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REACTIVITY AND SELECTIVITY OF HOMOLYTIC SUBSTITUTION REACTIONS ON THE PEROXYACID GROUP

Daniel LEFORT*, Jacques FOSSEY, Michel GRUSELLE, Jean-Yves NEDELEC and Jeanine SORBA

C.N.R.S., GR 12, 2, rue H. Dunant, 94320 THIAIS (France)

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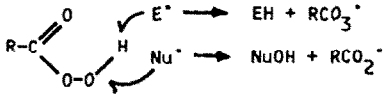
Abstract - Peracids in solution may undergo homolytic decomposition leading mostly to mixtures of acid and alcohols, these latters being formed from either the peracid or the solvent

$$RCO_3H \xrightarrow{SH} ROH,\ RH,\ RCO_2H,\ CO_2,\ SOH$$

The peracid behaves as source of radicals and also as substrate thus presenting two radicophile centers :



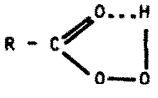
- with a nucleophilic radical (R° from peracid or S° from solvent) the site of attack is the O-O bond of the peracid yielding an alcohol (NuOH). The rate of this reaction increases with increasing nucleophilicity of the radical ; this reactivity is interpreted in terms of frontier orbital perturbation theory, taking into account both the orbital energy level difference and the orbital overlap.

- when the radical is electrophilic, it abstracts rather the hydrogen of the peroxidic group leading to decomposition of the peracid into acid.

Hydrogen abstraction from the solvent may be also observed in appropriate cases : this process can be used for free radical hydroxylation of hydrocarbons.

The relative importance of these three chain reactions in competition : O-O bound attack, hydrogen abstraction from the peracid and solvent transfer reaction were studied as a function of structure of the radicals, solvent properties and temperature.

Peracids are compounds that have been known of for a long time, and are used as oxidation reagents Their behavior is either electrophilic (epoxidation of olefins, oxidation of amines and sulfur compounds, hydroxylation of hydrocarbons) or nucleophilic (oxidation of ketones into esters) (1a). They are most commonly synthesized by reacting concentrated H_2O_2 with the corresponding acid, in a protonating medium (1) (2) (3). In solution, peracids exist uniquely in a chelated monomeric form (4) (5) ; this intramolecular hydrogen bond leads to a decrease in the acidity of the peracids, compared to that of acids (1).

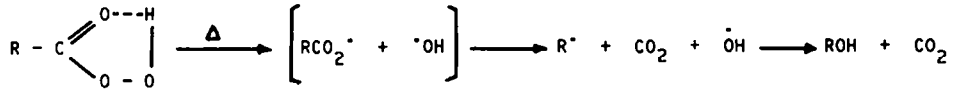


The stability of the peracids is a function of their molecular weight ; performic and peracetic acids in particular are unstable and call for special precautions during handling. A good number of peracids are sufficiently stable with respect to time (16) for it to be possible to study their reactions.

Kinetic studies of the decomposition of various peracids in ionizing media show that the rate depends greatly on pH, and reaches a maximum when the pH is equal to the pK of the peracid (16) (6) (7). This decomposition involves ionic species and gives rise to the formation of H_2O_2 or the release of oxygen, depending on the pH.

SWERN has shown that in different organic solvents, in particular benzene, the peracid decomposes into an acid following pseudo-first order kinetics (8).

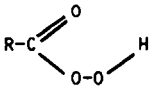
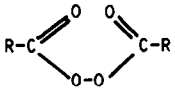
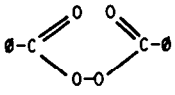
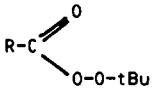
He remarks that if this was a radical reaction then one would expect to find the alcohol resulting from the decarboxylation.



Besides, such an alcohol had been identified among the decomposition products of acetic (9) and propionic (10) peracids.

Homolytic splitting of the O-O bond of the peracid is, a priori, easy since the dissociation energy is comparable to those of other categories of peroxide (Table I).

TABLE I

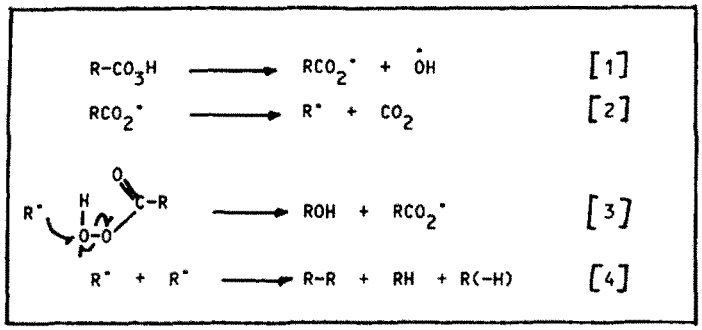
PEROXIDE	D(O-O) kcal/mole	Ref.
	47	11
	30	12
	32.7	1b
	35.5	1b
R-O-O-R	37.8	1b
R-O-O-H	43-44	1b-12

It is well known that peroxide compounds are used either as initiators of radical reactions (13), or as structural elements in synthesis (14). Curiously, radical chemistry of peracids has not undergone such developments. From 1959 onwards we have shown (15) that under certain very simple experimental conditions, peracids can give rise to very interesting radical reactions, and that they constitute a most fruitful model for studies of the regio- and stereoselectivities of homolytic substitution reactions as a function of the structure of the radical as well as for analysis of competition between different processes and applications to regioselective hydroxylations.

I - REACTIVITY AT THE O-O BOND OF PERACIDS : INFLUENCE OF THE NUCLEOPHILIC CHARACTER OF THE RADICALS

Reaction scheme

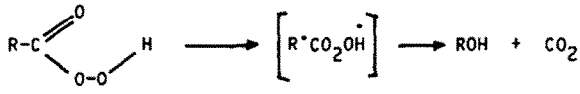
In earlier studies we have shown that when a solution of dodecanoic peracid in a hydrocarbon is boiled an alcohol is formed through decarboxylation of the peracid by a radical chain mechanism (15) (16) (Scheme I).



