Mechanisms of the formation of carboxylic acids and their anhydrides during the liquid-phase oxidation of cyclohexane

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The channels of formation and transformation of bifunctional (C_5, C_6) and monofunctional acids (C_1, C_5, C_6) and their anhydrides during the liquid-phase oxidation of cyclohexane are reviewed. Adipic acid and adipic anhydride are predominantly formed by the radical-chain oxidation of 2-hydroxycyclohexanone. Destructive transformations of 1-hydroxycyclohexyloxyl and cyclohexyloxyl (at a low conversion of cyclohexane) radicals, which are formed by the homolytic decomposition of 1-hydroperoxy-1-hydroxy- or 1-hydroxy-1-alkylperoxy-, and hydroperoxycyclohexane, respectively, afford 6-hydroxyhexanoic and caproic acids. 6-Oxohexanoic acid can be formed by the decomposition of 2-hydroperoxycyclohexanone *via* the nonradical and radical routes, as well as by the oxidation of 2-hydroxycyclohexanone with peroxide compounds. Valeric and 5-hydroxypentanoic acids are predominantly resulted from the destructive transformations of the 2-oxocyclohexyloxyl radical. The shortening of carbon chain is explained by decarboxylation, decarbonylation, and elimination of formic acid. The ring closure of 5-hydroxypentanoic acid to δ-valerolactone prevents its further oxidation. The schemes for the formation of 5-oxopentanoic and glutaric acids by the oxidation of 6-oxohexanoic acid at the C(5)—H bonds were proposed. The transacylation of the initially formed anhydrides with carboxylic acids leads to mixed anhydrides, and their alcoholysis by cyclohexanol affords all cyclohexyl esters of mono- and dicarboxylic acids.

Key words: cyclohexane, cyclohexanol, cyclohexanone, 2-hydroxycyclohexanone, liquid-phase oxidation, caproic acid, 6-hydroxyhexanoic acid, 6-oxohexanoic acid, adipic acid, adipic anhydride, valeric acid, 5-hydroxypentanoic acid, 5-oxopentanoic acid, glutaric acid, cyclohexyl esters.

Introduction

The liquid-phase oxidation of cyclohexane by molecular oxygen (most often in the presence of the cobalt compounds at 423—433 K and a pressure of 0.8—1.0 MPa) is used in two large-scale industrial processes: productions of caprolactam[1,2] and adipic acid.[2—4] The target products of caprolactam production are cyclohexyl hydroperoxide, cyclohexanol, and cyclohexanone, whereas other compounds (bifunctional compounds, carboxylic acids, and esters) are by-products.[1,2,5—7] The conversion of cyclohexane in the industrial production of caprolactam rarely exceeds 5—7% because of the possibility of involvement of the target products (mainly cyclohexanone) into radical-chain and nonradical transformations leading to by-products.[5] In the production of adipic acid, the liquid-phase oxidation of cyclohexane in the first step is performed to the 8—10% substrate conversion. In the second step, after distillation off of unreacted cyclohexane, the vat residue is oxidized with nitric acid.[2,3] The low conversion of cyclohexane in the first step is evidently explained by deviations from the α-mechanism of oxidative destruction that decrease the yield of adipic acid.[8]

Due to the high temperature of the cyclohexane oxidation process (423—433 K) and its multistep character, it is difficult to monitor the sequence of formation of the compounds containing carboxyl functional groups. Therefore, the mechanism of carbon chain destruction during cyclohexane oxidation remains unclear up to now. It was assumed that the main channel of oxidative destruction leading to adipic acid was related to the acid-base transformation of 2-hydroperoxycyclohexanone formed by cyclohexanone oxidation (Langenbeck—Pritzkow scheme).[1,9—12] The universal character of Langenbeck—Pritzkow scheme seemed doubtful for the authors.[13] The channels of oxidative destruction of cyclohexane related to radical-chain and nonradical transformations of 2-hydroxycyclohexanone and cyclohexane-1,2-dione (major products of 2-hydroperoxycyclohexanone transformation) and leading to adipic anhydride and adipic acid were substantiated.[14—22] The reactions of adipic anhydride with carboxylic acids affords mixed anhydrides, the involvement

