via Co/acetaldehyde technology [279], such as *p*-tolyl and 3,5-cresyl, and these derivatives could probably also be prepared using the MC method. These compounds can potentially be used as fire retardants [279,281]. The carboxyphosphates can be hydrolyzed to give carboxyphenols such as 1,3-dicarboxyphenol [279]:



(13.4)

The methyl group ortho to the phosphonic acid are apparently deactivated in 2,2′,5,5′-bis(dimethylpheny)phosphonic acid. At lower catalyst concentration one obtains the di-acid, while at higher concentration (which normally activates the reaction) one obtains the tri-acid (items 14 and 15):



(13.5)

14. Oxidation of non-aromatic compounds (see Table 14.1)

In this section, we discuss the oxidation of compounds which do not contain aromatic rings. Alkanes are generally less reactive than methyl substituted benzenes as is reflected by benzylic C–H bonds being ca. 10 kcal/mol weaker than alkane C–H bonds [15]. This explains why in long-chained benzene

Table 14.1
Summary of MC oxidations of non-aromatic compounds

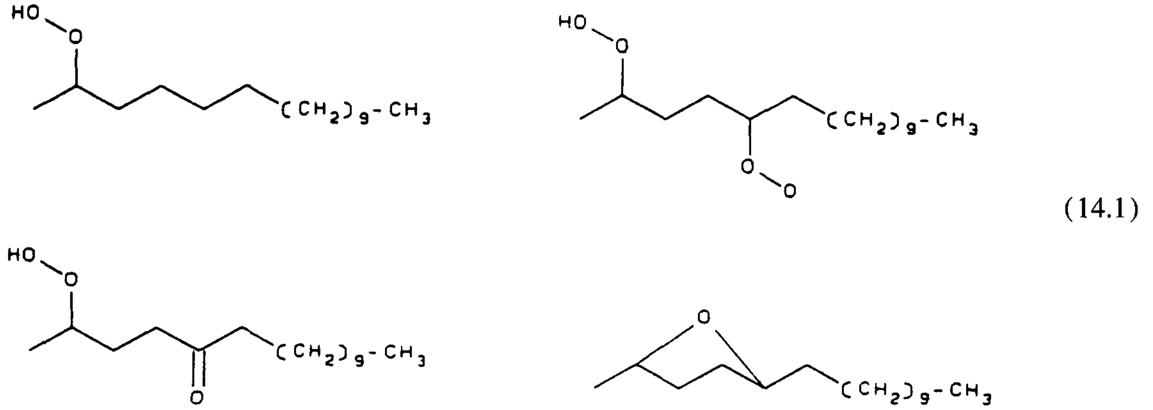
Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Saturated Alkanes:									
	$CH_3CH_2CH_3$ TO $CH_3C(=O)OH$ (propane to acetic acid)								
1.	Co/Mn/Br	HOAc	—	53	4.5	177	63	O_2	[121]
	$CH_3(CH_2)_2CH_3$ to CH_3COOH (n-butane to acetic acid)								
2.	Co/Br	HOAc	71	58	—	177	60	—	[289]
3.	Co/Br	HOAc	70	72	—	—	—	air	[40]
4.	Co/Mn/Br	HOAc	—	81	2.5	177	63	O_2	[121]
	$CH_3(CH_2)_3CH_3$ to CH_3COOH (n-pentane to acetic acid)								
5.	Co/Mn/Br	HOAc	—	53	4.0	177	63	O_2	[121]
	decahydronaphthalene to various acetate isomers								
6.	Co/Ce/Br	Ac_20	4.9	2.0	0.50	100	1.0	O_2	[41]
	methylcyclohexane to succinic anhydride								
7.	Co/Mn/Br	propionic acid	—	7.4	20	130	1.0	O_2	[290]
	methylcyclohexane to formic acid								
8.	Mn/Br	HOAc	—	19	1.0	180	24	air	[291]
	n-octane to mixture of octanones, diones, octanoic acid and others								
9.	Co/Br	benzoic acid	—	—	7.4	118	1.0	O_2	[292]
	n-decane to mixture of ketones and decanoic acid								
10.	Co/Br	benzoic acid	—	—	2.0	90	2.0	O_2	[292]
Saturated Alcohols:									
	ethanol to acetic acid								
11.	Co/Mn/Br	HOAc	—	79	—	194	17	air	[293]
	isopropyl alcohol to acetone								
12.	Co/Br	HOAc	—	70	4.0	110	1.0	O_2	[294]
	1-hexanol to n-hexanoic acid (38%) + 16% n-hexylcaproate								
13.	Co/Br	benzene	90	38	2.0	89–132	1.0	O_2	[11]
	1-hexanol to 1-hexanoic acid								
14.	Co/Br	HOAc	—	97	2.0	89–143	1.0	O_2	[294]
	3-heptanol to 3-heptanone and butyric acid								
15.	Co/Br	HOAc	—	—	3.5	92	1.0	O_2	[294]
	1-octanol to 1-octanoic acid and ocyl octanoate								
16.	Co/Br	HOAc	—	—	2.0	38	1.0	O_2	[294]
	1,10-decanol to acetate of alcohol-acid (acetoxydecanoic acid), to alcohol-acid (10-hydroxydecanoic acid), and to diacid (sebacic acid)								
17.	Co/Br	HOAc	—	—	6.0	90	1.0	O_2	[294]
Saturated Ketones:									
	cyclohexanone to adipic acid								
18.	Co/Br	HOAc	—	31	3.0	78	1.0	air	[295]
19.	Co/Mn/Br	HOAc,H_2O	—	36	20	115	1.0	O_2	[290]
20.	Co/Mn/Br	—	60	—	—	—	—	—	[296]
21.	HNO_3	—	100	87–91	—	—	—	—	[297]
	5,5-dimethyl-1,3-cyclohexanedione to 3,3-dimethyl glutaric acid								
22.	Co/Mn/Br	HOAc	—	89	3.0	100	14	air	[298]
	5-isopropyl-1,3-cyclohexanedione to 3-isopropyl glutaric acid								
23.	Co/Mn/Br	HOAc	—	87	3.0	100	14	air	[298]