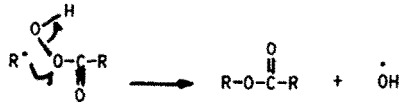
Scheme I

In addition to the usual arguments advanced to demonstrate the radical nature of this mechanism, we have established that the kinetic order is equal to 3/2, which is compatible with a chain-termination step involving two R• radicals (17).

In confirmation of the kinetic results, subsequent studies of the stereochemistry of reaction [3] (18), of CIDNP effects (19) and of reaction products from a peracid-diacyl peroxide mixture have verified that the alcohol is indeed formed through reaction [3] and not by a cage combination process that could be written :

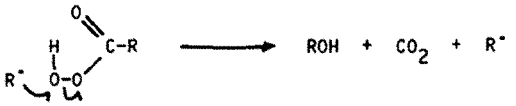


A homolytic substitution reaction on the other oxygen atom of the O-O bond could also have been anticipated :



In this case one would have found the corresponding ester in the reaction mixture, but this was never so ; it may be assumed that this reaction does not occur because the peroxide oxygen is much more accessible (reaction [3]).

In scheme I we have proposed a two-step reaction ([2] and [3]) for alcohol formation. In fact, we wondered whether in certain cases the alcohol formation and decarboxylation may occur simultaneously :

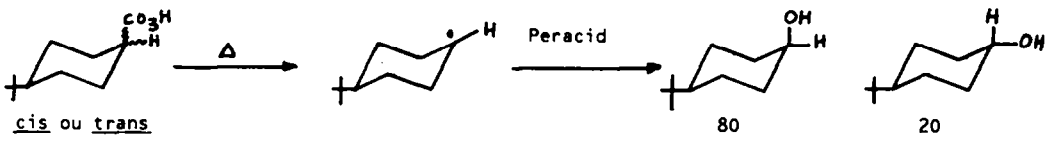


It was not possible to make a choice between the two processes on the basis of the kinetics and the analysis of the products. Nonetheless, the results show that there the two reactions are certainly not simultaneous in the case where the $RCO_2^{\bullet}$ radical is decarboxylated with difficulty (case of $\phi CO_2^{\bullet}$, which will be discussed later).

Upon referring to scheme I, it can be seen that a peracid is both a source of radicals and the substrate. The reaction is initiated without the addition of any other compound, as in many radical reactions. Alcohol formation reaction [3] lends itself very well to the study of the influence of the structure of a radical R• on its reactivity towards a peroxide bond, and also to the study of stereoselectivity.

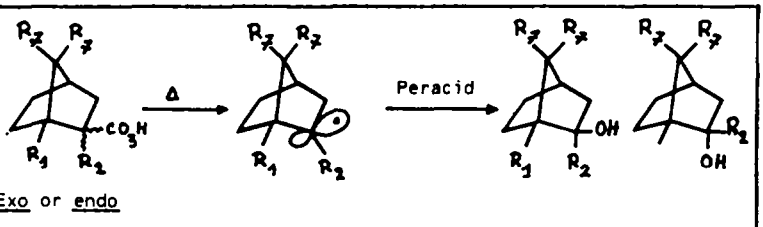
Stereoselectivity of the substitution reaction at the (O-O) bond (Reaction [3]).

By analogy with known results regarding the stereoselectivity of reactions of the ionic or concerted types, for the sp_2 carbon site of a t-butyl-4 cyclohexyl system (ketone reductions, epoxidation of juxtacyclic double bonds), we came to the conclusion that in reaction [3] a cyclohexyl radical behaves as if it was flat. For example, cis or trans t-but-4 cyclohexane carboxylic peracid gives rise to the same kinetic mixture of equatorial and axial alcohols :



The influence of a methyl group in position 2 or 3 shows that the stereoselectivity is a compromise, in the transition state, between bond interactions and steric effects (18a)-(18c).

Following the same approach, the 2-bicyclo-[2.2.1]-heptyl radical gives, on the other hand, stereochemical results compatible with a pyramidal structure. The entry of the peracid reagent by the exo face is always favored, even in the presence of a CH_3 at position 7, which is not the case for ionic-type reactions (table II) (18a)-(18c).



$R_1 = R_2 = R_7 = H$	94	6
$R_1 = R_2 = H \quad R_7 = CH_3$	70	30
$R_1 = H \quad R_2 = R_7 = CH_3$	58	42
$R_1 = CH_3 \quad R_2 = H \quad R_7 = CH_3$	71	29

Table II

As in the case of the cyclohexyl radical, the stereochemical results are a compromise between steric effects and bond interactions. Moreover, the influence of the methyl group at position 1 or 2 shows that the eclipse effects, often invoked to explain stereoselectivity of certain radical reactions, are only of negligible importance here (18a).

Another important conclusion of these stereochemical results is that the transition state resembles the starting products (radical-peracid) and that the C-OH bond is little formed.