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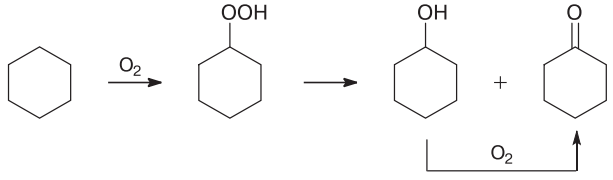
of which in cyclohexane oxidation results in the formation of all cyclohexyl esters of mono- and dicarboxylic acids.[8,14,23–25] The occurrence of homolytic channels of formation of the compounds containing carboxyl groups in the course of cyclohexane oxidation is accompanied by the formation of peroxy acids, which are responsible for the oxidation of cyclohexanone by peroxy acids *via* the Baeyer—Villiger scheme to form ε-caprolactone.[8,23,26–28] It is postulated[29–31] that during cyclohexane oxidation adipic acid is mainly formed from the cyclohexyloxyl radical, which is generated by homolytic transformations of cyclohexyl hydroperoxide. This contradicts the data of experiments on the oxidation of ^{14}C-labeled cyclohexane with additives of non-labeled cyclohexanone and cyclohexanol. These experiments showed that during cyclohexane oxidation 86—95% adipic acid are formed *via* cyclohexanone.[32] Since the possibility of intramolecular isomerization of the cyclohexylperoxyl radical was substantiated[5,33–35] and the products of cyclohexanol and cyclohexanone oxidation at CH bonds of all types were observed,[5,6,36–40] it became necessary to consider these routes of formation of carboxyl-containing compounds with the number of carbon atoms less than six.

In this review, we continue the previously started[5,6] consideration of the key problems of liquid-phase cyclohexane oxidation from the modern points of view. The data concerning the main channels and mechanisms of formation of compounds with carboxyl and anhydride functional groups under the conditions close to those used in industry for the liquid-phase oxidation of cyclohexane are systematized and discussed.

Oxidation of cyclohexane

Carboxylic acids and cyclohexanol esters are formed already in the initial steps of the cyclohexane oxidation process in the industrial production of caprolactam (Fig. 1).[41] This is explained by the conversion of the initially formed molecular product of oxidation, cyclohexyl hydroperoxide, to cyclohexanol and cyclohexanone at 423 K (Scheme 1).[1–8] The latter, being more reactive than cyclohexane, are involved in consecutive and consecutive-parallel radical-chain and nonchain transformations. As a result, a wide range of products is formed, and their number increases with an increase in the oxidation depth (see Fig. 1). Some of the formed products are highly reactive and, hence, exist in the reaction medium in relatively low concentrations. Their role in cyclohexane oxidation can often be evaluated only on the basis of model reactions.