Item	Catalyst	Solvent	Conv. (%)	Yield (%)	Time (h)	Temp. (°C)	*P* (atm)	O_2 source	Ref. No.
Saturated Aldehydes:									
	butyraldehyde to butyric acid								
24.	Co/Mn/Br	HOAc	71	58	4.0	115	1.0	O_2	[290]
	3,3-dimethyl-5-ketohexanoic acid to 3,3-dimethyl glutaric acid								
25.	Co/Mn/Br	HOAc	—	71	3.0	100	14	air	[298]
Ethers:									
	dibutylether to butyric acid and butylbutyrate								
26.	Co/Br	benzoic acid	—	50	2.0	130	1.0	O_2	[294]
Acids:									
	caproic acid (1-hexanoic acid) to a mixture of oxygenated products, including keto acids and dicarboxylic acids as keto caproic, oxalic, and adipic acids								
27.	Co/Br	caproic acid	—	—	1.2	127–165	1.0	O_2	[292]
	stearic acid to a mixture of oxygenated products including dicarboxylic acids and ketonic acids such as the isomeric ketostearic acids								
28.	Co/Br	stearic acid	—	—	3.3	140–144	1.0	O_2	[292]
Unsaturated Compounds:									
	$CH_2{=}CH_2$ to $CH_2(OAc)CH_2(OAc)$ (ethylene to ethylene glycol diacetate)								
29.	Co/Br	HOAc	53	19	2.0	165	17	air	[299]
	$CH_3CH{=}CH_2$ to $CH_2{=}CHCOOH$ (propene to acrylic acid)								
30.	Mn/Br	HOAc	22	22	4.0	200	20	air	[300]
	cyclohexene to cyclohex-2-enylacetate								
31.	Co/Br/NaOAc	HOAc,Ac_2O	—	11	5.0	80–111	1.0	O_2	[96,11]
32.	$Pd(OAc)_2$,$Cu(OAc)_2$	HOAc	—	85	—	—	1.0	—	[301]
	cyclohexene to 2-cyclohexen-1-one								
33.	Co/Br	HOAc/ heptane	—	—	0.75	95	1.0	O_2	[302]
	$CH_3(CH_2)_4CH{=}CH_2$ to $CH_3(CH_2)_4CH(OAc)CH_2(OAc)$ (1-heptene to the glycol acetate)								
34.	Mn	HOAc	33	28	5.0	150	—	—	[303]
	t-2-heptene to 2-heptene-4-one								
35.	Co/Br	HOAc	—	—	1.0	110	1.0	O_2	[302]
	1-octene to 3-acetoxy-1-octene								
36.	$Co(OAc)_2$,NaBr,NaOAc	HOAc,Ac_2O	—	—	1.0	60–122	1.0	O_2	[96]
	1-octene to 1-octenone-3								
37.	Co/Br	HOAc	—	—	2.3	25–36	1.0	O_2	[302]
	1-octene to formic acid, heptanoic acid and 5-acetylpentanoic acid								
38.	Co/Mn/Br	HOAc	—	—	5.0	170	27	air	[304]
	2-octene to 2-octen-one-4								
39.	Co/Br	HOAc	—	—	2.0	25–41	1.0	O_2	[302]
	2,4,4-trimethylpentene-2 to beta-*tert* butyl methacrylic acid								
40.	Co/Br	HOAc	—	—	1.3	80–100	1.0	O_2	[302]
	1-phenylbutene-2 to crotophenone								
41.	Co/Br	HOAc	—	—	1.0	50–105	1.0	O_2	[302]
	$CH_2{=}CHCH{=}CHCH_3$ to $CH_2{=}CHCH{=}CHCOOH$ (1,3-pentadiene to 2,4-pentadienoic acid)								
42.	Co/Mn/Br	—	70	—	85	—	—	—	[305]
	1,3-diphenyl-1,3-butadiene to 2,5-diphenylfuran								
43.	$Cu(OAc)_2$, LiBr	HOAc,Ac_2O	—	60	25	1.0	—	—	[306]

