Catalytic Effect of 4-Pyridone on the Free-Radical Oxidations of Secondary Alcohols with *t*-Butyl Peroxide[1]

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The rate of oxidation of secondary alcohols with *t*-butyl peroxide is enhanced by the presence of small amounts of 4-pyridone. The catalytic action of 4-pyridone arises from its ability to participate in the free-radical chain oxidation of the alcohol by the peroxide serving as a hydrogen atom carrier. Hydrogen atom transfer from an α-hydroxyalkyl radical to 4-pyridone yielding a 4-hydroxymonohydropyridyl radical apparently is a faster reaction than hydrogen atom transfer to the peroxide. The 4-hydroxymonohydropyridyl radical, however, reacts rapidly with the peroxide yielding *t*-butyl alcohol, a *t*-butoxy radical and 4-hydroxypyridine which on tautomerization regenerates the 4-pyridone. Reaction of the *t*-butoxy radical with the secondary alcohol yields the chain-carrying α-hydroxyalkyl radical. Similar catalytic action is not displayed by 2-pyridone or 3-hydroxypyridine.

The oxidation of primary and secondary alcohols to aldehydes and ketones, respectively, by *t*-butyl peroxide (I) occurs by a free-radical chain reaction as evidenced by induced decomposition of the peroxide resulting from a hydrogen atom transfer to the peroxide from an α-hydroxyalkyl radical derived from the alcohol.[2] The observations of hydrogen atom transfer from alcohol-derived radicals to ketones[3] and the facile hydrogen atom transfer reaction from certain monohydropyridyl radicals to *t*-butyl peroxide[4] suggested that 4-pyridone (II) might be a catalyst for the *t*-butyl peroxide oxidations of secondary alcohols.

The decomposition of I in inert solvents, that is, solvents that do not induce the decomposition of the peroxide, is a unimolecular reaction as shown in reaction 1. Recent work has shown that the unimolecular

$$\underset{\text{I}}{(CH_3)_3COOC(CH_3)_3} \xrightarrow{k_1} 2(CH_3)_3CO\cdot \qquad (1)$$

decomposition of I is influenced to some extent by the medium[5] but these solvents effects differ both in magnitude and kind from the induced decompositions observed in secondary alcohols. In the latter, the decomposition of I occurs by two modes—one being the unimolecular decomposition shown in reaction 1 and the other a reduction of the peroxide by the α-hydroxyalkyl radical (reaction 3), a radical resulting from interaction of the secondary alcohol with a *t*-butoxy radical (reaction 2). Reactions 2 and 3

$$(CH_3)_3CO\cdot + R_2CHOH \xrightarrow{k_2} (CH_3)_3COH + R_2\dot{C}OH \qquad (2)$$

$$R_2\dot{C}OH + (CH_3)_3COOC(CH_3)_3 \xrightarrow{k_3} R_2C{=}O + (CH_3)_3COH + (CH_3)_3CO\cdot \qquad (3)$$

comprise a free-radical chain sequence that accounts for the oxidation of the alcohol by the peroxide and the over-all rate of decomposition of the peroxide can be expressed by reaction 4. If the interactions of the

$$\frac{-d[Per]}{dt} = k_1[Per] + k_3[R_2\dot{C}OH][Per] \qquad (4)$$

alcohol-derived radicals with the peroxide account for an appreciable amount of the decomposition of the peroxide, the observed rate of reaction of the peroxide will be appreciably faster than that of the unimolecular reaction. The precise rate law for the decomposition of the peroxide depends on the termination step of the chain sequence. In the case of decomposition of *t*-butyl peroxide in acyclic secondary alcohols where the concentrations of the alcohol and peroxide are of the same order of magnitude, the cross-termination reaction 5 most likely occurs. The derived rate law for the decomposition of the peroxide based on a steady-state

$$(CH_3)_3CO\cdot + R_2\dot{C}OH \xrightarrow{k_5} (CH_3)_3COH + R_2C{=}O \qquad (5)$$

approximation of all radicals if termination by reaction 5 is operative is shown in equation 6. However, the reactions are not psuedo first order in peroxide when 4-pyridone is present, presumably because other termination processes occur. We have chosen, therefore, for comparison purposes, to report all rates in terms of the half-lives of the peroxide.

$$\text{rate} = \frac{-d[Per]}{dt} = \left[\frac{3}{4}k_1 \pm \frac{k}{2}\left(\frac{1}{4} + 2\frac{k_2k_3}{k_1k_5}[\text{alcohol}]\right)^{1/2}\right][Per] \qquad (6)$$