Scheme 1



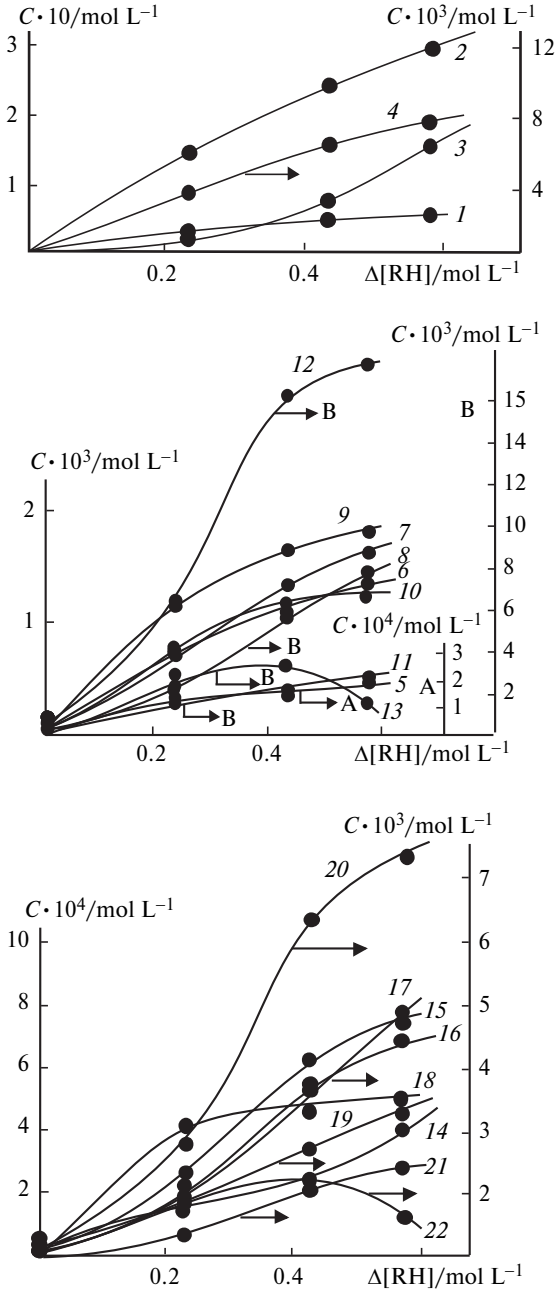


Fig. 1. Influence of the conversion (Δ[RH]) on the content of the following products of cyclohexane oxidation (423—428 K, 0.04% cobalt naphthenate, pressure 0.8 MPa): peroxide compounds (*1*), cyclohexanol (*2*), cyclohexanone (*3*), mixed carboxylic acid anhydrides (*4*), formic acid (*5*), butyric acid (*6*), valeric acid (*7*), caproic acid (*8*), succinic acid (*9*), glutaric acid (*10*), 5-oxopentanoic acid (*11*), adipic acid (*12*), 6-oxohexanoic acid (*13*), cyclohexyl formate (*14*), cyclohexyl butyrate (*15*), cyclohexyl valerate (*16*), cyclohexyl capronate (*17*), cyclohexyl succinate (*18*), cyclohexyl glutarate (*19*), cyclohexyl adipinate (*20*), dicyclohexyl adipinate (*21*), and cyclohexyl-6-oxohexanoate (*22*).

Peroxide and non-peroxide oxidation products and products formed without and with the carbon chain destruction are distinguished.[1—8]

Figures 1 and 2 provide some idea about the composition of the cyclohexane oxidation products. The range of changing the concentrations of the products under the industrial conditions (423—428 K, 0.04% cobalt naphthenate, pressure 0.8 MPa, oxidation shop of caprolactam production at the Kemerovo JCP "Azot")[41] is shown in Fig. 1. The kinetics of accumulation of a series of products of non-catalyzed and cobalt naphthenate-catalyzed cyclohexane oxidation with oxygen (stainless steel reactor, 423 K, pressure 1.0 MPa) is presented in Fig. 2.

1-Hydroperoxy-1-hydroxycyclohexane, 2-hydroperoxycyclohexanone, 2-hydroxycyclohexanone, cyclohexane-1,2-dione, and, possibly, cyclohexane-1,2-diol were found among the products formed without cyclohexane ring destruction upon the oxidation of cyclohexane and its derivatives. The products formed with cyclohexane ring destruction include ε-caprolactone and δ-valerolactone; 6-oxohexanoic, 5-oxopentanoic, 6-hydroxyhexanoic, caproic, valeric, formic, adipic, glutaric, and succinic acids; mixed anhydrides of mono- and dicarboxylic acids; esters of cylohexanol and listed above mono- and dicarboxylic acids; and others.[1—8]

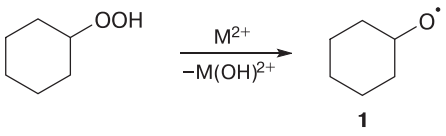
Interest in studying the reactions of cyclohexane oxidation in the gas phase at moderate and high temperatures increases in the recent decades.[33—35] The products of cyclohexane gas-phase oxidation, such as cyclohexene, cyclohexene oxide, products of cyclohexane ring destruction, and some others, can possibly be formed under the liquid-phase reaction conditions as well. For example, 2-cyclohexenone and 1,2-epoxycyclohexanone are formed by the liquid-phase oxidation of cyclohexanone at the β-C—H bonds.[39—40]

Caproic and bifunctional C_6 acids

The considered group of carboxyl-containing compounds comprises caproic, 6-hydroxyhexanoic, 6-oxohexanoic, and adipic acids. It is known that caproic, adipic, and 6-hydroxy- and 6-oxohexanoic acids can be formed not only from the cyclohexyloxyl radical[29—31] but also in the steps of oxidation of cyclohexanol,[1,8,11] and cyclohexanone,[1,8,11,13,19,41,42] whereas the three last products can also be formed from 2-hydroxycyclohexanone.[8,22,43] Therefore, it seems reasonable to crucially consider all alternative channels of formation of these acids.

