THE JOURNAL OF Organic Chemistry®

VOLUME 41, NUMBER 1
JANUARY 9, 1976

Autoxidations of Cyclohexane and Its Autoxidation Products

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Received June 3, 1975

The rates, products, and mechanisms of t-Bu_2O_2-initiated oxidations of cyclohexane at 100° and N,N'-azobis(1-cyanocyclohexane)-initiated oxidations of cyclohexanone at 80° are described. The initial oxidation of cyclohexane gives mostly cyclohexyl hydroperoxide and gives cyclohexanol and cyclohexanone as chain termination products. On further reaction, much of the hydroperoxide is converted directly to ketone. Both cyclohexanol and cyclohexanone catalyze the decomposition of hydroperoxide into radicals, which increase the rate of oxidation. The further oxidation of cyclohexanone is complex, even at 80°. The major primary product is 2-hydroperoxycyclohexanone whose decomposition, also catalyzed by cyclohexanone, leads to other hydroperoxides, ϵ-caprolactone, adipic and glutaric acids, adipaldehyde acid, cyclohexane-1,2-dione, and δ-valerolactone. The oxidation of cyclohexanone is catalyzed by both cobalt and manganese, the latter giving high yields of adipic acid. Relative reactivities toward *tert*-butylperoxy radicals follow: cyclohexane, 1.0; cyclohexyl hydroperoxide, 56; cyclohexanol, 55; cyclohexanone, 13; and cyclohexyl acetate, 0.5. Rates of oxidation of pure compounds at the same rate of initiation at 100° follow: cyclohexane, 1.0; cyclohexanol, 40; and cyclohexanone, 27.

This paper describes some studies of high conversion oxidations of cyclohexane, in Pyrex glass, with special attention to (1) the relative reactivities of the compounds involved toward a common peroxy radical, (2) the role of thermal decomposition of the hydroperoxide, (3) the intermediates that lead to carbon–carbon cleavage, and (4) effects of cobalt and manganese salts. Cyclohexane was selected for study because of its symmetry, which leads to simpler products and makes it a useful model for oxidation of alkanes, and because its oxidation is industrially important. Our conclusions are summarized in the last section.

In low conversion experiments, cyclohexyl hydroperoxide is formed from air oxidation of cyclohexane in a sufficient yield for synthetic preparation of the hydroperoxide.[1] Cyclohexanol[2] oxidizes cleanly to an equilibrium mixture of cyclohexanone, hydrogen peroxide, and 1-hydroxycyclohexyl hydroperoxide. The oxidation of cyclohexanone[3] to adipic acid goes through 2-hydroperoxycyclohexanone and adipaldehyde acid with ϵ-caprolactone, valeric acid, and glutaric acid as by-products.

Most of the published work on oxidations of cyclohexane is in the Russian literature.[4] This work has usually been carried out without added initiator, and with markedly different results in glass and steel vessels. In glass, the rate is slightly slower than in steel, with an obvious induction period, and the maximum concentration of hydroperoxide attained is about three times that in steel.[5] In glass, addition of ^{14}C-labeled cyclohexanol to oxidizing cyclohexane at 155° showed that the alcohol is quantitatively converted to cyclohexanone (without cleavage) and that labeled adipic acid and some labeled CO_2 are eventually formed.[4,5] Whereas hydroperoxide is clearly the major primary product in glass, cyclohexanone is the major primary product in steel where the peroxide is apparently decomposed on the walls. Adding cyclohexyl hydroperoxide initially to a cyclohexane oxidation at 145° in steel had no significant effect on the reaction; however, if cyclohexanone is added in amounts found normally after about 10 hr of reaction, the reaction begins at the maximum rate that normally would be delayed for several hours.[4,6] Thus, in steel cyclohexanone appears to be more important in the initiation step than is the hydroperoxide.

Tanaka[7] recently described a cobalt-catalyzed oxidation of cyclohexane in acetic acid solution at 80–100°, with higher rates of reaction and higher yields of adipic acid at high conversions than have been reported previously, but the mechanism is obscure. A comparison with our own results shows that the rate of reaction in cyclohexane is markedly increased by cobalt, but the improvement in selectivity must arise from the effect of cobalt on the subsequent oxidation of oxygen-containing products.

In view of the Russian results, we have confined our own studies to glass vessels. After some preliminary investigations at 60–130°, 100° was chosen for most of our oxidations of cyclohexane.

Experimental Section

Chemicals. Cyclohexane and cyclohexanone from Matheson Coleman and Bell (Chromatoquality) and cyclohexanol from Eastman Chemical Co. (White Label) were distilled before use. Cyclohexyl hydroperoxide was made according to the procedure of Walling and Buckler.[8] Initiators were obtained through normal chemical suppliers and either distilled or recrystallized before use.

Reaction Procedures. Runs were made in a 100-ml Pyrex flask fitted with a glass break-seal. Reactants were introduced through a side arm and then degassed. The initiators N,N'-azobis(2-methylpropionitrile) (ABN) and N,N'-azobis(1-cyanocyclohexane) (ABC) were added in solvents that were then removed under vacuum. When di-*tert*-butyl peroxide was used, it was added through a septum from a tared syringe after the vessel had been degassed. The

Table I
Oxidations of Cyclohexane (RH), Cyclohexanol (ROH), and Cyclohexanone (R=O)

			Reaction				Products, M			
Charge	Concn, M	Initiator,[a] M	Temp, °C	Time, hr	$-\Delta\dot{O}_2$	Chain length[b]	RO_2H	Net ROH	R=O	Acid, as dibasic
RH	8.79	0.0105 (ABN)	60	17.1	0.016	2.8	0.0086	0.004	0.0017	0
RH	8.79	0.0312 (ABN)	60	20.0	0.056	3.0	0.0078	0.0088	0.0069	0
RH	8.67	0.0095 (ABN)	70	5.0	0.015	2.5	0.0069	0.0010	0.0016	0
RH	8.46	0.0109 (ABC)	91	14.3	0.046	2.4	0.0362	0.0053	0.0064	0
RH	8.33	0.0112	100	24.9	0.025	18	0.0163	0.0016	0.0005	0
RH	8.15	0.0108	130	15.0	0.042	28.4	0.0058	0.1487	0.110	0.0876
ROH	8.81	0.0151	100	2.0	0.089	596	0.0696		0.0616	0
ROH	8.81	0.010	100	4.0	0.152	720	0.127		0.200	0.0036
ROH	8.81	0.0154	100	220	0.355	220	0.0005		0.503	0.0085
ROH RH	4.38 4.18	0.0094	100	24.0	0.087	66	0.0011		0.0080	0.0016
ROH DCB[c]	3.58 3.53	0.0108	100	25.3	0.344	285	0.0430		0.332	0.0311
ROH RH	0.19 8.15	0.010	100	24.0	0.012	10	0.0104	0.1639	0.0013	trace
R=O	9.04	0.010	100	2.0	0.045	440	0.0147			0.0151
R=O	9.04	0.0098	100	2.5	0.180	1520	0.0382	0		0.1085
R=O	9.04	0.519	100	15.0	0.388	99	0	0		0.356
R=O	9.04	0.098	100	24.0	1.893	150	0.0118			0.645
R=O RH	0.17 8.17	0.010	100	38.0	0.065	57	0.0330	0.0260[d]	0.1541	0.0013

[a] Initiator is $t\text{-}Bu_2O_2$ except where indicated otherwise; at 100° $k_d = 6.0 \times 10^{-3}\ hr^{-1}$. For ABN, $k_d = 0.035\ hr^{-1}$ at 60°, $0.14\ hr^{-1}$ at 70°. For ABC, $k_d = 0.13\ hr^{-1}$ at 91°. [b] Moles oxygen per mole radical formed from initiator. [c] *o*-Dichlorobenzene. [d] Total ROH before correction for ROOH.

arm having the septum was sealed off; the oxygen was added through the other arm, which was connected to the vacuum line, and that arm was sealed off. The untransferred portion of the oxygen was measured using the same gas buret–Toepler pump that was used to measure the initial oxygen.