derivatives, the attack is first next to the benzene ring; i.e., benzylic methylene groups are much more reactive than aliphatic methylene groups. The reactivity of aliphatic compounds, typical of free radical oxidations, follow the reactivity pattern alcohols ≃ acetates ≃ ketones > tertiary C–H > secondary C–H bond > primary carbon bond.

14.1. Oxidation of alkanes

The catalyst modified free radical attack of hydrocarbons gives a complex set of products. Therefore, we will first start with a brief discussion of the *primary* products formed from THERMAL oxidation. There are four classes of primary products from the thermal autoxidation of n-hexadecane namely hydroperoxides, di-hydroperoxides, cyclic ethers and α–γ and α–δ hydroperoxy-ketones [285]. An example of each are:



(14.1)

There are 8 geometrical isomers of the hydroperoxides and they constituent roughly 80% of the oxygenated products. Only about 1% of the oxygenated products are cyclic ethers. The hydroperoxy-ketones and cyclic ethers are thought to occur via intramolecular attack. Chain cleavage occurs via the peroxy ketones to give methyl ketones [285]. At higher conversions even more complex mixtures form. For example during the thermal autoxidation of n-octane, at 4% conversion, the selectivity to peroxides is 30%, 2,3,4-octanones is 30%, 2,3,4-octanols is 16%, acetic + caproic acid is 11%, propanoic + valeric acids is 18% and n-buteric acid is 5% [286]. Heterogeneous and homogeneous catalysis can change the rate of formation as well as the distribution of products, see for example ref. [287]. Non-MC type autoxidations are commercially being used to produce acetic acid from n-butane [288]. A C_4–C_8 mixture of alkanes has been used in the past to produce formic, acetic, and propionic acid [288].

n-Propane, n-butane, and n-pentane have been subjected to MC oxidation (see items 1–5). A complex mixture results but the highest yields are to acetic acid.

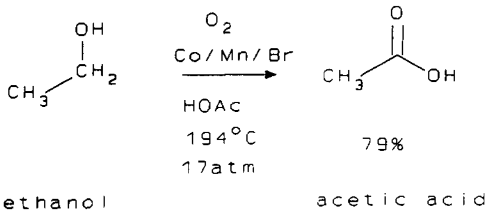
	Yield (mol-%)				
	Acetic acid	Formic acid	Propionic acid	Carbon oxides	Esters
n-Propane	53	16	–	22	10
n-Butane	81	–	–	6.4	12.8
n-Pentane	53	4.6	18	–	6.9

A 93% yield of acetic acid from n-butane can be obtained via recycle. This is obtained by distillation of the effluent from the reactor, removing the acetic acid, and then re-cycling the remainder back to the reactor. The absence of bromide from the cobalt and manganese or the absence of the metals from the bromide result in a much slower reaction [121] indicating that MC catalysts are much more active than non-MC catalysts with aliphatic hydrocarbons just as they are in benzylic oxidations (see Section 3.5). n-Octane and n-decane are reported to give a mixture of ketones, diones, and carboxylic acids in unspecified yields (items 9, 10). Considering the commercial importance of the oxidation of cyclohexane to a mixture of cyclohexanol–cyclohexanal ('keto' oil), it is surprising that there are no reports on the MC oxidation of cyclohexane.