Influence of the structure of the radical $R^{\cdot}$ on its reactivity towards the O-O bond

In general terms, the activation energy of radical reactions is a function of polar, steric and enthalpic factors, the relative importance of which will clearly depend on the reaction considered. In the case of interest to us, and by analogy with hydrogen transfer reactions, one can reasonably use POLANYI's relation, with suitable precautions, between the activation energy E and the enthalpy ΔH for the substitution reaction [3] (17) :

$$E = C + \alpha\Delta H$$

where α is a proportionality coefficient which varies from 0 to 1, depending on whether the transition state resembles the initial state or the final state, and C is a constant which depends on polar factors. For two radicals $R_1^{\cdot}$ and $R_2^{\cdot}$, the difference in activation energy is :

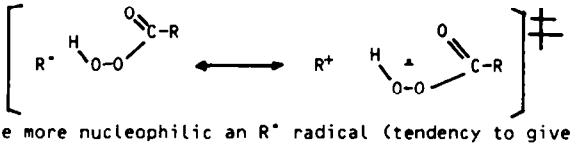
$$E_1 - E_2 = C_1 - C_2 + \alpha(\Delta H_1 - \Delta H_2)$$

with

$$\Delta H_1 - \Delta H_2 = D(R_1CO_2-OH) - D(R_2CO_2-OH) - D(R_1-OH) + D(R_2-OH)$$

The experimental values for the dissociation energies of the R-OH bonds of various alcohols are little influenced by the nature of R : D(R-OH) = 91 $\pm$ 2 kcal./mole. If one also assumes that the nature of R has little influence on the dissociation energy of the O-O bond of peracids : $D(R_1CO_2-OH) = D(R_2CO_2-OH)$, it follows that the enthalpies of the transfer reaction with a peracid are little affected by the nature of R, whence $\Delta H_1 - \Delta H_2 = 0$. In addition, as this reaction [3] is strongly exothermic (ΔH greater than 40 kcal./mole) the transition state is near to the initial state, which had already been shown by the stereochemical results. In consequence, α will be close to 0 and the enthalpic effects small. The difference $E_1 - E_2$ therefore amounts to $C_1 - C_2$, where only the polar factors intervene.

Our studies on the mechanism of the decomposition of α-halogenated peracids (20), as well as those of TOKUMARU (21) on the behavior of benzoic peracid in different solvents, have demonstrated the relation between the reactivity of the radicals towards the O-O bond of the peracids (reaction [3]) and their nucleophilic characteristics. There was every reason for proposing, therefore, a transition state represented by the two following limiting forms :

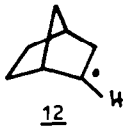


[5]

Plainly, the more nucleophilic an R$^\bullet$ radical (tendency to give carbocation), the more reactive it is at the O-O bond of a peracid.

In order to confirm this hypothesis, it was necessary to have a range of results with radicals of different nucleophilic characteristics. The choice of these radicals produced by reaction [2] was made as a function of the stability of the carbocations resulting either from an electronic effect of a group at position α of the radical center, in which case the stability of the carbocation is given by the ionization potential (I.P.) (22) (25), or from a strain in the ring, in which case the carbocation stability is linked to the rate of solvolysis (k_{S_N}) of the corresponding halogen-containing compounds (see table II) (26) (27).

The nucleophilic character of a radical can also be assessed according to the s character of the orbital containing the unpaired electron (28) (29) (30) ; and it can be predicted that the sp_3 radical 7 will be much less nucleophilic than a π radical such as 11 (cf. table III). With this in mind we have also compared the reactivity of the 2-norbornyl 12 and 4-ter-butyl-1-cyclohexyl 13 radicals :

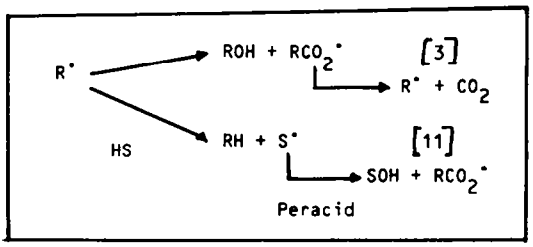


12

13

Certain data in the literature indicate that the first radical 12 has a pyramidal structure corresponding to a single minimum energy (31) (34), whereas the cyclohexyl radical 13 has two pyramidal forms, with two energy minima and a low inversion barrier (about 1.5 kcal./mole) (35).

The reactivity of a radical is defined by the rate constant of the reaction [3] , but it is known that in a chain reaction it is difficult to reach the absolute rate constant of each of the stages. Nonetheless, the aim that we set ourselves will be achieved if a sequence of relative reactivities can be obtained. To do this we have used the characteristics of the competitive reactions, dealt with in detail later, of the radical studied with the peracid and the hydrogen donor solvent HS :



For two radicals $R_1^\bullet$ and $R_2^\bullet$ we can write

$$\frac{k_o 2}{k_o 1} = r\frac{k_s 2}{k_s 1} \quad \text{with } r = \frac{[R_2OH]f}{[R_1OH]f} \times \frac{[R_1H]f}{[R_2H]f}$$

By applying the ARRHENIUS and POLANYI equations and by using the ROH and RH concentrations at the end of the reaction, we have been able to establish a sequence of relative rate constants for the different radicals under study, with the 1-bicylo-[2.2.2]-octyl 8 radical as reference (17) (Table III).

TABLE III

Reactivity of radicals R•
at the O-O bonds of peracids

R•	$k_{rel.}$	D(R-H) kcal./mole	I.P.(R•) e.v.	k_{S_N1} R-Br(s^{-1})
 7	4×10^{-4}	99.4		10^{-13}
 8	1	93.2		10^{-6}
$Ad_1^\bullet$ 9	9	92		10^{-3}
 10	50	≅ 91		
$R-\dot{C}(CH_3)_2$ 5	100	92	7.90	1
$R-\dot{C}H(CH_3)$ 3	11	94.5	8.78	
$R-\dot{C}HCl$ 2	0.4	94.7	9.32	
$R-CH_2^\bullet$ 1	1.6×10^{-2}	98	9.84	
 12	3	≅ 94		
 13	8	94		

Some conclusions can be drawn from the data in this table. The stability of the radicals is usually deduced from the values of the dissociation energies D (R-H) (36) (46), and it can be seen that radicals of the same stability have different reactivities towards peracids. Thus, the tertiary 1-bicyclo-[2.2.2]-octyl 8 radical is of comparable stability to the α,α-dimethyl radical 5, but has an activation energy about 2.5 kcal./mole higher. Likewise, there is an activation energy difference of about 1.5 kcal./mole between primary radical 1 and tertiary radical 7. The stability

of the radical is not, therefore, a determinant factor in its reactivity at the O-O bond of a peracid. If the steric factor plays a determinant role in the radical reactivity, the tertiary radicals at the head of the bridge should give similar results, and further, as these radicals are less bulky (47) (49) than the α,α-dimethyl radical 5, one would expect greater reactivity, which is not the case.