The runs were terminated by quickly cooling the flasks to 25°. After sealing the vessels on the vacuum line, flask contents were frozen at −195°; the seal was broken, and the noncondensable gases were measured using the gas buret–Toepler pump. The gas sample was then allowed to react in a Cu–CuO furnace at about 300° to convert oxygen to CuO and CO to CO_2. With the furnace trap at −195°, only N_2 and Ar are volatile and may be measured. CO is estimated as CO_2 by warming the furnace trap to −80° and measuring in the buret. Oxygen was estimated by difference of total noncondensables and CO_2. The reaction vessel was then warmed to −80° to release the CO_2, which was then measured.

Instead of vessels with glass break-seals, we also used vessels with a glass stem that is fitted with Swageloc fitting (Zytel ferrules) to a bellows-type stainless-steel valve (Whitey Research Tool Co.). This arrangement not only reduces the time required to prepare and analyze samples but also eliminates the possible hazard of sealing vessels containing oxygen and hydrocarbon mixtures.

Analyses. Hydroperoxide was then determined by refluxing a weighed sample (~1 ml) with 1 g of KI in 20 ml of 2-propanol (10% acetic acid) for 5–10 min, and then titrating with 0.02 *N* $Na_2S_2O_3$.

Acid was determined by dissolving the weighed sample in neutralized 95% EtOH and titrating with 0.05 *N* NaOH to a phenolphthalein end point.

Cyclohexanol and cyclohexanone were determined by first reducing the reaction mixture with a 100% excess of triphenylphosphine,[9] the amount being determined from hydroperoxide titration. Determinations were made on a chromatograph having a flame-ionization detector (Hewlett-Packard) and 10 ft of 0.125 in. column packed with 5% Carbowax 20M on Chromosorb G. *p*-Xylene was used as an internal standard. The "net ROH" is the difference between the total ROH found after reduction and the RO_2H found before reduction.

Oxidation products of cyclohexanone were determined first by direct GC analysis for ε-caprolactone and cyclohexane-1,2-dione. Then a second sample was reduced with triphenylphosphine, and after the volatile materials were removed, the residue was treated with methanol (1 ml) and boron trifluoride (several drops) to esterify the acids. The esters were then determined by GC.

In a third sample, after reduction with triphenylphosphine, the cyclohexanon-2-ol was esterified with acetic anhydride and pyridine catalyst at 80° for 3 hr and the ester was determined by GC.

Preparation of Cyclohexyl *tert*-Butyl Peroxide (CBP). CBP was prepared in a pressure bomb by decomposing 0.03 mol of *tert*-butylperoxy isopropyl carbonate (Pittsburgh Plate Glass Co., Chemical Division) at 115° for 16 hr in the presence of 0.02 mol of *tert*-butyl hydroperoxide and 200 ml of cyclohexane solvent. After most of the excess cyclohexane was removed by distillation at atmospheric pressure, the residue was fractionated at 20 Torr pressure on a spinning-band column to give 0.0058 mol (29%) of the desired product. The purity of the peroxide was easily determined by GC with 0.125-in. columns packed with 2% or 30% Carbowax 20M on Chromosorb P at 80°120°. The thermal decomposition of the peroxide was followed by the same method.

Results

Preliminary Oxidations. To determine the best conditions for studying the oxidation of cyclohexane, several exploratory runs were made between 60 and 130°. *N,N′*-Azobis(isobutyronitrile) (ABN) was used for the free-radical initiator at 60–70°, *N,N′*-azobis(1-cyanocyclohexane) (ABC) at 91°, and di-*tert*-butyl peroxide at 100 and 130°. Data are summarized in Table I. Below 100° kinetic chains are too short to study the chain oxidation of cyclohexane. Cyclohexanol and cyclohexanone were oxidized at 100° using di-*tert*-butyl peroxide. Cyclohexanol oxidizes 40 times as fast as cyclohexane under the same conditions; cyclohexanone is 27 times as fast. To determine how cyclohexanol and cyclohexanone affect the oxidation of cyclohexane, mixtures have been oxidized at 100° also. Cyclohexanol (2%) reduces the rate of oxidation of cyclohexane by ½; a similar amount of cyclohexanone accelerates the rate by a factor of 3.

Oxidation Products of Cyclohexane at 100°. Neat cyclohexane has been oxidized at 100° using 0.01 *M* di-*tert*-butyl peroxide as an initiator. Oxygen consumption was measured, hydroperoxide and acid were determined by titration, and cyclohexanol and cyclohexanone were determined by GC analysis after the hydroperoxide was reduced

Table II
Oxidations of Neat Cyclohexane (8.33 *M*) at 100°, 0.01 *M* t-Bu_2O_2 Initiator

		Products, *M*						Oxygen balance, %
Time, hr	$-\Delta O_2$, *M*	RO_2H	Total ROH	Net ROH	R=O	Acid	CO_2	
48A[a]	0.0428	0.0375	0.0388	0.0013	0.0020	0	0	94
72A	0.0690	0.0576	0.0666	0.0090	0.0072	0	0	100
96A	0.107	0.0822	0.101	0.0189	0.0158	0.001	0	103
144A	0.207	0.0876	0.137	0.0498	0.0638	0.006	0.001	93
169A	0.352	0.103	0.174	0.0708	0.0904	0.009	0.004	73[b]
192A	0.526	0.107	0.327	0.220	0.1844	0.006	0.009	108
48B[a]	0.0327	0.0238	0.0246	0.0007				79
72B	0.0610	0.0477	0.0540	0.0063	0.0016			87
96B	0.0956	0.0729	0.0834	0.0105	0.0037			87
144B	0.159	0.0967	0.156	0.0589	0.0409			117
192B[b]	0.276	0.105	0.205	0.100	0.0516			95[b]
216B	0.441	0.113	0.249	0.136	0.0392	0.0402		108
24	0.0200	0.0134	0.0136	0.0002				68
48.8	0.0350	0.0298	0.0302	0.0004				86
96	0.0667	0.0521	0.0552	0.0031	0.0190			109
96	0.0853	0.0590	0.0647	0.0051	0.0136	Trace		88
144	0.176	0.0621	0.0756	0.0135	0.0568	0.0100	0.0023	87
144	0.334	0.0867	0.144	0.0572	0.0776	0.0259	0.0085	77
192	0.414	0.0892	0.169	0.0796	0.105	0.0438	0.0138	86
192	0.360	0.130	0.184	0.0546	0.0844	0.0320	0.0193	95

[a] In the two six-part runs (labeled by A or B after time) with repeated additions of oxygen, product concentrations are cumulative. Reaction vessel was treated with EDTA solution before reaction. [b] After about 150 hr, a small heavy layer separates, probably mostly adipic acid and water. Since only the top layer was analyzed in the 169-hr A point and 192-hr B point, oxygen balances are low for these points.

with triphenylphosphine. Results are summarized in Table II. Initial experiments were carried out using all-glass vessels for each run; however, later experiments were run in a vessel with a valve that permitted several analyses during one reaction. Each time that the reaction was stopped and analyzed, it could be recharged with oxygen for oxidation. This technique eliminated some of the irregularities in conversion-time plots based on several experiments. In an attempt to improve reproducibility further, reaction vessels were washed with EDTA solutions to remove trace metal ions. Figure 1 shows oxygen consumed and products found vs. time for the oxidation of cyclohexane using data from the first series in Table II.