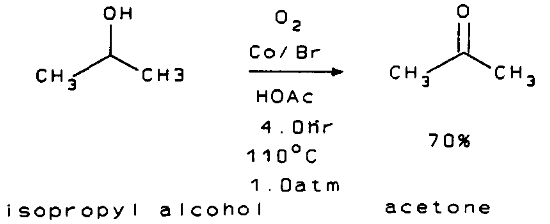
The MC oxidation of methylcyclohexane yields a mixture of formic acid (19%), acetic acid (8.7%), glutaric acid, adipic acid, succinic acid (7.4%), and acetylvaleric acid (items 7 and 8). Decahydronaphthalene has been oxidized to various acetate isomers (item 6).

14.2. Oxidation of alcohols, aldehydes, ethers, and acids

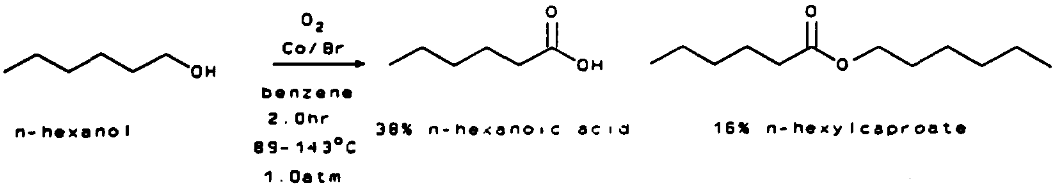
Since alcohols are more reactive than aliphatic C–H bonds, one can obtain good yields of acids from primary alcohols, or ketones from secondary alcohols (items 11–17). Three examples are:



(14.2)

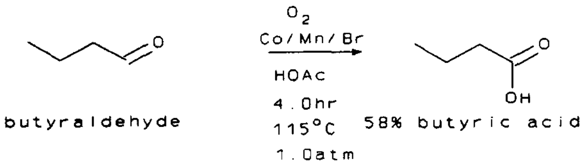


(14.3)



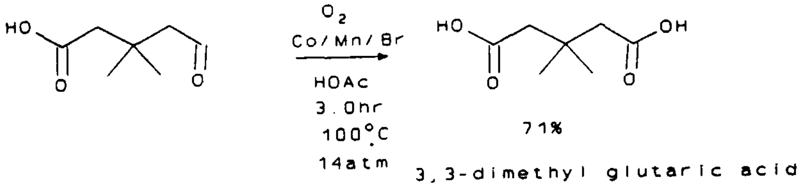
(14.4)

Similarly for aldehydes we have item 24:



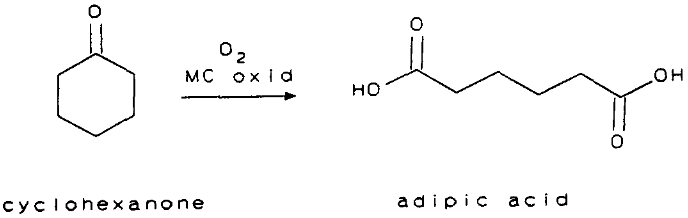
(14.5)

and item 25:



(14.6)

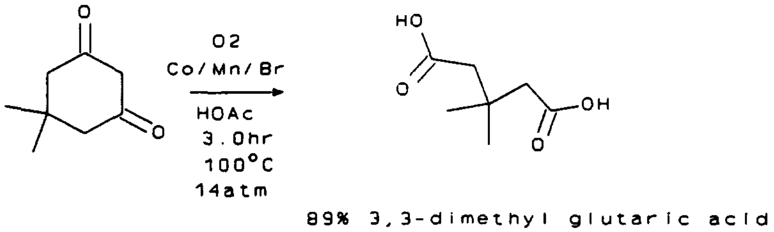
Carboxylic acids can be prepared from ketones (items 18–23). One can prepare adipic acid from cyclohexanone (items 18–20):



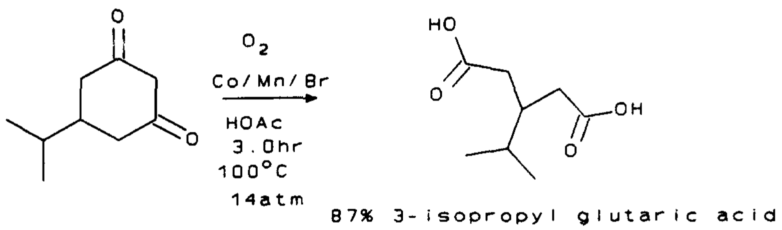
(14.7)

Yields from 31 to 60% have been reported. A maximum 31% yield to adipic acid was obtained by varying catalyst concentration, cyclohexanone concentration, temperature, time, and air flow rate. This is distinctly inferior to the industrial method using nitric acid which gives a 88–90% yield (item 21).