In contrast, there is a good correlation between the reactivity of a radical and its ability to give a carbocation, that is to say its nucleophilic character, linked either to the rate of solvolysis of the corresponding bromides (radicals 7, 8, 9, 10 and 5) or to their ionization potential (radicals 5, 3, 2, 1) (Figure 1).

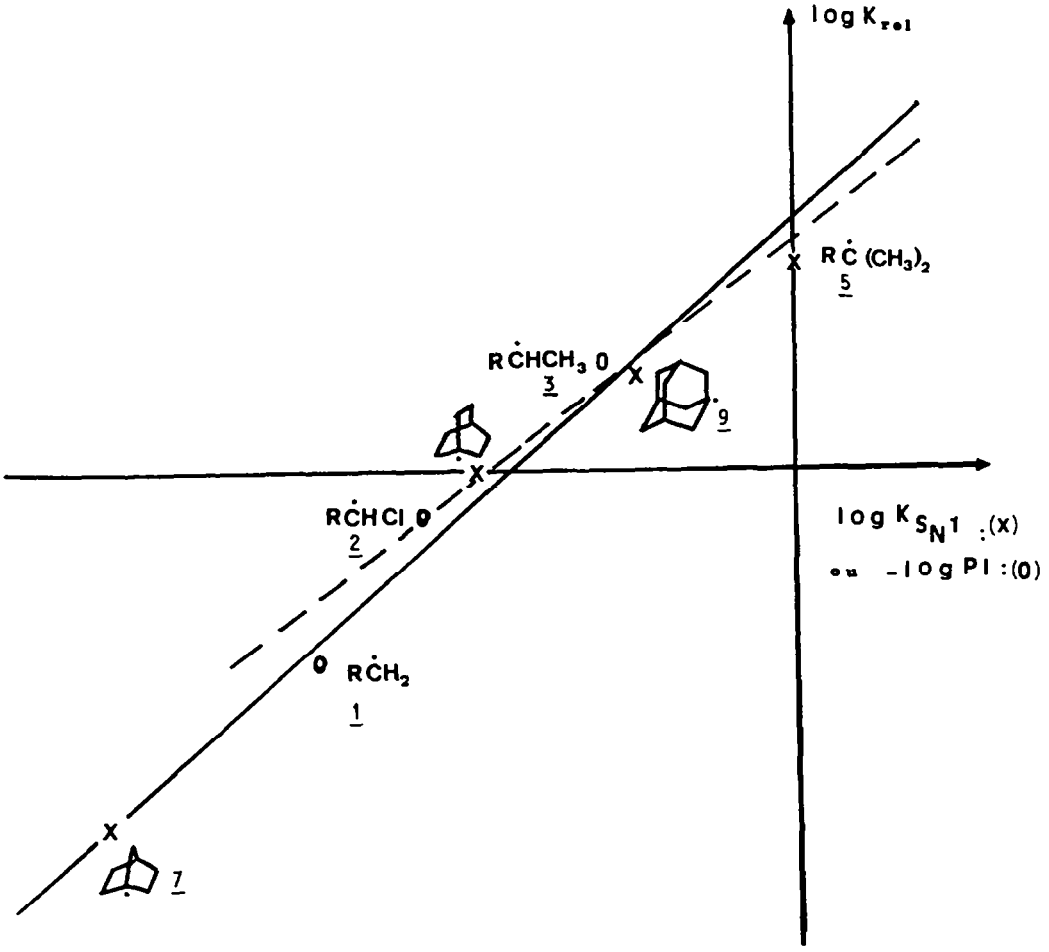


Figure 1 : Plots of log $k_{rel.}$ Vs either log k_{S_N1} (x) for radicals 5, 7, 8, 9 or - log PI (O) for radicals 1, 2, 3, 5.

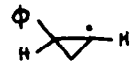
A relation is also observed with the hybridization state of the carbon bearing the unpaired electron (28) (30) ; the sp^3 bicyclo-[2.2.1]-heptyl radical 7 is very unreactive and on comparing the secondary radical 3, the cyclohexyl radical 13, which is flat or slightly pyramidal, and the 2-bicyclo-[2.2.1]-heptyl radical 12 which is pyramidal a decreasing reactivity is observed 3 > 13 > 12.

Bearing in mind their σ structure, radicals such as phenyl 15 or cyclopropyl 4 are very weakly nucleophilic and do not react with the peracid to give the phenol or phenylcyclopropanol that one might expect (Table IV). The decomposition of the corresponding peracids has given some very interesting informations which will be discussed later.

TABLE IV

PERACID DECOMPOSITION PRODUCTS

(0.1 M - cyclohexane - boiling - mole/mole peracid)

R·		ROH	RH	RCO_2H	Cyclohexanol
$R'CH_2^{\cdot}$	1	0.54	0.23	0.24	0.36
$R'\dot{C}HCl$	2	-	0.05	0.43	0.11
$R'\dot{C}HCH_3$	3	0.97	0.01	-	0.03
	4	0	0.79	0.22	0.75
$R\dot{C}(CH_3)_2$	5	0.89	< 0.05	0.11	0.01
$\emptyset\text{-}CH_2^{\cdot}$	6	0.27	0	0.52	0
	7	0.17	0.79	0.05	0.77
	8	0.87	0.12	0.01	0.15
$Ad_1^{\cdot}$	9	0.94	0.03	0.03	0.04
	10	0.95	0.01	0.04	0.02
	12	0.91	0.03	0.03	0.03
	13	0.97	0.02	0.17	0.02
$R' = CH_3(CH_2)_9^{-}$					

The important result of this study is that the reactivity of a radical at the O-O bond of a peracid increases with its nucleophilic strength, and that this reaction has a low activation energy. In the case of the 1-bicyclo-[2.2.1]-heptyl 7 radical, this has been calculated as approximately 4 kcal./mole (17), by using the variation in the ROH/RH ratio as a function of temperature.

