'Oxenoid' oxygen insertion *vs.* a radical mechanism in the oxidation of alkanes and alcohols: the case of aromatic peracids

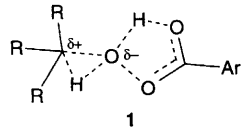
Anna Bravo, Francesca Fontana, Francesco Minisci* and Anna Serri

Dipartimento di chimica del Politecnico, via Mancinelli 7, I-20131 Milano, Italy

Adamantane is oxidised by MCPBA in a free-radical process, whose selectivity is discussed; by this method, cyclohexanol can be directly oxidised to caprolactone.

Aromatic peracids represent a class of oxidants, characterized by high selectivity in the oxidation of nonactivated C=H bonds, for which both an 'oxenoid' insertion[1] (**1**) and a free-radical mechanism[2] involving aroyloxyl and aryl radicals as hydrogen abstracting species have been proposed. The suggested radical mechanism, however, is not consistent with the selectivity of the alkane oxidation. We therefore propose a different free-radical mechanism, based on our previous studies[3] concerning the reaction of alkoxy radicals with hydroperoxides [reaction (1)].

Reaction (1) is very fast and is strongly affected by the ability of the solvent to form hydrogen bonds with hydroperoxides.[3,4] Thus it seems reasonable to hypothesize also for reaction (2), by analogy with reaction (1), a high rate constant and an important solvent effect. Acylperoxy radicals are well-known hydrogen abstracting species in the autoxidation of aldehydes [reactions (3) and (4)]. The oxidation of alkanes would occur according to reaction (5). Reaction (5*a*) prevails over reaction (5*b*) and reactions (2) and (5*a*) are the propagating steps of the free-radical chain leading to the main reaction product ROH. The competitive decarboxylation of aroyloxy radicals[5] would lead to the classical reactions of aryl radicals. The high regioselectivity is mainly explained by the electrophilic character of the acylperoxy radical and the stereoselectivity observed with some alkanes[1,2] should be ascribed to a fast cage reaction of the alkyl radical with the peracid reaction (5), an oxygen rebound mechanism]. A great deal of evidence and new synthetic developments support the oxidation mechanism of adamantane, cyclohexane, cyclohexanol, cyclopentanol, heptan-1-ol and heptan-2-ol by MCPBA [reaction (5)]. The evidence is as follows: (*i*) adamantane reacts at room temperature in 1,2-dichloroethane under argon to give 1-hydroxyadamantane **2**,



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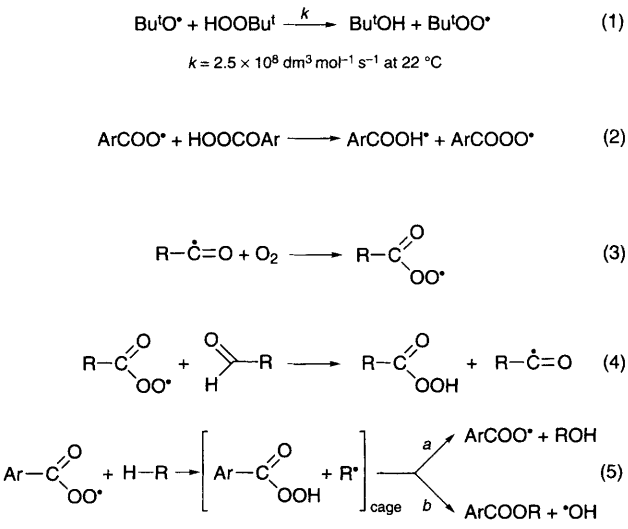

Table 1 Oxidation of adamantane by MCPBA[a]