Table I shows the half-lives of *t*-butyl peroxide at 125° in several alcohols containing varying amounts of added reagents. The rate of decomposition of the peroxide is considerably faster in secondary alcohols from which an α-hydroxyalkyl radical can be formed than in *t*-butyl alcohol which, having no α hydrogens, cannot participate in the chain sequence 2 and 3. The presence of 4-pyridone in small amounts (1–10 mol % of the amount of *t*-butyl peroxide originally present) markedly enhances the rate of decomposition of the peroxide in all of the secondary alcohols but has no effect on the decomposition rate in *t*-butyl alcohol. An explanation for the rate enhancement is that the α-hydroxyalkyl radical transfers its hydrogen atom to 4-pyridone (reaction 7) yielding the 4-hydroxymonohydropyridyl radical (A·) which reduces the

$$R_2\dot{C}OH + \underset{\text{II}}{O{=}\langle\rangle NH} \longrightarrow R_2C{=}O + \underset{\text{A}\cdot}{HO{-}\langle\cdot\rangle NH} \qquad (7)$$

$$\text{A}\cdot + (CH_3)_3COOC(CH_3)_3 \xrightarrow{k_4} (CH_3)_3COH + (CH_3)_3CO\cdot + HO{-}\langle\rangle N \longrightarrow \text{II} \qquad (8)$$

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(3) J. N. Pitts, R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Rechtenwald, and R. B. Martin, *ibid.*, **81**, 1068 (1959); E. S. Huyser and D. C. Neckers, *ibid.*, **85**, 3641 (1963).

(4) E. S. Huyser, C. J. Bredeweg, and R. M. VanScoy, *ibid.*, **86**, 414 (1964).

(5) E. S. Huyser and R. M. VanScoy, *J. Org. Chem.*, **13**, 3524 (1968).

TABLE I

HALF-LIVES OF *t*-BUTYL PEROXIDE AT 125° IN SECONDARY ALCOHOLS

Alcohol[a]	Initial ratio of alcohol to peroxide	Added reagent (mole %)[b]	Half-life, min
t-Butyl alcohol	5.00	None	468
	4.94	4-Pyridone (9.86)	468
2-Butanol	4.92	None	266
	4.95	None	274
	4.68	4-Pyridone (0.93)	190
	5.21	4-Pyridone (5.27)	124
	4.95	4-Pyridone (9.88)	105
	5.02	2-Pyridone (5.14)	338
	4.69	2-Pyridone (9.66)	~375
	4.91	3-Hydroxypyridine (9.90)	275
	4.94	3-Hydroxypyridine (9.95)	268
2-Octanol	5.01	None	280
	4.90	4-Pyridone (1.19)	236
	6.89	4-Pyridone (5.44)	150
	4.85	4-Pyridone (9.79)	140
	4.95	2-Pyridone (9.99)	~350
Cyclopentanol	19.35	None	256
	5.01	None	248
	4.99	4-Pyridone (10.50)	160
Cyclohexanol	19.89	None	370
	4.90	None	425
	5.01	4-Pyridone (10.13)	240
Cycloheptanol	20.38	None	148
	5.11	None	150
	4.58	4-Pyridone (9.08)	59
Cyclooctanol	19.56	None	120
	5.00	None	120
	4.62	4-Pyridone (8.82)	44

[a] The respective registry numbers are 75-65-0, 78-92-2, 123-96-6, 96-41-3, 108-93-0, 502-41-0, and 696-71-9. [b] Based on amount of peroxide initially present.

peroxide by another hydrogen atom transfer reaction (reaction 8). In order for the 4-pyridone to exercise a positive catalytic effect, it is necessary that not only must reaction 7 compete favorably with reaction 3, but reaction 8, the hydrogen atom transfer from A· to the peroxide, must also be very rapid. The formation of 4-hydroxypyridine with its aromatic ring resulting from transfer of the nitrogen-bonded hydrogen of A· may well provide the driving force for this reaction. Tautomerization of 4-hydroxypyridine to 4-pyridone would regenerate the catalyst.

Table II shows that the rate enhancement by 4-pyridone is truly catalytic in that the reagent, present in 1 mol % relative to the peroxide, is not consumed

TABLE II

CONCENTRATION MEASUREMENTS OF 4-PYRIDONE IN THE REACTION OF *t*-BUTYL PEROXIDE AND 2-BUTANOL AT 125°

Time, min	% reaction of peroxide: Without catalyst[a]	With catalyst[b]	4-Pyridone remaining[c]
0	0	0	16.0
40	11	19	15.7
80	20	30	14.9
100	28	36	14.9
140		43	13.7
160	33	50	14.4
220	42		

[a] Initial molar ratio of alcohol/peroxide 4.92:1. [b] Initial molar ratio of alcohol/peroxide/4-pyridone 5:1:0.01. [c] Millimoles per liter.

although the rate of reaction of the peroxide is faster than that of a reaction without the catalyst.