Oxidations of Cyclohexane. The products of oxidation of cyclohexanone are surprisingly complex. Careful GC analyses of the reaction mixtures after reduction of hydroperoxides with triphenylphosphine revealed δ-valerolactone, ϵ-caprolactone, cyclohexane-1,2-dione, and 2-cyclohexylidenecyclohexanone. Treating the reduced reaction mixture with acetic anhydride allowed determination of 2-hydroxycyclohexanone and 1-cyano-1-hydroxycyclohexane as their acetates. Treating the reduced reaction mixture with either diazomethane or methanol and $BF_3 \cdot OEt_2$ permitted determination of the acids: succinic, glutaric, adipic, and adipaldehyde. Because of complications, no attempt was made to detect the presence of monofunctional acids such as caproic or valeric acids. In all cases, identification was based on comparison of GC retention times with those of authentic samples and checked by NMR, ir, or mass spectroscopy of material isolated by GC.

Table III and Figure 2 summarize the oxidation of cyclohexanone at 80°. To determine the dependence of rate on initiator, ABC concentrations were varied from 0.01 to 0.10 *M*. Acetic acid (2 *M*), 0.01 *M* trifluoroacetic acid, or 0.1 *M* pyridine has little effect on rate or products in the ABC-initiated reactions. Oxidations in the presence of cobaltous or manganous acetates, in the presence of about 2 *M* acetic acid, are significantly faster than oxidations with 2 *M* acetic acid initiated with ABC.

The product analyses account for 76–82% of the oxygen consumed in ABC-initiated reactions, 86–102% in the Mn-catalyzed reactions. In the Co-catalyzed experiment, 91% of the oxygen was accounted for.

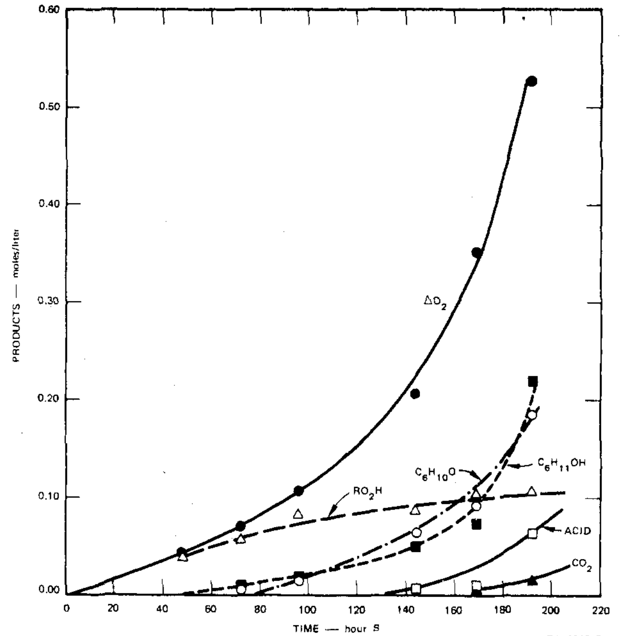


Figure 1. Oxidation of cyclohexane at 100°C in presence of 0.01 *M* t-Bu_2O_2 (A points in Table II).

Relative Reactivities toward *tert*-Butylperoxy Radicals. Cyclohexane, cyclohexyl hydroperoxide, cyclohexanol, cyclohexanone, cyclohexyl acetate, and tricyclohexyl borate were oxidized in the presence of 0.5 *M* *tert*-butyl hydroperoxide, with the results shown in Table IV. In each such oxidation the peroxy radicals corresponding to the substrate are rapidly converted by hydrogen transfer to *tert*-butylperoxy radicals that are responsible for both attack on substrate (k_p) and termination (k_t). Since the termination constant is known, the value for attack on substrate by *tert*-butylperoxy may be determined.[10] The expression for the rate of oxygen absorption (R_O) is

$$R_O = k_p[RH](R_i/2k_t)^{1/2} - R_i(1 - 2a)/2a \qquad (1)$$

Table III
Oxidation of Cyclohexanone (8.97 M) at 80°

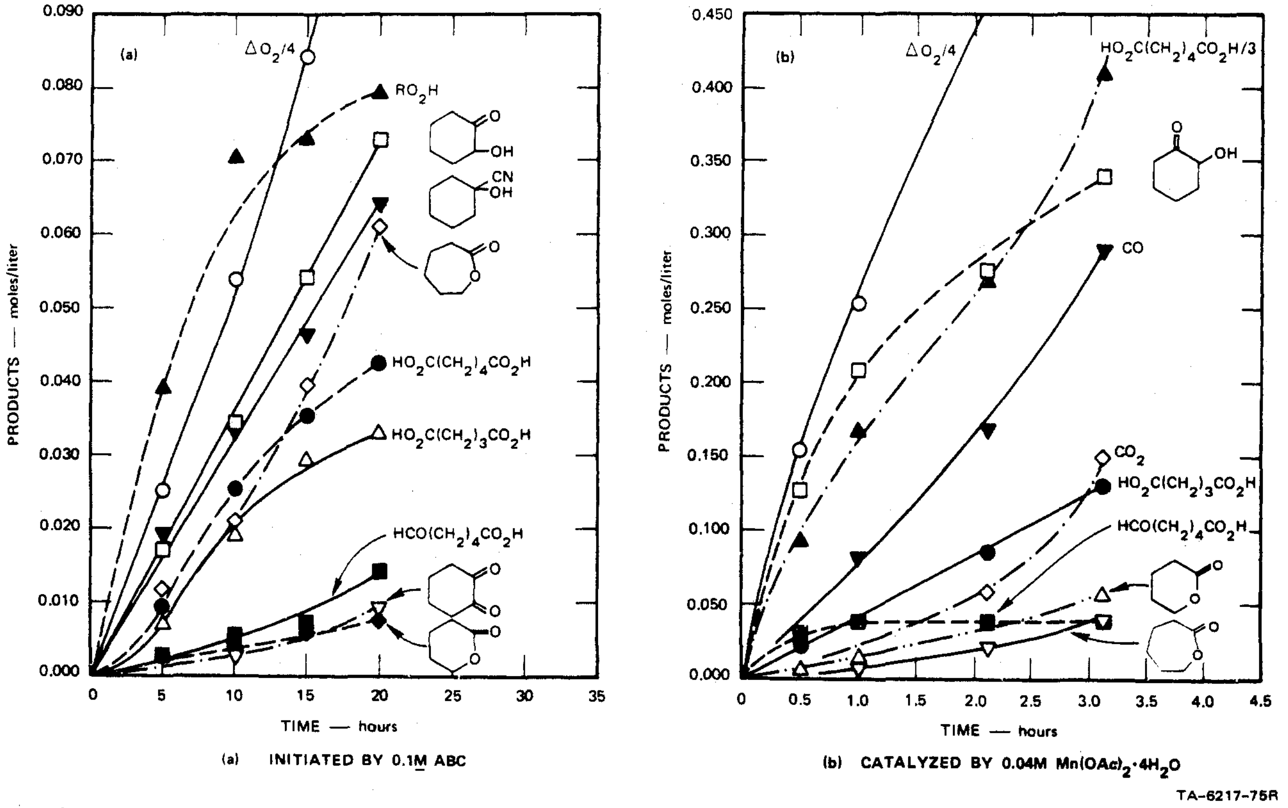
			Products, mM										
ABC, M	Time, hr	R_O, mM/hr	$-\Delta O_2$	RO_2H[a]	Acid, as dibasic	Dimethyl glutarate	Dimethyl adipate	Methyl adipaldehyde ester	2-Acetoxycyclohexanone	1-Acetoxy-1-cyanocyclohexane	Cyclohexane-1,2-dione	δ-Valerolactone	ε-Caprolactone
0.010	2.73	6.08	16.6	8.0	7.9				5.9				
0.010	8.98	6.48	58.3	21.9	28.9								
0.050	1.67	6.72	11.2	22.8	11.7								
0.10	1.67	2.20	36.7	16.1	15.0	1.7	2.5 (5.0)[b]	2.5	7.8				
0.10	5.0	20.6	103	38.8	22.6	6.9	9.4 (9.5)[b]	2.8	17.2	34.2	2.3	2.4	11.8
0.10	10.0	21.7	217	70.6	51.0	20.7	25.6 (38.1)[b]	5.3	34.2	34.2	2.8	3.6	19.0
0.10	15.0	22.5	337	73.1	93.5	29.4	35.3 (49.7)[b]	7.2	54.1	46.3	6.4	6.2	39.5
0.10	20.0	22.2	445	79.4	135	32.7	42.4 (54.4)[b]	14.2	73.0	64.5	8.3	7.6	61.3
0.10[c]	1.67	20.6	34.4	12.1	9.9	1.1	4.0	2.3	10.6				
0.10[d]	2.52	24.4	61.5	20	15		7.5		17.2				
0.10[e]	3.20	25.8	82.5	22	36		10.6		12.3				
Co[f]	0.53	488	259 ± 27	1.5	263	14.1 (14.4)[b]	84.5 (86.5)[b]	8.3 (8.3)[a]					
Mn[g]	0.35	1080	380	5.9	294	22.2	161				80.5		
Mn[h]	0.5	1240	621			21.8 (12.6)[i]	283 (292)[i]	29.2	129		13.1	7.3	4.4
Mn[h]	1.0	1020	1020			42 (est)	472	39.3	210		35.6	13.1	6.8
Mn[h]	2.1	903	1900			80.6 (108)[i]	811 (782)[i]	38.1 (46.7)	276		43.4	36.0	20.5
Mn[h]	3.1	1020	3150			131 (158)[i]	1230 (1225)[i]	39.1 (47.3)	341		62.2	54.5	43.3