Formation of caproic and bifunctional C_6 acids from cyclohexyloxyl radical. Cyclohexyloxyl radical (**1**) is formed upon the thermal, catalytic (Scheme 2), and by free-radical-induced decomposition of cyclohexyl hydroperoxide.[1,5,6,8,29—31,42—45]

Scheme 2



1

M is metal.

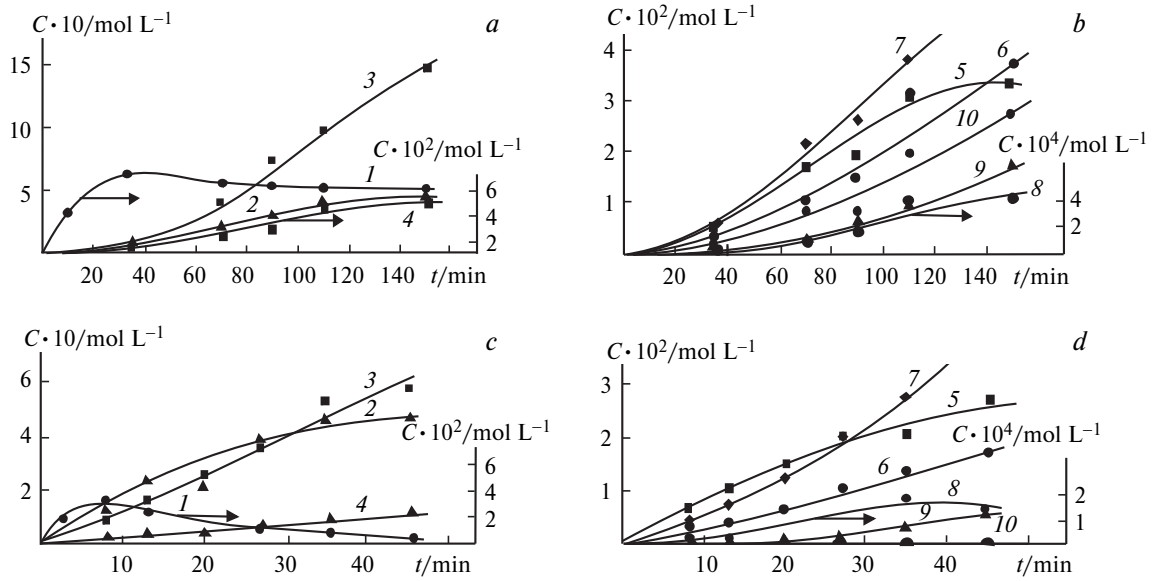
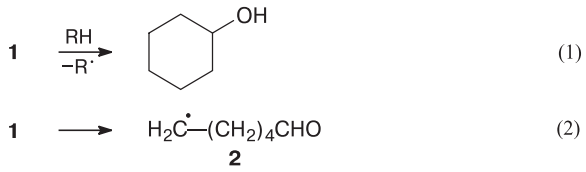


Fig. 2. Kinetic curves of accumulation of the following products of non-catalyzed (423 K) (*a*, *b*) and cobalt naphthenate-catalyzed (423 K, cobalt(II) naphthenate ($8.5 \cdot 10^{-4}$ mol L^{-1})) (*c*, *d*) cyclohexane oxidation: peroxy compounds (*1*), cyclohexanol (*2*), cyclohexanone (*3*), 2-hydroxycyclohexanone and 2-hydroperoxycyclohexanone (*4*), 6-hydroxyhexanoic acid (*5*), 6-oxohexanoic acid (*6*), adipic acid (*7*), adipic anhydride (*8*), monocyclohexyl adipinate (*9*), and ε-captolactone (*10*).