Theoretical interpretation

The results can be discussed in terms of frontier orbital interactions (17) (52) between the single occupied molecular orbital of the radical (SOMO) and either the highest occupied molecular orbital (HOMO) or the lowest unoccupied molecular orbital (LUMO) of the substrate, that is to say the antibonding orbital of the O-O bond (cf. figure 2)

The nucleophilic-type SOMO-LUMO interaction (2 orbitals-1 electron) is always stabilizing. The energetic effect ΔE(PMO) associated with this interaction is proportional to the square of the overlap integral between the 2 orbitals, and inversely proportional to the energy difference $\Delta e_{SOMO-LUMO}$ before the interaction.

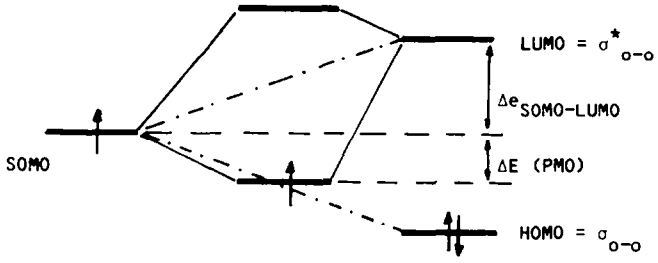


Figure 2. Schematic representation of orbital interactions

$$\Delta E(PMO) = \frac{Sij^2(\varepsilon_i - H_ij/Sij)^2}{\varepsilon_i - \varepsilon_j}$$

i = SOMO, j = LUMO
ε = orbital energy
S = overlap integral
H = matrix element

The smaller the difference $\Delta e = \varepsilon_i - \varepsilon_j$, that is to say the higher the SOMO energy level, the stronger the SOMO-LUMO interaction and the stronger the nucleophilic reactivity of the radical. For localized radicals, the SO orbital energies can be classified according to the ionization potentials or according to the stability of the carbocations. As an example, the α,α-dimethyl 5 radical has a SOMO of higher energy level than the 1-bicyclo-[2.2.2]-octyl 8 radical.

The case of the benzyl radical is different and because of delocalization the spin density at the radical site is about 0.6 instead of 1 for the localized radicals examined up to now. In terms of the orbital energy difference Δe, the benzyl radical should be more reactive than a primary alkyl radical since its I.P. is lower (7.2 and 9.84 respectively) (table V). But in terms of orbital overlap, delocalization of the benzyl radical leads to a smaller numerator in the preceding equation and, according to the results, this factor prevails over that corresponding to Δe. This conclusion shows, furthermore, that the reaction process of a nucleophilic radical at the O-O bond of a peracid corresponds to an orbital interaction.

II - DECOMPOSITION OF PERACIDS BY ELECTROPHILIC RADICALS

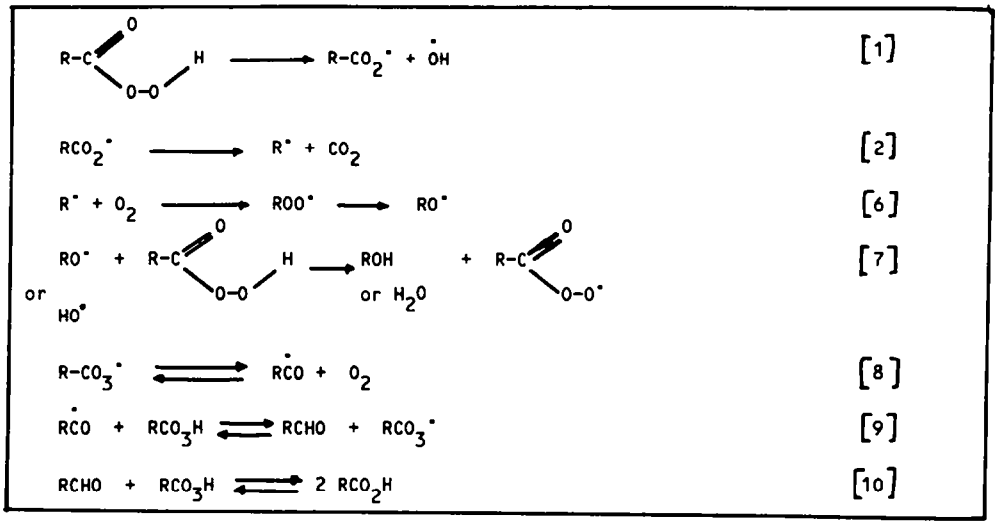
Until now we have considered the reactivity of nucleophilic radicals at the O-O bond of peracids and the formation of alcohols resulting from decarboxylation. Two questions now arise :

- how does an electrophilic radical react ?
- what is the mechanism of the formation of the acid which always accompanies the alcohol and whose quantity varies with the nature of the radical, the reaction conditions and the nature of the solvent (see section III) ?

The two questions are connected and the reply to the first provides the explanations to the problems posed by the second.