[a] By titration; reduced compound appears as corresponding alcohol. [b] After esterification, sample transesterified with methanol–sodium methoxide; increase in ester value indicates presence of complex adipate. [c] 7.75 M cyclohexanone, remainder of reaction mixture is acetic acid. [d] 8.96 M cyclohexanone, 0.01 M trifluoroacetic acid. [e] 8.77 M cyclohexanone, 0.10 M pyridine. [f] 0.0057 M $Co(OAc)_2$, 8.00 M cyclohexanone, balance acetic acid. [g] 0.0037 M $Mn(OAc)_2 \cdot 4H_2O$, 7.99 M cyclohexanone, balance acetic acid. [h] 0.0043 M $Mn(OAc)_2 \cdot 4H_2O$, 7.8 M cyclohexanone, balance acetic acid. [i] Esterification by methanol and $BF_3 \cdot OEt_2$ rather than diazomethane.

Table IV
Oxidations of Cyclohexane and Derivatives at 80° with 0.1 *M* ABC and 0.5 *M* *tert*-Butyl Hydroperoxide in *tert*-Butylbenzene

Substrate	Concn, *M*	Initial $R_O \times 10^2$, *M*/hr	$k_p/(2k_t)^{1/2}$, $(M\ \text{hr})^{-1/2}$		k_p, $(M\ \text{sec})^{-1\,a}$	Relative reactivity per C_6 group
None		−0.74				
C_6H_{12}	1.50	0.30	0.11	0.10^b	0.175	1.0
C_6H_{12}	2.06	0.45	0.09			
C_6H_{12}	2.51	0.77	0.10			
C_6H_{12}	3.68	0.96	0.075			
$C_6H_{11}OH$	0.0099	−0.40	5.6	5.6^b	9.7	55
$C_6H_{11}OH$	0.048	0.27	3.4			
$C_6H_{11}OH$	0.26	0.61	0.84			
$C_6H_{11}OH$	1.00	1.83	0.41			
$C_6H_{11}O_2H$	0.0098	0.25^c	5.6^d		9.8	56
$C_6H_{10}O$	0.098	−0.49	0.42	$\sim 1.3^{b,e}$	2.26	13
$C_6H_{10}O$	0.206	−0.45	0.23			
$C_6H_{10}O$	0.308	−0.31	0.23			
$C_6H_{11}OAc$	2.01	−0.03	0.058	0.047^b	0.082	0.5
$C_6H_{11}OAc$	3.98	0.35	0.044			
$C_6H_{11}OAc$	5.92	0.69	0.039			
$(C_6H_{11}O)_3B$	0.99	0.73	0.081^f		0.14	0.8

[a] Calculated from $k_p/(2k_t)^{1/2}$ using $k_t = 5.6 \times 10^3\ M^{-1}\ \text{sec}^{-1}$ and $R_i = 3.75 \times 10^{-3}$ *M*/hr for 0.1 *M* ABC. [b] Preferred value based on plot of data. [c] Rate of formation of cyclohexanone. [d] Corrected for contribution of reaction 7 (see text). [e] Corrected for cyclohexanone as hydroperoxide adduct as determined by ir (see text). [f] Per C_6H_{11} group.



(a) INITIATED BY 0.1M ABC

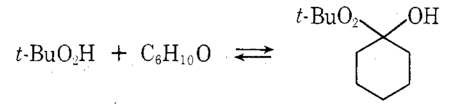
(b) CATALYZED BY 0.04M Mn(OAc)$_2$·4H$_2$O

Figure 2. Oxidations of cyclohexanone at 80°C.

where R_i is the rate of initiation and *a* is the efficiency of termination in interactions of two *tert*-butylperoxy radicals. The negative term in eq 1 allows for evolution of oxygen and is evaluated from the decomposition of hydroperoxide in the absence of oxidizable substrate. The other term corresponds to oxygen consumed by chain propagation with substrate. There can be a net evolution of oxygen in the absence of sufficient substrate.

Although eq 1 predicts that values of $k_p/(2k_t)^{1/2}$ should remain constant as [RH] is increased, the data for cyclohexanol and cyclohexanone clearly show significant decreases. In the case of cyclohexanol, we attribute this decrease to incomplete reaction of hydroperoxy radicals with *tert*-butyl hydroperoxide and their participation in propagation and termination. Since the cross termination reaction between $t\text{-BuO}_2\cdot$ and $HO_2\cdot$ has a rate constant about 10^5 times that for 2 $t\text{-BuO}_2\cdot$,[11] relatively little $HO_2\cdot$ can have a large effect on the rate. The amount of $HO_2\cdot$ and its contribution to termination is expected to decrease as the concentration of cyclohexanol is decreased. Hence, the relative reactivity has been estimated from data at the lowest concentrations of cyclohexanol.

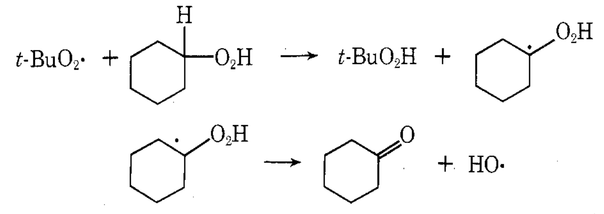
When hydroperoxide is added to cyclohexanone, and ir absorption of the carbonyl group decreases, indicating the



(2)

equilibrium in eq 2. The relative reactivities in Table IV were determined using the carbonyl absorption as a measure of free cyclohexanone.