The homolytic decomposition of hydroperoxide is accelerated by oxygen-containing compounds (alcohols, ketones, carboxylic acids, *etc.*).[1,5,6,8,43,44] The main route of the transformation of radical **1** in a medium of oxidized cyclohexane is the dehydrogenation of the substrate to form cyclohexanol.[1,5,6,8,11,42–44] During the thermal decomposition of *tert*-butylcyclohexyl peroxide in cyclohexane at 413 K, 56% cyclohexyloxyl radicals are transformed into cyclohexanol (Scheme 3, reaction (1)).[42] Radical **1** underwent the destructive decomposition with cyclohexane ring opening to a substantially lower extent, which affords 6-oxohexyl radical **2** (Scheme 3, reaction (2)).[1,5,6,8,29–31,42–44]

Scheme 3



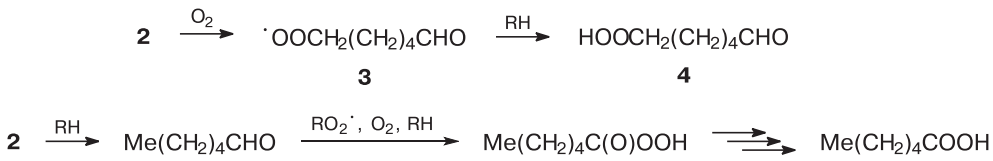
In a medium of oxidized cyclohexane, radical **2** can react with both molecular oxygen and substrate RH (Scheme 4).[1,42–44]

The reaction of radical **2** with oxygen in a medium of oxidized cyclohexane leads to peroxyl radical **3** and then to hydroperoxide **4**, whose transformations can theoretically be the source of both hydroxy- and oxohexanoic acids and adipic acid (see Scheme 4). According to the known concepts on the mechanisms of oxidation processes,[44] in the kinetic region of oxygen absorption, the reactions of alkyl radicals with oxygen should be substantially faster than the reactions at the CH bonds of the substrate. The reaction of radical **2** with cyclohexane affords caproic aldehyde, the radical-chain oxidation of which through the peroxy acid step should result in caproic acid. The probability of transformation of oxohexyl radical **2** into caproic acid increases under the industrial process of cyclohexane oxidation when the oxidizing gas with a low oxygen content (about 3%) is used.[6] In this case, caproic acid is formed in substantial amounts (see Fig. 1).

The transformation of hydroperoxide **4** into 6-hydroxyhexanoic (**7**), 6-oxohexanoic (**8**), and adipic acids is a multistep process that can include decarbonylation and decarboxylation steps with the formation of products with the number of carbon atoms less than six.[1,8,11,42] The dependences of the accumulation of a series of by-products upon cyclohexane oxidation (418 K, conversion to 7.5%) on the cyclohexane conversion were obtained.[29–31] To explain the observed course of the curves of accumulation of 6-hydroxyhexanoic (**7**) and adipic (**9**) acids, the authors[29] assumed that these acids are resulted predominantly from the radical-chain transformations of radical **2** (Scheme 5).

The principal possibility of transformation of the hydroxy and aldehyde groups of the initially formed products into carboxyl groups during cyclohexane oxidation cannot be denied. However, some transformations presented in Scheme 5 are of low probability. Transformations **3** → **5** and **5** → **6** should proceed *via* the nine- and seven-mem-