α-, γ-Diketones are cleaved to their carboxylic acids (items 22 and 23):



(14.8)

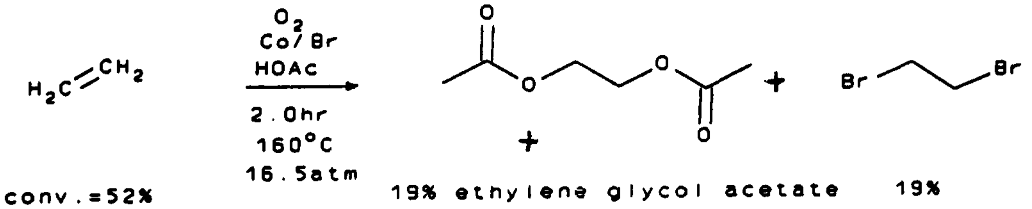


(14.9)

The oxidation of dibutylether (item 26), caproic acid (item 27), and stearic acid (item 28), have also been reported.

14.3. Oxidation of alkenes

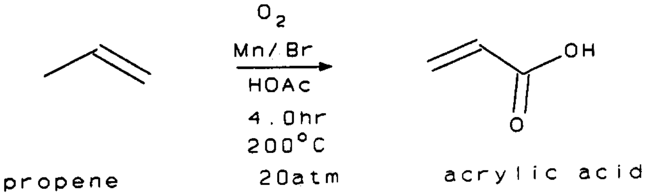
The MC oxidation of ethylene has been reported to give good yields of ethylene glycol diacetate (item 29):



(14.10)

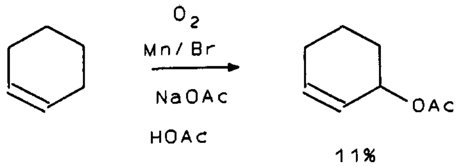
The selectivity of the reaction favors the diacetate with increasing temperature and bromine concentration. The diacetate was also obtained directly from 1,2-dibromoethane, suggesting that 1,2-dibromoethane is the main precursor of the ethylene diacetate. *t*-Heptene has also been reported to oxidize to the glycol acetate, using a non-MC manganese(II) catalyst (item 34).

Acrylic acid forms from the MC oxidation of propene as the major product (item 30):



(14.11)

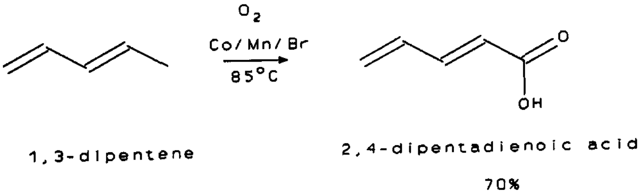
Cyclohexene gives the allylic acetate in 11% yield (item 31), which is distinctly inferior to a Pd/Cu catalyst (item 32):



(14.12)

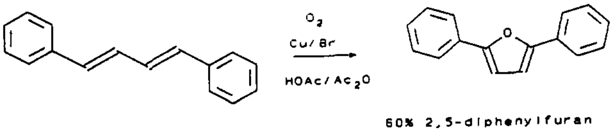
Other allylic products from the oxidation of olefins have been reported (see items 33, 35–37, 39).

1,3-Pentadiene yields 2,4-pentadienoic acid in 70% yield (item 42):



(14.13)

The high yield transformation of *t*,*t*-1,4-diphenyl-1,3-butadiene to 2,5-diphenylfuran is interesting (item 43):



(14.14)

It is claimed that the Cu/Br catalyst acts as both dioxygen activation and halogenation agent[1–314].

Acknowledgements

I would like to thank Alan Bemis and Peter Thornley for their encouragement over the years and Amoco for its support. I would like to thank the following co-workers: Robert Buntrock, Larry Satek, Jeff Broeker, Dan Pourreau, Neal Nowicki, Gayle Chany, David Young, Robert Gipe, Rise Whitworth, Kristi Fjare. Special thanks to Janet Hoffman who prepared the manuscript.

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