Obtaining relative reactivity data for the oxidation of cyclohexyl hydroperoxide in the presence of *tert*-butyl hydroperoxide is more complicated, since reaction of this substrate does not result in oxygen consumption. Instead, α-attack of the hydroperoxide yields ketone by the reactions



(3)

(4)

Hence, if only *tert*-butylperoxy radicals participate in propagation and termination, the rate of formation of cyclohexanone measures the reactivity of cyclohexyl hydroperoxide in reaction 3.

$$d[C_6H_{10}O]/dt = k_p[C_6H_{11}O_2H](R_i/2k_t)^{1/2} \qquad (5)$$

However, the cyclohexyl hydroperoxide which is present inevitably reacts with the propagating peroxy radicals,

$$t\text{-BuO}_2\cdot + c\text{-C}_6H_{11}O_2H \rightleftarrows t\text{-BuO}_2H + c\text{-C}_6H_{11}O_2\cdot \qquad (6)$$

so that some cross-termination occurs:

$$t\text{-BuO}_2\cdot + c\text{-C}_6H_{11}O_2\cdot \rightarrow t\text{-BuOH} + c\text{-C}_6H_{10}O + O_2 \qquad (7)$$

Since the latter reaction is 10^2–10^3 times as fast as termination by 2-t-BuO$_2$·,[12] a small amount of c-$C_6H_{11}O_2$· can have a large effect on the rate of oxidation. If reaction 7 is unimportant, then added cyclohexyl hydroperoxide should have no effect on R_O in eq 1, since reactions 3 and 4 do not consume oxygen. However, if added hydroperoxide reduces R_O, the contribution of reaction 7 is equivalent to a corresponding reduction in rate of initiation. It was found necessary to work at concentrations of 2.0 *M* *tert*-butyl hydroperoxide and 0.01 *M* cyclohexyl hydroperoxide where the latter hydroperoxide retarded the rate of oxygen formation by only 50%. Since R_O is proportional to R_i under these conditions (eq 1) this amount of retardation indicates that reaction 7 accounts for ½ of the termination and that an amount of cyclohexanone is formed corresponding to ¼ the rate of initiation (R_i = 3.75×10^{-3} *M*/hr). Thus, the observed rate of formation of cyclohexanone from peroxy attack is 2.5×10^{-3} *M*/hr (from Table IV) − 0.1×10^{-3} *M*/hr = 2.4×10^{-3} *M*/hr. The value for $k_p/(2k_t)^{1/2}$ obtained by substitution of this value for $d[C_6H_{10}O]/dt$ in eq 5 must also be corrected for the effect of reaction 7 on the apparent value of k_t. Since R_O is reduced by 50% by the addition of cyclohexyl hydroperoxide, the apparent k_t is twice as fast as for the reaction of 2 t-BuO$_2$· (eq 1). Therefore the value of $k_p/(2k_t)^{1/2}$ (eq 5) was corrected for termination by only 2 t-BuO$_2$· by multiplying by $\sqrt{2}$.

Decompositions of Cyclohexyl Hydroperoxide. The rate of decomposition of cyclohexyl hydroperoxide has been investigated at 100° in the absence of both oxygen and added free radical initiator. First the decomposition was studied at 0.1 and 0.5 *M* in cyclohexane using 96% pure hydroperoxide containing about 2% each of cyclohexanol and cyclohexanone. The individual effects of about 0.1 *M* adipic acid, cyclohexanol, cyclohexanone, boric acid, and tricyclohexyl borate were determined on the decomposition of 0.1 *M* hydroperoxide. Concentrations of cyclohexanol and cyclohexanone were followed with conversion, but with limited success, although reproducibility per sample was usually within 5% for duplicate analyses. Data in Table V are plotted in Figure 3. The curves for 0.1 *M* hydroperoxide indicate autocatalysis up to >50% conversion. This relation is consistent with a faster reaction between hydroperoxide and one or more of the decomposition products. Cyclohexanol, cyclohexanone, and to a lesser extent adipic acid accelerate the decomposition of hydroperoxide. The magnitude of the effect indicates that the small amount of impurity in the 0.1 *M* hydroperoxide run is probably accelerating the decomposition initially. Since the initial rate of decomposition of 0.5 *M* hydroperoxide is ~70 times that for 0.1 *M* peroxide, the decomposition is not a simple unimolecular reaction.

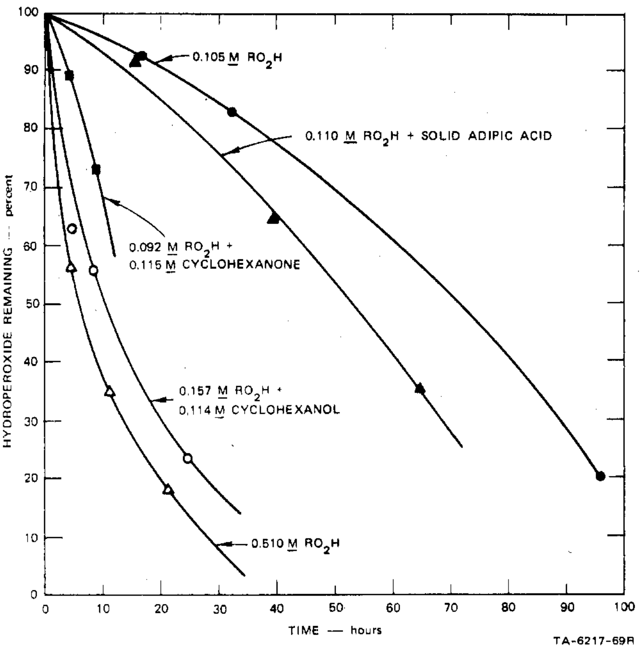
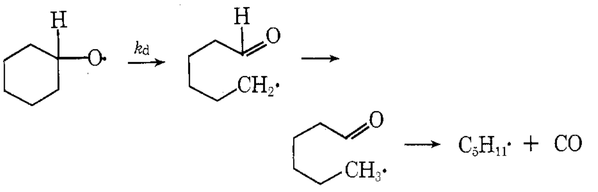


Figure 3. Effects of concentration and decomposition products on decompositions of cyclohexyl hydroperoxide (RO_2H) in cyclohexane at 100°.

Chemistry of the Cyclohexyloxy Radical. Cyclohexyl *tert*-butyl peroxide (CBP) was selected as the source of cyclohexyloxy radicals because of its ease of preparation and because, unlike secondary peroxides,[13] it cannot decompose to hydrogen and ketone.

CBP (0.0988 mmol) was heated with 1.0 ml of isopropyl acetate at 130° for 64 hr in a sealed tube. Analysis of the noncondensable products indicated formation of about 0.035 mmol of each of carbon monoxide and methane. Since the carbon monoxide results from cleavage of the cyclohexyloxy radical (reaction 8), at least 35% and possibly all (since no cyclohexanol is found) of the cyclohexyloxy radicals cleave under the reaction conditions. The presence of carbon monoxide indicates that pentane or pentene should also be present. A GC analysis showed peaks with the necessary retention times, but positive identification has not been made.