An important phenomenon has been observed (15) in which if the solution of a peracid in a hydrocarbon is not brought to boiling, decomposition results uniquely in the formation of the corresponding acid, whereas boiling of the solution induces decarboxylation and the formation of alcohol (reaction [3]). It is clear that oxygen, if it is not eliminated by boiling, plays a role. A study of this problem (66) led to the proposal of a radical chain mechanism for acid

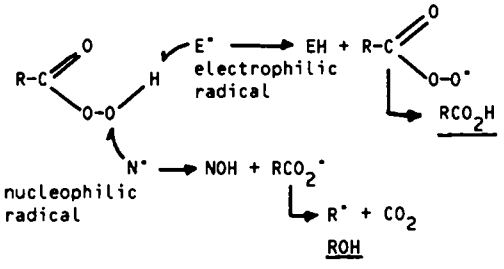
formation : the R$^{\bullet}$ radical produced by reaction [2] is quickly trapped by O_2, and the electrophilic peroxy or alkoxy radical does not react at the O-O bond but withdraws H from the peracid (scheme II).



scheme II

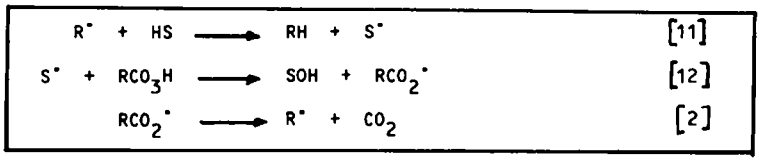
We have established that the overall rate of this succession of reactions leading to the acid (scheme II) is slower than that which gives the alcohol (scheme I or III). Reaction [3] leads to the chief product in the absence of O_2 and is very exothermic (40 kcal./mole), whereas in the presence of oxygen all reactions other than those of "trapping", which ultimately control the overall rate, [7] to [10] are either athermic or endothermic.

The regioselectivity of the reaction of a radical with a peracid group can be summarized in the following way, depending on its electrophilic or nucleophilic character :



III - INFLUENCE OF SOLVENT - COMPETITION BETWEEN DIFFERENT MECHANISMS

In addition to the two possibilities just described it should be added that for a radical to react with a peracid the solvent can intervene as a source of radicals through removal of hydrogen. In such a case one observes a hydroxylation reaction of the solvent, according to scheme III.



scheme III

There are then three competitive processes occurring in the decomposition of a peracid.

- decarboxylation to give alcohol (scheme I)

- transformation into acid (scheme II)
- transfer to the solvent and solvent hydroxylation (scheme III).

The results of table IV show the reality of this competition and the examples that follow give explanations of the relative importance of each of the three processes as a function of the structure of the R$^{\bullet}$ radical and of the nature of the solvent.

When a radical is very nucleophilic (3, 5, 9, 10, 12, 13) the reaction of the O-O bond of the peracid is strongly favored and that with the solvent is negligible, and essentially one obtains the alcohol ROH and very low levels of solvent transfer products (RH and cyclohexanol).

If the radical is less nucleophilic (8, 1) the solvent transfer reaction (Scheme III) is no longer negligible ; the nucleophilic cyclohexyl radical formed reacts favorably with the peracid leading to cyclohexanol and RH in significant amounts ; importantly this solvent transfer reaction induces the decarboxylation of the peracid and leads to regeneration of the radical R$^{\bullet}$.

For weakly nucleophilic radicals (7, 4) the reactions of scheme I are unimportant, even abolished, and the solvent transfer reaction becomes dominant, with equivalent quantities of RH and cyclohexanol being formed. Note that this situation corresponds to the hydroxylation of a hydrocarbon.

The case of the phenyl-cyclopropyl radical 4 is interesting as we have observed that at high initial peracid concentrations this radical reacts with the peracid by withdrawal of hydrogen (scheme II) rather than with the solvent. In effect, for initial peracid concentrations in cyclohexane of 0.1 and 0.5 M, one obtains respectively (in mole per mole of peracid) 0.22 and 0.86 acid and 0.75 and 0.04 cyclohexanol (54). The phenyl cyclopropyl radical 4 can, therefore, be considered as electrophilic towards the peracid. As we shall see later, this is also true for $\Phi^{\bullet}$ and $\Phi CO_2^{\bullet}$ radicals. This electrophilicity is due to the σ character of the radical.

The case of the benzyl radical is very instructive in several respects. This radical is considered very nucleophilic in the case of homolytic substitution reactions of protonated bases (55) and from its I.P. (7.2 e.v. (56)) one might expect that its reactivity at the O-O bond is identical to that of tertiary radicals such as 5 and 9. In fact, the amount of benzyl alcohol obtained (table V) shows that this radical is less reactive than a primary radical such as 1, and necessarily less so than tertiary radicals 5 and 9 (57). This is due to the fact that the unpaired electron of the benzyl radical is delocalized and we have given a theoretical interpretation to this reactivity. One notes also that almost no toluene or cyclohexanol are formed (57) ; for enthalpic reasons the benzyl radical does not withdraw H from cyclohexane, and as the solvent transfer reaction does not occur (scheme III) there is no formation of cyclohexanol. Kinetically there is no aiding of decomposition as in the case of benzoic peracid, which we shall see later, and the rate of decomposition of phenylacetic peracid in cyclohexane is about 10 times slower than that of benzoic peracid (57). Because of the slowing down of reaction [3] and the inexistence of scheme III, the phenylacetic peracid then decomposes into acid according to scheme II and this chain reaction is probably initiated by $\dot{O}H$ radicals derived from homolytic splitting [1]. Comparison of the behavior of the benzyl radical with that of the primary aliphatic radical 1 is a good illustration of the competition between the three mechanisms. In the case of the primary alkyl radical 1, the occurrence of process III (formation of equivalent quantities of hydrocarbon and cyclohexanol) assists the decarboxylation reaction and accelerates the overall rate of decomposition, and the quantity of acid resulting from process II is then minimal. Indeed, in solution in benzene, where process III is suppressed, one observes with radical 1 a drop in the amount of alcohol ROH, a rise in the quantity of acid and a slowing down of the overall decomposition rate by a factor of about 7.