Scheme 4



Scheme 5

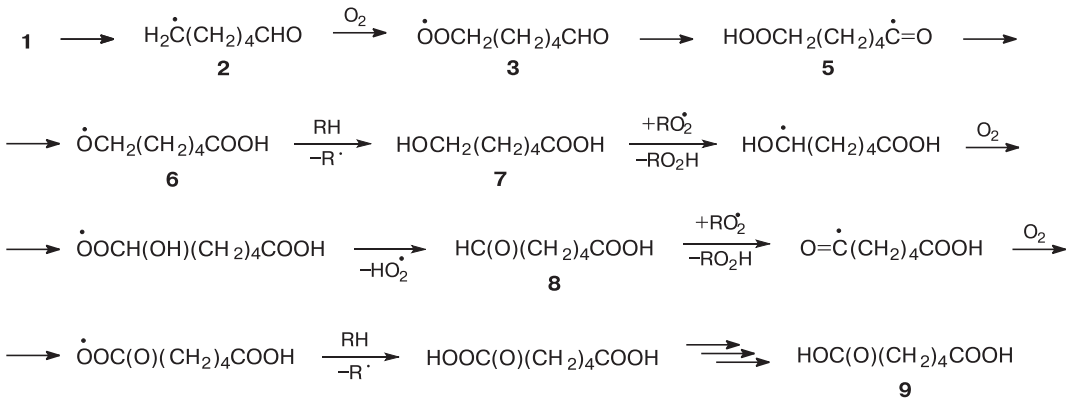


Table 1. Influence of the number of atoms in the cyclic transition state (*N*) on the relative ring closure rate of ω-bromocarboxylic acids to lactones at 423 K[46]

N	Relative ring closure rate
5	$1.5 \cdot 10^6$
6	$1.7 \cdot 10^4$
7	97.3
8	1.00
9	1.12
10	3.35
11	8.51

bered transition states. It is known that the formation of the cyclic transition state becomes less probable with an increase in the cycle size. This is explained by an increase in the entropy factor upon the formation of the "folded" conformation of the acyclic molecule.[46] The data on the influence of the number of atoms in the cyclic transition state on the relative rate of ring closure of ω-bromocarboxylic acids to lactones (Scheme 6) presented in Table 1 show that the ring closure occurs with the lowest rate in the cases of the eight- and nine-membered reaction cycles.

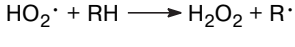
Scheme 6

The fact that intramolecular transformations **3** → **5** and **5** → **6** are poorly competitive compared to the corresponding intermolecular interactions is also confirmed by the data[47] obtained when studying the direction of hydrogen atom detachment by ω-formyl radicals (Table 2). Side reactions of decarbonylation (for example, of radical **2**[8]) and decarboxylation[8,11] also should decrease the selectivity of the transformation of 6-oxohexyl radical **2** into 6-hydroxyhexanoic, 6-oxohexanoic, and adipic acids. Under the conditions of cyclohexane oxidation, the probability of these reactions is fairly high. The oxidation of 6-oxohexanoic acid at the C(5)—H bonds affords formic acid and 5-oxohexanoic acid found among the cyclohexane oxidation products.[41]

Formation of caproic and bifunctional C_6 acids from cyclohexanol and cyclohexanone. The problems of kinetics, reactivity, and mechanisms of cyclohexanol transformation under the radical-chain conditions are rather comprehensively considered in the monograph[11] and reviews.[5,6] Cyclohexanol is mainly oxidized at the α-CH bonds (Scheme 7).[1,5,6,11]

Predominantly $HO_2^{\bullet}$ radicals lead the chain (Scheme 8).

Scheme 8



There are mobile equilibria between cyclohexanone and α-hydroxycyclohexylperoxyl radical **10** (see Scheme 7, route *a*)[6,48–50] and between cyclohexanone and α-hydroxycyclohexyl hydroperoxide **11** (see Scheme 7, route *b*).[5,11,44] When the reaction medium contains hydroperoxides, for example, cyclohexyl hydroperoxide or 2-hydroperoxycyclohexanone, they reversibly add to cyclohexanone to form hemiperketal **12** (Scheme 9).[5,6,8,11,44]

Scheme 7

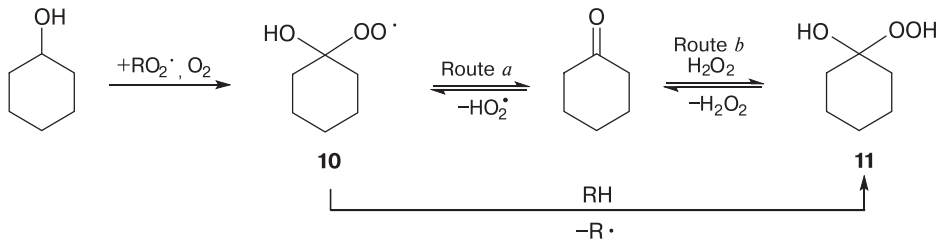
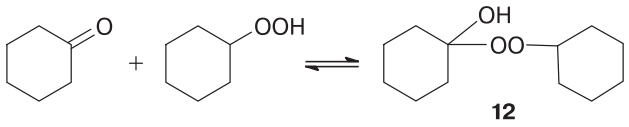