(8)

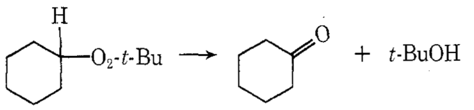
In a series of sealed tubes, 0.064 *M* CBP was decomposed

Table V
Decomposition of Cyclohexyl Hydroperoxide at 100°

Additive	Time, hr	Concn, M			Yield decomposition products[a]
		$C_6H_{11}O_2H$	$C_6H_{10}O$	$C_6H_{11}OH$	
None	0	0.510	0.010	0.015	
	5.0	0.288	0.112	0.165	114
	11.5	0.177			
	22.3	0.093	0.205	0.331	122
None	0	0.105	0.002	0.003	
	16.0	0.098	0.004	0.002	
	32.0	0.087	0.013	0.009	113
	95.5	0.021	0.057	0.085	163
Cyclohexanone	0	0.092	0.115	0.003	
	4	0.082	0.135	0.014	
	8.5	0.067	0.134	0.011	108
Cyclohexanol	0	0.157	0.003	0.114	
	4.7	0.098	0.012	0.111	
	9.0	0.088	0.018	0.108	
	25.0	0.038	0.047	0.137	50
Adipic acid[b]	0	0.110	0.002	0.003	
	15.5	0.100	0.007	0.006	80
	39.5	0.071	0.023	0.020	97
	64.5	0.040	0.035	0.076	163
Boric acid[b]	0	0.105	0.002	0.003	
	3.0	0.071	0.004	0.014	
	5.25	0.048	0.009	0.014	
	8.25	0.030	0.012	0.030	54
	15.5	0.008	0.012	0.056	62
Tricyclohexyl borate (0.109 M)	0	0.113	0.002	0.003	
	4	0.104			
	20	0.057	0.046		
	28	0.022	0.072		

[a] (Increase in alcohol + ketone) × 100%/(decrease in hydroperoxide). [b] 1 mol/mol ROOH, insoluble in reaction mixture.

in cyclohexane for up to 2 hr at 140°, with the results in Table VI. This decomposition gives 8–9% cyclohexanone, probably in the cage reaction 9. Of the remaining free cyclohexyloxy radicals, 56% give cyclohexanol by hydrogen abstraction (reaction 10), and 44% is in unidentified and probably mostly acyclic products. The 44% includes products left after evolution of CO corresponding to about 8% of the cyclohexyloxy radicals that escape the initial cage.



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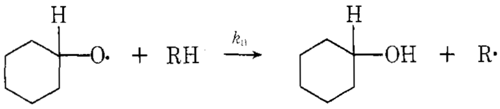


(10)

Discussion

Oxidation of Cyclohexane at Low Conversion. The oxidation of cyclohexane at 100° initiated by 0.10 M di-*tert*-butyl peroxide gives about 0.5% conversion in 48 hr. At this conversion, hydroperoxide accounts for 87.5% of the oxygen consumed while cyclohexanol accounts for 1.4%, and cyclohexanone accounts for 4.7% (assuming 1 mol of water per mole of ketone). The missing oxygen corresponds to one molecule for every 14 molecules found as peroxide. The chain length averages 23 ($\Delta O_2/t\text{-BuO}\cdot$ formed). From the known amount of initiation, 0.00075 M each of cyclohexanol and cyclohexanone should be present if termination occurs by two cyclohexylperoxy radicals. Actually twice as much cyclohexanol and three times as much cyclohexanone are found. However, in the next 24 hours, 14 times as much cyclohexanol and 10 times as much cyclohexanone are found as expected from the calculated initiation and termination. Thus, during the first 0.1–0.3% of reaction only one molecule each of cyclohexanol and cyclohexanone appear to be formed per termination step. Since our CBP results showed that cyclohexyloxy radicals are readily converted to cyclohexanol in cyclohexane, the absence of excess cyclohexanol demonstrates that few or no free cyclohexyloxy radicals are formed either from nonterminating interactions of cyclohexylperoxy radicals or from reaction 11, suggested by Berezin et al.[14]

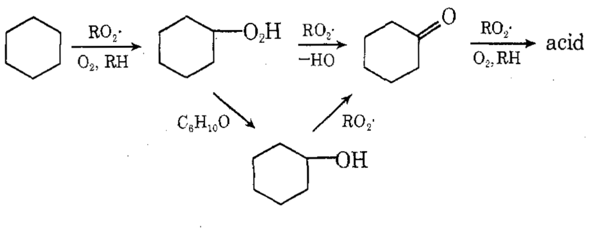
Table VI
Decomposition of CBP in Cyclohexane at 140.2°

Time, min	CBP mM	Products, mM[a]			
		CO	$C_6H_{10}O$	$C_6H_{11}OH$	$(C_6H_{11})_2$
0	64	0	1.2	0.11	0.26
20	50	0.4	2.75	4.88	19.0
30	39	0.8	3.02	12.7	19.4
60	40	1.4	5.40	16.8	26.6
127	21	2.8	5.68	24.2	24.9
1200	0	4.4	6.64	33.2	21.9

[a] All values except for CO are averages of three replicate analyses by GC. Precision is generally better than ±5%.

$$RO_2\cdot + RH \rightarrow RO\cdot + ROH \qquad (11)$$

Oxidation of Cyclohexane at High Conversion. A simple sequence for the further oxidation of cyclohexane is the first line in reaction 12, although it neglects the presence of cyclohexanol in the products.



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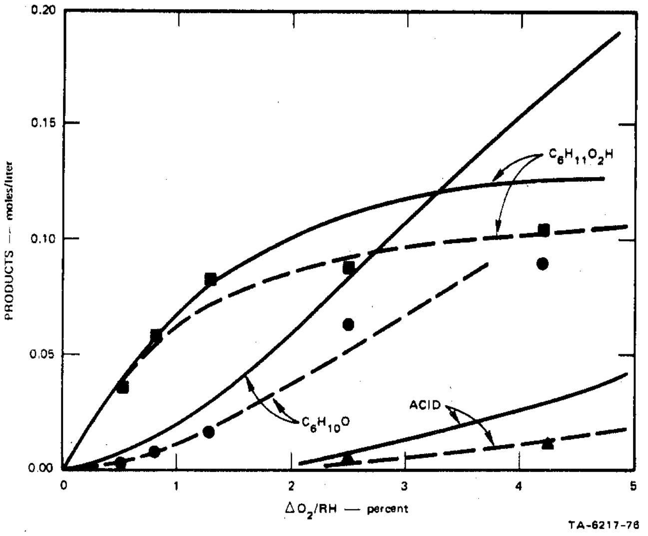
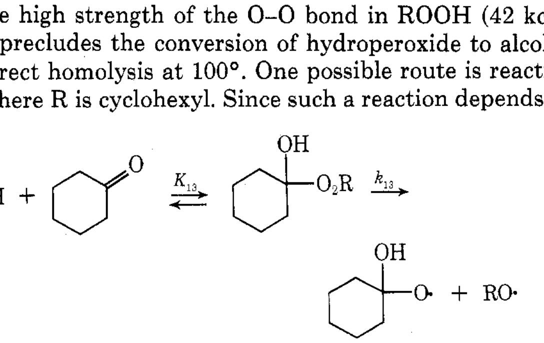


Figure 4. Formation of products in oxidation of cyclohexane at 100°C. Solid lines are calculated from independently measured relative reactivities; dashed lines and points are experimental.

If we assume that cyclohexane, cyclohexyl hydroperoxide, and cyclohexanone have the relative reactivities in Table IV and that these values do not change with conversion, it is possible to calculate the concentrations of hydroperoxide, cyclohexanone, and acid as the reaction proceeds, using the technique described by Benson,[15] which considers only the products formed in propagation. Figure 4 is a plot of the calculated concentration of products against conversion, with experimental points from the A series in Table II.

While there is qualitative agreement between the experimental and the calculated curve based on relative reactivities, all the calculated concentrations are too high, mostly because of neglect of cyclohexanol in the model and not because of neglect of termination products. Experimentally, cyclohexanol is present to about the same extent as cyclohexanone. We conclude that hydroperoxide is being converted to cyclohexanol by a partly nonradical reaction in addition to the radical attack that leads to ketone. Hence, the true relative reactivity of the hydroperoxide toward peroxy radicals may be smaller than the value used. The actual main sequence then requires incorporation of the second line in reaction 12.