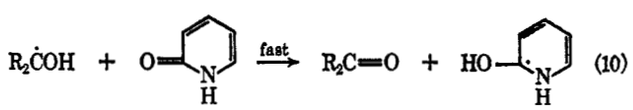
The observed rate of decomposition of the peroxide in the 4-pyridone catalyzed reactions would be given by eq 9. The effectiveness of the catalyst in enhancing

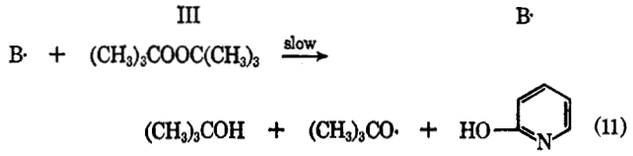
$$\frac{-d[Per]}{dt} =$$

$$k_1[Per] + k_3[R_2\dot{C}OH][Per] + k_4[R_2\dot{C}OH][4\text{-pyridone}] \quad (9)$$

the reaction rate would therefore depend on both the reactivity of 4-pyridone toward reaction with the alcohol radical and on the concentration of 4-pyridone in the reaction mixture. Our data show that the catalytic effect does vary amongst the secondary alcohols studied and that the catalytic effect is concentration dependent.

3-Hydroxypyridine, as would be expected on the basis of structural requirements, displays no significant catalytic effect on the reaction. 2-Pyridone (III) might, however, be expected to behave similarly to 4-pyridone. We found that 2-pyridone impedes the reaction rate rather than enhances it (see Table I). One explanation for this behavior may be that hydrogen atom transfer to the carbonyl function of 2-pyridone (reaction 10) is fast but the resulting 2-hydroxymonohydropyridyl radical (B·) reacts slowly with the peroxide (reaction 11) and thus acts as a retarder. It





is not immediately obvious why reaction 11 should be slow since the driving force responsible for the rapid transfer of a hydrogen atom from B· to the peroxide, namely, formation of the aromatic ring, should be operative in this reaction as well. The lack of reactivity of B· cannot be attributed solely to the steric interaction caused by the 2-hydroxy group, a steric effect not present in the case of the 4-hydroxymonohydropyridyl radical A·. The 2,6-dimethyl-3,5-dicarboethoxymonohydropyridyl radical, which would be expected to experience even more steric hindrance than B· in reactions with *t*-butyl peroxide, transfers its hydrogen atom readily to the peroxide.[4] One plausible explanation is that the 2-hydroxymonohydropyridyl radical B· is more effectively solvated by the hydroxylic alcohol because of its greater polarity than is the 4-hydroxymonohydropyridyl radical A·. The energy of desolvation of the tightly solvated radical would then have to become part of the activation energy requirement for the hydrogen atom transfer to the peroxide.

Examination of the data in Table I shows that the half-lives of the peroxide in these secondary alcohols vary to a significant extent even in the absence of 4-pyridone. If it is assumed that the rate of the unimolecular decomposition is approximately the same for each alcohol, namely, about that of *t*-butyl alcohol, the differences in the rate serve as a measure of the ability of the alcohol to participate in the chain sequence 2 and 3. The half-lives of the peroxide in the acyclic

alcohols are almost identical. The varying extent of induced decomposition of the peroxide in the cycloalkanols, however, indicates that conformational aspects of the alcohol possibly play a significant role in these reactions. The apparent order of reactivity of the cycloalkanols toward participation in the chain sequence 2 and 3, namely, $C_6 < C_5 < C_7 < C_8$, parallels the reactivity of cyclic compounds in reactions that convert a carbon from the tetrahedral sp^3 configuration to the planar sp^2 configuration.[6] The hydrogen atom abstraction reaction 2, therefore, appears to play a significant role in these reactions. Conformation strain is introduced into the cyclohexane ring in this reaction and the ability of cyclohexanol to participate in the chain sequence 2 and 3 is significantly less than that of the acyclic alcohols. On the other hand, relief of conformation strain is experienced in hydrogen abstractions from cycloheptane and cyclooctane ring systems and the extent of induced decomposition of the peroxide is greater than in the open chain alcohols. Although some relief of conformational strain would be expected in the hydrogen abstraction from cyclopentanol, its ability to participate in the chain reaction, although greater than that of cyclohexanol, is about the same as 2-butanol and 2-octanol.