Solvent	Conv. (%)	*T*/°C	Yield (%) **2**[b]	**3**[b]	**4**[b]	**5**[b]	Mono- and di-haloadamantanes
CH_2Cl–CH_2Cl[c]	30.2	18	70.1	1.6	19.3	18.1	not obs.
CH_2Cl–CH_2Cl[d]	29.4	18	77.2	1.3	11.4	not obs.	not obs.
CH_2Cl–CH_2Cl[e]	44.1	65	56.0	2.0	10.5	24.9	not obs.
CH_2Cl–CH_2Cl[e] $CBrCl_3$ (0.25 mmol)	73.3	65	25.1	0.8	4.8	not obs.	63.0
CH_2Cl–CH_2Cl[e] $CBrCl_3$ (0.5 mmol)	74.9	65	7.3	traces	traces	not obs.	77.2
CH_2Cl–CH_2Cl[e] $CBrCl_3$ (1 mmol)	95	65	not obs.	not obs.	not obs.	not obs.	85.1
Benzene[c]	9.4	18	75.2	traces	18.3	not obs.	not obs.
Benzene[d]	11.4	18	74.5	0.9	17.7	not obs.	not obs.
Benzene[e]	21.0	65	84.6	4.5	10.8	not obs.	not obs.
CH_2Cl_2[e]	15.3	40	58.5	1.9	10.4	21.3	not obs.
$CHCl_3$[e]	49.9	60	29.4	1.2	2.5	9.5	18.1 (1-Cl)
CCl_4[e]	>99	65	*ca.* 1	not obs.	not obs.	not obs.	88.2

[a] 1 mmol of MCPBA, 1 mmol of adamantane in 5 ml of solvent for 100 h at 18 °C and 20 h for all the other temperature. [b] Conversion of adamantane; all yields based on converted adamantane, except for yields of **5**, based on MCPBA; [c] Argon atmosphere. [d] Oxygen atomosphere. [e] Air atmosphere. In benzene solution *m*-chlorobiphenyl is formed in (*c*), 5% and (*e*), 18%, but not in (*d*). Two experiments have been carried out in $CHCl_3$ and in CCl_4 in the absence of MCPBA according to procedure (*e*) and no chlorination took place. An experiment carried out according to procedure (*c*) in the absence of MCPBA, but in the presence of 1-adamantanol and MCPBA did not give **4**.