Table 2. Influence of the number of atoms in the cyclic transition state (*N*) on the direction of hydrogen atom detachment by the ω-formylalkyl radical ($^{\bullet}(CH_2)_nCHO$) (333 K, dodecane, N_2)[47]

$^{\bullet}(CH_2)_nCHO$	*N*	Direction of H atom detachment (%)		
		intramolecular, from CHO group	from solvent	from other CH bonds of radical
4	6	74	12	14
5	7	29	19	52
6	8	38	8	54

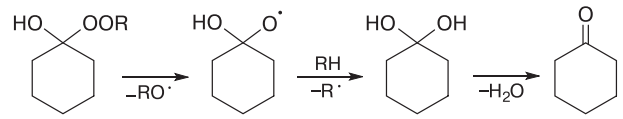
Scheme 9



12

Peroxides **11** and **12** underwent homolytic decomposition (Scheme 10)[5,6,11,42,44] along with reversible dissociation to cyclohexanone and the corresponding peroxide compound.

Scheme 10



11, **12** **13**

R = H (**11**), *cyclo*-C_6H_{11} (**12**)

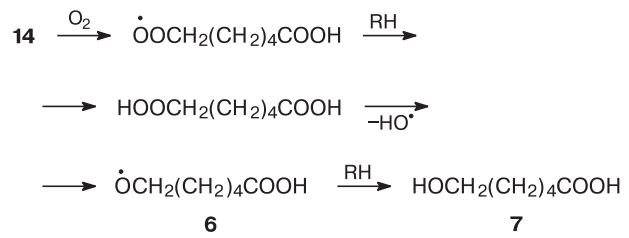
At temperatures below 353 K, 1-hydroxycyclohexyloxyl radical **13** predominantly detaches the hydrogen atom from the substrate to regenerate cyclohexanone (see Scheme 10). At higher temperatures, the destruction of radical **13** with the ring opening is possible to give ω-carboxyalkyl radical **14**.[8,42,43] The latter reacts with the substrate to give caproic acid (Scheme 11).

Scheme 11

14

The alternative reaction of radical **14** with oxygen proceeds according to Scheme 12 to afford 6-hydroxyhexanoic acid (**7**).

Scheme 12

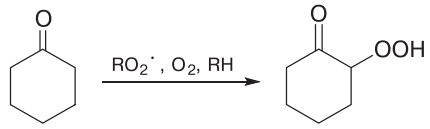


6 **7**

It is noteworthy that radical **14** is more readily underwent destruction than radical **2**, and its conversion to caproic and 6-hydroxyhexanoic (**7**) acids requires a less number of steps than the process with radical **2** (see Schemes 5 and 12).

Since the reactivity of the α-CH bonds in cyclohexanone is substantially higher than the reactivity of the CH bonds of cyclohexane, cyclohexanone is oxidized *via* the free radical mechanism with the formation of 2-hydroperoxycyclohexanone (**15**) (Scheme 13).[1,5,6,8,11]

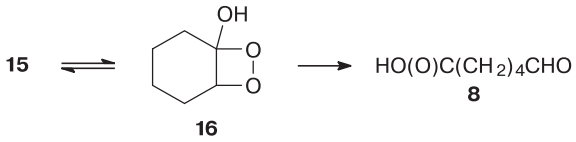
Scheme 13



15

It is most probable that compound **15** is transformed into 6-oxohexanoic acid (**8**) *via* dioxetane intermediate **16** (Scheme 14).[6,8,43]