It should not be inferred, however, that the hydrogen atom abstraction reaction is the limiting factor in the oxidation of secondary alcohols by the chain sequence 2 and 3. The observation that 4-pyridone has a catalytic effect in each alcohol is significant since the interaction of 4-pyridone in the chain sequence does not involve any change in the configuration of the α carbon of the alcohol and hence should not have any effect on the conformational aspects of the reaction. If the limiting reaction of the chain sequence were the hydrogen abstraction, a process that does not involve 4-pyridone, no catalytic effect would be observed. The best explanation for the observation that both the conformational aspects and the catalysis are observed in these reactions is that the chain prograting reactions 2 and 3 proceed at about comparable rates. Any factor that would increase or decrease the rate of either reaction would effect the over-all rate of the induced decomposition of the peroxide since the rate of each reaction in the chain sequence would be increased or decreased in order to maintain steady-state concentrations (or nearly so depending on the kinetic chain length) of the chain-carrying radicals. That cross-termination (reaction 5) occurs in the reactions of many secondary alcohols as evidenced by the observation that the reactions are psuedo first order in peroxide supports the suggestion that neither reaction 2 nor 3 is rate limiting and the chain-carrying radicals have comparable concentrations. The deviation from the psuedo-first-order reactions in the presence of 4-pyridone may be caused by an imbalance in the steady-state concentrations of the chain-carrying radicals causing termination to occur, in part, by coupling of *t*-butoxy radicals. The steady-state concentration of the α-hydroxyalkyl radicals is likely decreased relative to the *t*-butoxy radicals because of the rapid reaction of the former with 4-pyridone.

Experimental Section[7]

Materials.—The following alcohols were obtained from the indicated commercial sources and redistilled before using: 2-Octanol (Eastman Organic), 2-butanol (J. T. Baker), *t*-butyl alcohol (Fisher), cyclopentanol (Matheson Coleman and Bell) and cyclohexanol (Fisher). Cycloheptanol [bp 54.5–55° (1.5 mm)] and cyclooctanol [bp 66° (1.5 mm)] were prepared by $NaBH_4$ reduction of cycloheptanone (Aldrich) and cyclooctanone (Aldrich), respectively. 4-Pyridone (Aldrich) was purified by the method described previously which consisted of recrystallizing it from chloroform as the dihydrate. The dihydrate is then dehydrated by heating under vacuum at 90°, mp 147–148° (lit.[8] mp 147.5–150°). 3-Pyridone (Aldrich) was recrystallized from benzene and melted at 125–127° (lit.[9] mp 126°). 2-Pyridone (Aldrich) was recrystallized from benzene and melted at 105–107° (lit.[10] mp 106–107°). Commercial *t*-butyl peroxide (Wallace and Tierman, Inc.) gave a single peak on gas chromatographic analysis and was used without further purification. Gas chromatographic analyses were performed on an F & M Model 5750 gas chromatograph using an 8 ft × 1/8 in. column packed with 2% diethylene glycol succinate and 8% SF-96 on Chromosorb W. The chromatograms were traced on a Mosely recorder equipped with a Disc integrator. Spectrophotometric analysis were made on a Beckman DU-2 spectrometer.

Determination of Decomposition Rate of *t*-Butyl Peroxide.—Solutions consisting of the reagents in the amounts shown in Table I were in each case divided into eitht Pyrex tubes, sealed and placed in a constant-temperature bath set at 125°. Tubes were removed at various time intervals and immediately cooled to 0°. A portion of the contents of each tube was accurately weighed out along with a known amount of an internal standard for chromatographic analysis. Benzene was used as the internal standard for the higher boiling alcohols and chlorobenzene for the lower boiling alcohols. The peak areas of the peroxide and the internal standard were used to determine the amount of peroxide remaining in the sample.

Determination of Catalyst Consumption.—In a reaction of 2-butanol with approximately 1 mol % 4-pyridone relative to *t*-butyl peroxide, the amounts of both peroxide and 4-pyridone in each sample were determined. The peroxide was determined by the method described above. The 4-pyridone was determined spectrophotometrically making use of its absorption maximum at 257 mμ (ϵ 1.48 × 10^4). The data found are given in Table II.

Registry No.—I, 110-05-4; II, 108-96-3.

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(7) All melting points are uncorrected.

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