TABLE V

DECOMPOSITION OF DIVERSE PERACIDS

(0.1 M, boiling, products formed in mole/mole of peracid)

PERACID RCO_3H	RADICAL	SOLVENT[a]	$10^4 k$ s^{-1}	RH	ROH	RCO_2H	SOH[e]
ΦCH_2CO_3H	$\Phi-CH_2^{\cdot}$ 6	S-H	2.6	0	0.27	0.52	0.13
		Φ-H	1.7	0	0.27	0.60	-
$CH_3(CH_2)_9CH_2CO_3H$	$CH_3(CH_2)_9CH_2^{\cdot}$ 1	S-H	38.2	0.17	0.53	0.09	0.21
		Φ-H	7.1	0	0.27	0.40	-
ΦCO_3H	$\Phi-CO_2^{\cdot}$ 14	S-H	24.0	0.40[b]	0[d]	0.60	0.95
	or $\Phi^{\cdot}$ 15	Φ-H	2.6	0	0[d]	0.98	-
$\Phi(CH_2)_3CH_2CO_3H$	$\Phi(CH_2)_3CH_2^{\cdot}$ 16	S-H		0.10[c]	ε	0.84	0.10

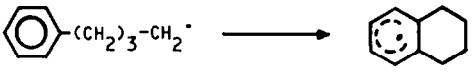
a) S-H and Φ-H stand respectively for cyclohexane and benzene b) Φ-H c) traces of tetralin have been observed d) phenol was not observed e) SOH stands for cyclohexanol.

When the results of the dodecanoic and phenylacetic peracids (sources of primary alkyl and benzyl radicals, respectively) in solution in benzene are compared, where only processes I and II occur, one notes in effect that the benzyl radical is less reactive than the primary alkyl radical and that as a result the rate of decomposition is about four times slower. Nevertheless, when the benzyl radical is substituted by one or two CH_3, one observes the same respectivity sequence as in the alkyl radicals :

$$\Phi-CH_2 \; < \; \Phi-\dot{C}H(CH_3) \; < \; \Phi-\dot{C}(CH_3)_2$$

and one obtains increasing amounts of the corresponding alcohol (57).

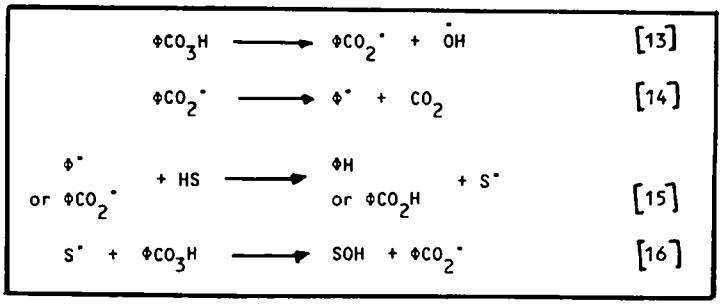
The 4-phenyl butyl radical 16 manifests, for another reason, an analogous behavior in this sense because its cyclization



16 17

generates the new cyclohexadienyl radical 17, which cannot react either with the peracid or with the solvent, and the transformation into acid according to scheme II becomes very largely preponderant. In corroboration of this feature, 4-phenyl-butyric peracid, a lower homologue, whose 3-phenyl propyl radical does not give rise to cyclization, is decarboxylated normally in 3-phenyl propanol (58).

Benzoic peracid is particularly interesting both for the reactivity of the radicals produced and for its use as a hydroxylation agent. The benzoylozy radical 14 has a slower decarboxylation rate than that of the $RCO_2^{\cdot}$ radicals envisaged previously and the two radicals $\Phi CO_2^{\cdot}$ and $\Phi^{\cdot}$ therefore occur simultaneously in the medium. Neither of these react with the O-O bond, but they do very easily withdraw a hydrogen from the cyclohexane used as solvent and give rise to the transfer reaction (scheme IV analogous to scheme III) :



scheme IV

Effectively one observes (table V and (53)) that 1 mole of cyclohexanol is formed per mole of decomposed peracid. This study has contributed two important conclusions :

- the decomposition of benzoic peracid in solution in a hydrocarbon leads quantitatively to the homolytic hydroxylation of the solvent. We shall see what use can be made of such a reaction.

- the intervention of a hydrogen donor solvent like cyclohexane assists the decomposition of the peracid (reactions [10] and [11]). If the solvent is not a hydrogen donor the decomposition rate drops markedly (by a factor of about 10) and the peracid is decomposed uniquely into acid through the reactions of scheme II.

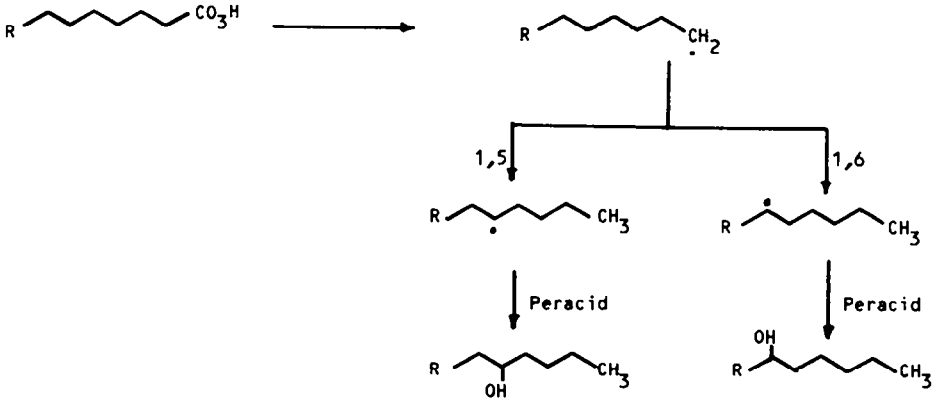
It is evident from the overall set of results that the solvent plays an important role in the mechanism of homolytic decomposition of peracids. The withdrawal of hydrogen from the solvent leading to a nucleophilic radical induces the decomposition of the peracid and accelerates its overall rate. If R· reacts neither with the O-O bond nor with the solvent then the two chain reactions I and II are slowed down and the peracid is transformed into acid through scheme II.