The high strength of the O–O bond in ROOH (42 kcal/mol) precludes the conversion of hydroperoxide to alcohol by direct homolysis at 100°. One possible route is reaction 13, where R is cyclohexyl. Since such a reaction depends on



(13)

the accumulated ketone, it would be unimportant at low conversions, as observed. Further, this reaction predicts that the overall oxidation would be autocatalytic, as observed; after 6% conversion, the rate of oxygen absorption has increased tenfold (Figure 1). Little of this increase is caused by replacement of cyclohexane by more reactive products, since 2 mol % of cyclohexanol retards the rate of oxidation of cyclohexane and 2 mol % cyclohexanone only slightly accelerates the rate (Table I); however, the effects of these products on the decomposition of the hydroperoxide in cyclohexane (Figure 4) further supports occurrence

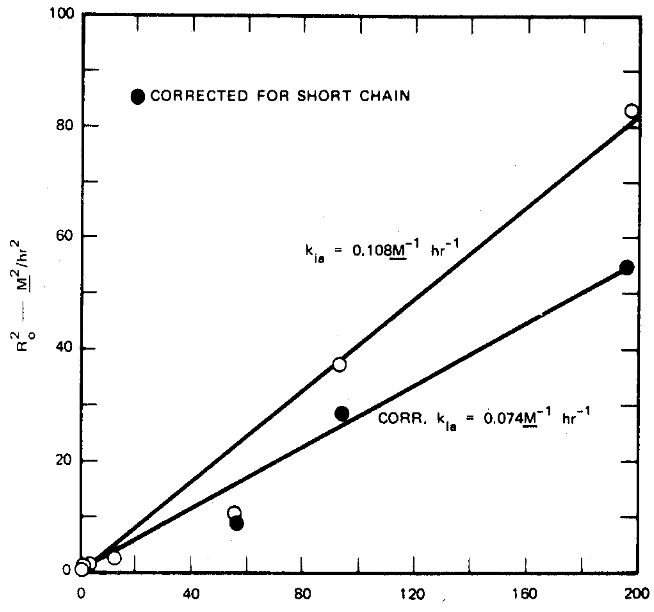


Figure 5. Autocatalytic initiation for oxidation of cyclohexane at 100°C.

of reaction 13 in the oxidation. Kazantseva and co-workers[16] have recently shown that 4-methylcyclohexanone not only increases the rate of radical production from cyclohexyl hydroperoxide but also increases the rate of the nonradical decomposition even more.

Equation 14 gives the rate of oxidation of cyclohexane, with initiation from both the added *tert*-butyl peroxide and reaction 13, propagation by attack of cyclohexylperoxy radicals on cyclohexane, and termination by two cyclohexylperoxy radicals

$$R_O = \frac{k_p}{(2k_t)^{1/2}}[C_6H_{12}]\{2k_d[t\text{-}Bu_2O_2] + 2k_{ia}[RO_2H][C_6H_{10}O]\}^{1/2} - \{k_d[t\text{-}Bu_2O_2] + k_{ia}[RO_2H][C_6H_{10}O]\} \quad (14)$$

where k_{ia} (= $K_{13}k_{13}$) is the rate constant for the autocatalytic initiation and k_d is the rate constant for decomposition of initiator. If the second term on the right side of the equation is neglected (it is 2–5% of the total at low conversion but it could be as large as $R_O/2$ at high rates) and the equation is then squared, the two initiation terms can be separated.

$$R_O^2 = (k_p[C_6H_{12}])^2(2k_d[t\text{-}Bu_2O_2]/2k_t) + (k_p[C_6H_{12}])^2(2k_{ia}[RO_2H][C_6H_{10}O])/2k_t \quad (15)$$

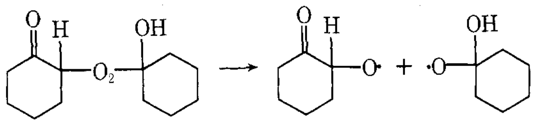
Figure 5 plots R_O^2 (as determined from tangents at each point on the best curve of ΔO_2 vs. time in Figure 1) against the products of the concentrations of hydroperoxide and ketone. By combining the values of the intercept and slope, $k_{ia} = 0.108\ M^{-1}\ hr^{-1}$. If initiation occurs only by decomposition of di-*tert*-butyl peroxide and reaction 13, the actual rate of initiation may be calculated at each point. From these values, R_O^2 may be corrected using the second term on the right in eq 14 and a new value of k_{ia} determined; successive adjustment gives $k_{ia} = 0.074\ M^{-1}\ hr^{-1}$ (or $2.05 \times 10^{-5}\ M^{-1}\ sec^{-1}$). A reported value for the *tert*-butyl hydroperoxide–cyclohexanone decomposition is about $0.6 \times 10^{-5}\ M^{-1}\ sec^{-1}$.[17] The agreement between these values gives substantial support to the sequence in eq 12. However, as the rate increases, the termination reaction produces significant amounts of cyclohexanol and cyclohexanone. At the completion of the reaction in Figure 1, the actual chain length appears to be about 4; therefore, as much as 25% of the consumed hydrocarbon could be in termination products.

At higher temperatures, 1-hydroxycyclohexyloxy radicals formed in reaction 13 apparently cleave to complicate the products,[18] but not in our work at 100°. Instead, cleavage is associated with oxidation of cyclohexanone, as shown in the following discussion.

Oxidation of Cyclohexanone. Although the free radical initiated oxidation of cyclohexanone was studied at 80° instead of the 100° used for cyclohexane, the products were more complex. At 0.7% conversion all products are present that are present at 4% conversion and in about the same proportions. The suggestion by Pritzkow[3] that an acid-catalyzed decomposition of the α-ketocyclohexyl hydroperoxide is responsible for the complex mixture of products may be ruled out, at least at our high rates of initiation, since the presence of acetic acid, trifluoroacetic acid, or pyridine does not have any large effect on rates, distribution of products, or the fraction of the oxygen appearing as hydroperoxide (Table III). Therefore, the intermediates must be largely free radical in nature. Apparently organic acids do shorten the induction period in uncatalyzed oxidations of cyclohexane, but the mechanism is obscure.[19] Acid does not accelerate the ABC-initiated reaction.

The α-hydroperoxy ketone must be an important intermediate since it accounts for a large fraction of the first products. We conclude that most of products result from decomposition of the hydroperoxide, although at least some of the products must arrive from chain termination reactions.

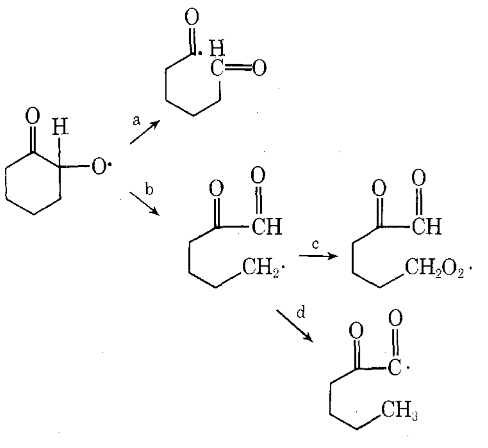
The cyclohexanone concentration is so high that a reaction like 13 must be the main route for decomposition of 2-hydroperoxycyclohexanone, as proposed by Berezin et al.[4]



(16)

At the temperature of our reaction, hydroxycyclohexyloxy radicals should initiate chains and be converted back to cyclohexanone (plus H_2O), although at higher temperatures cleavage of this radical may also be important.

The 2-ketocyclohexyloxy radicals formed in reaction 16 may abstract hydrogen or cleave. The amount of the alcohol thus formed is small since we find about the same amount of hydroperoxide before triphenylphosphine reduction as alcohol afterwards. Cleavage probably predominates and the competition between two possible routes explains the complexity of the observed products.