2-hydroxyadamantane **3**, 1-adamantyl-*m*-chlorobenzoate **4** and chlorobenzene **5** (Table 1). In benzene solution **2**, **3**, **4** and *m*-chlorobiphenyl **6** are formed. Compounds **5** and **6** clearly arise from the chlorophenyl radical by hydrogen abstraction from the solvent and by homolytic substitution of benzene, respectively. (*ii*) In the absence of adamantane under the same conditions as (i), **5** and **6** are not formed. This means that adamantane induces the homolysis of MCPBA. (*iii*) Under the same conditions as in (i) but with an oxygen atmosphere, **2**, **3** and **4** are formed with similar selectivity, while **5** and **6** are absent. O_2 intercepts all the carbon-centred radicals escaping from the solvent cage, but not the adamantyl radical, which reacts rapidly with MCPBA in the cage. (*iv*) No reaction takes place in the absence of MCPBA under the conditions reported in (iii). (*v*) In $CHCl_3$, 1-chloroadamantane **7** is formed in addition to **2–5**. It is, however, well-known[6] that tertiary alkyl radicals abstract both hydrogen and chlorine atoms from $CHCl_3$ at similar rates.(*vi*) In CCl_4 or in the presence of $CBrCl_3$ adamantane halogenation largely prevails over its oxidation (Table 1). (*vii*) No halogenation takes place under conditions (v) and (vi) in the absence of MCPBA. (*viii*) In the presence of TEMPO the oxidation is inhibited. (*ix*) The oxidation is inhibited in Bu^{t}OH, supporting, for reaction (2), a solvent effect similar to the one observed[3,4] for reaction (1). (*x*) In dichloroethane solution cyclohexane is much less reactive than adamantane. In a competitive experiment at 20 °C C–H in adamantane is 100 times more reactive than C–H in cyclohexane. At 60 °C the reaction products are cyclohexanol, cyclohexanone and caprolactone in the ratio 1:2:2 at low (10%) conversion of cyclohexane (cyclohexane–MCPBA = 5:1). Bromination of cyclohexane largely prevails in the presence of $CBrCl_3$. (*xi*) The oxidation of adamantane has been carried out under the conditions in which aldehyde autoxidation (butanal, benzaldehyde and *m*-chlorobenzaldehyde) takes place reactions (3) and (4)] (Table 2): **2**, **3** and esters with the same structure as **4** have been obtained with the same high selectivity observed with MCPBA. Since aliphatic peracids are unsuitable for alkane hydroxylation,[2] due to the very fast decarboxylation of the RCOO· radical (10^{10} s^{-1} as compared with 10^6 s^{-1} for PhCOO·), the results with butanal strongly support the mechanism of reaction (5). The acylperoxy radical, formed according to reaction (3), thus provides a new, more useful procedure for selective alkane oxidation. (*xii*) In the presence of cyclohexanone, adamantane is not oxidized by MCPBA, caprolactone being the only reaction product (Baeyer–Villiger reaction). However, adamantane is selectively oxidized during the autoxidation of *m*-chlorobenzaldehyde in the presence of cyclohexanone, clearly indicating that the species responsible for the oxidation is not the peracid formed *in situ*, but the acylperoxy radical generated according to reaction (3). No oxidation takes place in any of the examples listed in Table 2 in the absence of aldehyde. (*xiii*) The prevailing formation of cyclohexanone and caprolactone in the oxidation of cyclohexane at low conversions is in striking contrast with previous reports[7] stating that primary and secondary alcohols are unreactive with peracids in the absence of catalysis. Actually, cyclohexanol, cyclopentanol, heptan-1-ol and heptan-2-ol give the corresponding carbonyl compounds and the products of further oxidation (lactones, esters and carboxylic acids) simply by warming for a few hours at 60 °C with MCPBA in dichloroethane or keeping the mixture at room temperature for longer periods. (Table 3). Chlorobenzene is also a by-product in this case, and Bu^{t}OH, when used as solvent, inhibits the reaction. The previously reported[7] inertness of alcohols towards MCPBA should therefore be ascribed to solvent effects,which inhibit reaction (2) by forming hydrogen bonds with peracids.

Table 2 Oxidation of adamantane and aldehydes by oxygen

Aldehyde	Conv. (%)[a]	*T*/°C	Yield (%) **2**[b]	Yield (%) **3**[b]	1-Adamantyl ester (%)[b]
C_3H_7CHO[c]	47	70	78	traces	13
C_6H_5CHO[c]	31	70	84	traces	12.2
C_6H_5CHO[d]	36	40	82	1.3	6.1
m-ClC_6H_4CHO[d]	34	40	75	2.1	8.2
m-ClC_6H_4CHO[e]	20	70	72	2.8	7.3

[a] Adamantane conversion. [b] Yields based on converted adamantane. [c] 2 mmol of aldehyde in 5 ml of dichloroethane are dropped during 3 h to a solution of 1 mmol of adamantane in 5 ml of dichloroethane and oxygen is bubbled for 24 h. [d] As in (*c*) by using 0.1 mmol of $(Bu^tOOCO)_2$. [e] As in (*c*) in the presence of 3 mmol of cyclohexanone.

Table 3 Oxidation of alcohols by MCPBA[a]

Alcohol	Conversion (%)[b]	Reaction products (%)[c]
Cyclohexanol	75	caprolactone (87)
Cyclohexanol[d]	85	caprolactone (89)
Cyclopentanol	79	valerolactone (92)
Heptan-1-ol	70	heptanoic acid (78) hexyl formate (6.8) heptanal (2.6)
Heptan-2-ol	79	hexyl acetate (42.9) 2-heptanone (45.1) methyl hexanoate (2.5)

[a] 1 mmol of alcohol and 2 mmol of MCPBA in 5 ml of dichloroethane at 60 °C for 20 h. [b] Alcohol conversion. [c] Yields based on converted alcohol. [d] As in (*a*) at 20 °C for 70 h 10–15% of chlorobenzene, based on MCPBA, is formed in all cases.

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