IV - SYNTHETIC APPLICATIONS

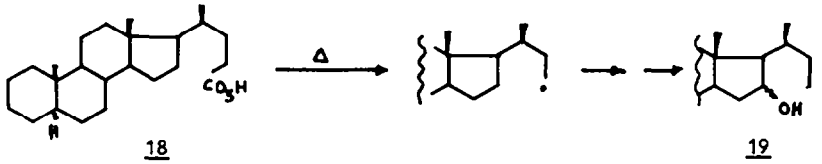
Hydroxylation of C-H bonds by homolytic reactions, whose principle we have just described, can occur by intra- or intermolecular processes.

a) Intramolecular hydroxylation

Extensive studies have been performed on intramolecular hydrogen transfer in those cases where the atom bearing the unpaired electron is nitrogen or oxygen. In contrast, the transfers of hydrogen from carbon to carbon, although demonstrated repeatedly, have been little studied. The study of the decomposition of long chain aliphatic peracids has allowed the characteristics of these intramolecular transfers to be specified (59) (60).



Measurement of the relative quantities of the secondary alcohols shows that transfer 1,5 is approximately 3 times greater than transfer 1,6, and that the other transfers are practically inexistent. This regioselectivity of the intramolecular transfers of hydrogen atoms is explained in entropic term and by the requirement for colinearity, in the transition state, of the radical center and the C-H bond. A theoretical study of this problem has been made (60). The presence of a phenyl substituent certainly diminishes the activation energy of the reaction of the withdrawal of a benzyl hydrogen, as compared with that of an aliphatic hydrogen, but is insufficient to render possible a transfer of hydrogen over a short distance (61). These fundamental studies have found their application in the regioselective hydroxylation of the D ring of steroids (62). Peroxycholanic acid 18 decomposed in solution in n-octane leads to the formation of hydroxy-16 norcholane 19, with a yield greater than 35 % and an α/β ratio of about 3.



18 19

b) Intermolecular hydroxylation

The hydroxylation of hydrocarbons such as methylcyclohexane, adamantane or the cis and trans decalins is effected with a regioselectivity of 70 to 80 % in favor of tertiary C-H bonds when using benzoic peracid and employing the reactions of scheme IV. This result is in accord with the characteristics of the two successive steps of the withdrawal of H [15] (tertiary H > secondary H) and the reaction of the radical with the peracid [16] (tert. > sec.). Moreover, the stereoselectivity of hydroxylation of the tertiary hydrogens is 97 % with trans-decalin in favor of trans 9-decalol and can reach the same percentage with cis-decalin in favor of the cis- 9-decalol but only at higher peracid concentration (63). This is in accord with the known behavior of decalyl-9 radicals and confirms our observation according to which a tertiary radical reacts rapidly with the O-O bond of a peracid. In more general terms, these results show that a radical reaction can be both regio- and stereoselective.

CONCLUSION

The present studies have shown that peracids give rise to radical reactions consequent upon the homolytic splitting of the O-O bond, as in the case of other peroxides.

Because of the fact that the peracid is both a source of radicals and the substrate, it constitutes an excellent model for studying the characteristics of S_H2 reactions at the peroxyacid group as a function of the structure of the radicals and the reaction conditions.

In the case of a nucleophilic radical, the S_H2 reaction occurs at the O-O bond and results in an alcohol [3] and a decarboxylation [2]. If the orbital containing the unpaired electron is not delocalized, the reactivity of the radical increases with its nucleophilicity, correlated with its ionization potential or more generally with the difference in energy levels between its SOMO orbital and the σ^*_{O-O} of the peracid. The consequences of this type of interaction are that a σ radical (sp^3 like the 1-bicyclo-[2.2.1]-heptyl 7 or cyclopropyl 14 radicals or sp^2 like the phenyl 15 radical) is very unreactive and gives little or no alcohol according to [3], whereas alkyl radicals of the π type lead to a quasi-quantitative decarboxylation into alcohol with a reactivity sequence tertiary 5 > secondary 3 > primary 1, without steric bulkiness playing a detectable role. This conclusion that reactivity varies with the nucleophilicity of the radical and not with its stability, contrary to the generally acknowledged axiom, has been observed in other cases in radical chemistry (64) (65). If the radical is delocalized, the orbital overlap integral between the radical and the substrate becomes an important reactivity factor and a radical seemingly more nucleophilic on the basis of the ionization potential proves to be less reactive than a non-delocalized primary radical ; this is the case for the benzyl radical 6.

If the radical is electrophilic, the reaction does not occur at the O-O bond and it is the H atom of the peroxyacid group which is removed, the decomposition into acid following a radical chain mechanism. This explains why there is no decarboxylation and formation of alcohol when the solution is not boiling, that is in the presence of O_2 which supplies the electrophilic RO° radicals.

In radical reactions the solvent intervenes most often by virtue of its H donor character, and very frequently one is confronted with a problem of competition between different processes. As the activation energies are generally low, very small differences between them can have important consequences for the path taken by the reaction process. The peracid playing the roles of the source of radicals and the substrate, it has been possible to determine with clarity, in function of the nature of the solvent (H donor or not), the influence of the structure of the radical on the relative importance of the three processes : radical attack at the O-O bond of the peracid, withdrawal of the H atom from the peracid or transfer reaction with the solvent.

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