(17)

Route a leads easily to adipaldehyde acid, adipic acid, and monoperadipic acid, which can convert cyclohexanone to ϵ-caprolactone. Route b leads to glutaric acid and δ-valerolactone by route c and valeric acid related compounds by route d.

In the presence of cobalt or manganese, the rates are much faster than the ABC-initiated rates and much less hydroperoxide is found. With cobalt, the ratio of adipic to glutaric acid is about the same as found in the ABC-initiated reaction, suggesting that free-radical cleavage of the 2-ketocyclohexyloxy radical still predominates, although it is now formed by reaction of hydroperoxide with cobaltous salts. With manganese, much less glutaric acid is formed, which suggests that while some cleavage of 2-ketocyclohexyloxy radicals may occur, there is another important cleavage mechanism that produces less decarbonylation or decarboxylation. This mechanism may be similar to the ionic cleavage induced by the manganese which was proposed by Hertog and Kooyman.[20] Our rate and product results with cobalt and manganese have been confirmed and extended by Kamiya and Kotake,[21] who have shown convincingly that the rate-determining step in oxidations by manganic acetate is the enolization of cyclohexanone.

Conclusions

The di-*tert*-butyl peroxide initiated oxidation of cyclohexane at low conversions at 100° gives high yields of cyclohexyl hydroperoxide with cyclohexanol and cyclohexanone as chain termination products. On further oxidation, hydroperoxide is converted directly to cyclohexanone without much chain cleavage or by-product formation. The accumulating ketone also catalyzes the decomposition of hydroperoxide into radicals, increasing the rate of oxidation, regenerating ketone, and producing cyclohexanol, which is readily oxidized to more ketone. Cyclohexanol also accelerates decomposition of hydroperoxide. These conclusions are supported by thermal decompositions of hydroperoxide in the absence of oxygen. As these catalytic effects lead to faster oxidation, they also lead to shorter kinetic chains and higher proportions of chain termination products.

Relative rates of oxidation at the same rate of initiation at 100° follow: cyclohexane, 1; cyclohexanol, 40; and cyclohexanone, 27. Relative reactivities toward *tert*-butylperoxy radicals follow: cyclohexane, 1.0; cyclohexyl hydroperoxide, 56; cyclohexanol, 55; cyclohexanone, 13; and cyclohexyl acetate, 0.5.

Hydroperoxide appears to be converted to cyclohexanol by formation of the hemiperketal, which decomposes faster by O–O cleavage than the simple hydroperoxide. The cyclohexyloxy radicals formed react mostly by hydrogen abstraction at 100°, but more cleavage occurs at higher temperatures. Integration of data on peroxide decomposition and relative reactivities gives a satisfactory account of the observed rates and products of oxidation of cyclohexane to cyclohexanone at 100°.

The further oxidation of cyclohexanone is more complex, even where it was studied at 80°. The major primary product is 2-hydroperoxycyclohexanone and the decomposition of this compound, also catalyzed by cyclohexanone, leads to a variety of products. At 4% conversion, the oxidation gives about 30% hydroperoxide, 20% ϵ-caprolactone, 16% adipic acid, and 12% glutaric acid. The remaining 22% comprises adipaldehyde acid, cyclohexane-1,2-dione, and δ-valerolactone. The product mix depends on competing abstraction and cleavage reactions of alkoxy radicals and inter- and intramolecular hydrogen transfer and oxygen addition reactions of alkyl and acyl radicals formed by cleavage. The oxidation of cyclohexanone is catalyzed by both cobalt and manganese. The latter gives outstanding yields of adipic acid.

This investigation has brought out the relative simplicity of the oxidation of cyclohexane to cyclohexanone at 100°, and the variety of the subsequent reactions of cyclohexanone at 80°. It has also indicated what reactions should become important in the presence of metals and at higher temperatures. Therefore, it should provide an improved point of departure for study of oxidations of cyclohexane at higher temperatures and for other aliphatic hydrocarbons at all temperatures.

Registry No.—Cyclohexane, 110-82-7; cyclohexanol, 108-93-0; cyclohexanone, 108-94-1; cyclohexyl hydroperoxide, 766-07-4; cyclohexyl acetate, 622-45-7; tricyclohexyl borate, 2467-16-5; cyclohexyl-*tert*-butyl peroxide, 15619-54-2; *tert*-butylperoxy isopropyl carbonate, 2372-21-6.

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Cycloaddition of an Enamine to an Activated Cyclopropane

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Received July 8, 1975

The cycloaddition of *N*-pyrrolidinylcyclohexene (**5**) to 1,1-dicyano-2,2-dimethylcyclopropane (**9**) proceeded by an SN2 route (across the 1–3 bond) rather than by way of a zwitterionic intermediate (across the 1–2 bond). The adduct (**12**) rearranged upon partial hydrolysis to a spiro structure (**13**) which was further hydrolyzed to 2-oxo-4,4-dimethylcyclopentanepentanoic acid (**14**). This keto acid was synthesized.

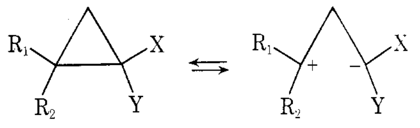
Considerable data now support the existence of zwitterionic intermediates (**2**) in the ring opening of suitably activated cyclopropanes (**1**). For instance, Cram[1] has demonstrated that nucleophiles, electrophiles, and polar solvents strongly increase the rate of racemization of such systems. In addition, both Cram[1] and Danishefsky[2] have shown that such systems suffer nucleophilic ring opening almost exclusively at the more highly substituted carbon (presumably by way of the more stable carbonium ion).

On the other hand, both authors have proven that nucleophilic attack occurs with *complete inversion*,[1,2a,b] leading to the conclusions that nucleophilic attack must be considerably faster than bond rotation and that racemization, at least in the presence of nucleophiles or polar solvents, probably involves a measure of nucleophilic participation as well (and also, perhaps, electrophilic aid).

Conversely, enamines attack **3** exclusively at the terminal carbon.[3] Danishefsky has suggested that the reaction involves zwitterionic intermediate **4**.

Where would an enamine attack cyclopropane **1**? Cycloaddition of enamine **5** to unalkylated cyclopropane **6** gave adduct **7** as shown by hydrolysis to keto acid **8**.[4]

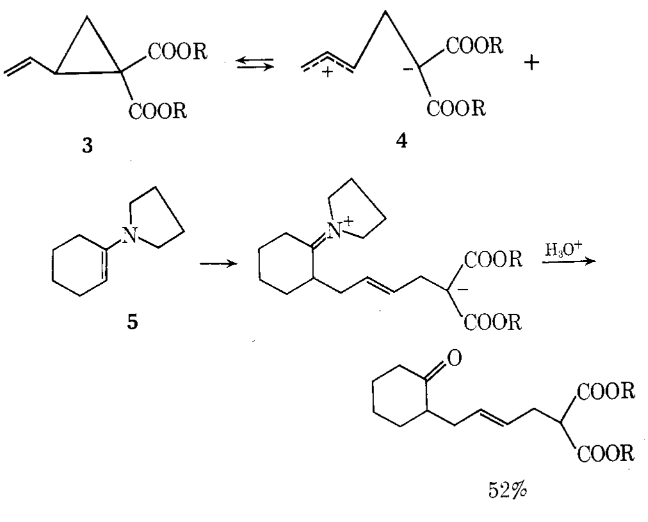
We have examined the reaction of enamine **5** with 1,1-dicyano-2,2-dimethylcyclopropane (**9**).[5] A zwitterionic intermediate (**10**) would give **11**; SN2 attack would give **12**. In the event, **12** was produced in 47% yield. The results are summarized in Chart I.



1 **2**

X,Y = CN, COOR, SO$_2$R

R$_1$,R$_2$ = H, alkyl, vinyl, aryl



52%