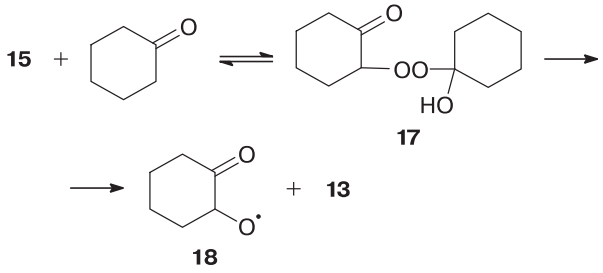
Scheme 14



16

2-Hydroperoxycyclohexanone (**15**), like cyclohexyl hydroperoxide, can be involved in intermolecular reactions with oxygen-containing compounds, which will accelerate its homolytic decomposition. In oxidized cyclohexanone, the reaction with the substrate is preferable and leads to hemiperoxyketal **17**, which decomposes to form 1-hydroxycyclohexyl (**13**) and 2-oxocyclohexyloxyl (**18**) radicals (Scheme 15).[1,5,6,8,11,43]

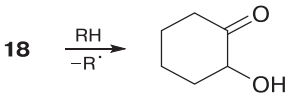
Scheme 15



17 **18**

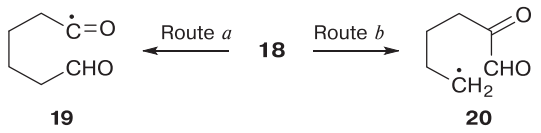
2-Oxocyclohexyloxyl radical **18** is transformed into 2-hydroxycyclohexanone (Scheme 16).[6,8,11,43]

Scheme 16



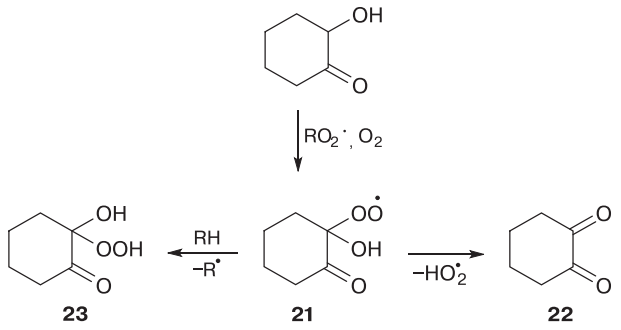
The transformation of radical **18** with the carbon chain destruction can proceed *via* two routes (Scheme 17). Route *a* in Scheme 17 explains the formation of 6-oxohexanoic acid (**8**) and monoperoxyadipic and adipic (**9**) acids[6,8,11,42,43] in the course of cyclohexanone oxidation. The significance of Scheme 17, including route *b*, for the formation of the destruction products with the number of carbon atoms less than six will be considered below.

Scheme 17



Formation of bifunctional C_6 acids from 2-hydroxycyclohexanone and cyclohexane-1,2-dione. 2-Hydroxycyclohexanone is oxidized *via* the radical-chain mechanism at the most reactive α-CH bond (Scheme 18).[5,6,8,11,14–22,51,52]

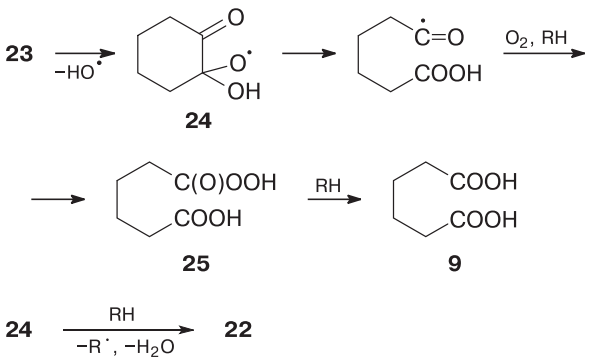
Scheme 18



Hydroxyperoxyl radical **21** either eliminates the $HO_2^{\bullet}$ radicals transforming into cyclohexane-1,2-dione (**22**), or detaches hydrogen from the substrate to form 2-hydroxy-2-hydroperoxycyclohexanone (**23**) (see Scheme 18). Hydroxyhydroperoxide **23** reversibly dissociates to cyclohexane-1,2-dione and H_2O_2 or undergoes destruction *via* the homolytic and non-homolytic mechanisms.[6,8,20,43] The homolytic decomposition of compound **23** proceeds predominantly with cyclohexane ring opening and in the presence of oxygen affords adipic acid (through the step of monoperoxyadipic acid **25**). This reaction also affords cyclohexane-1,2-dione (**22**) (Scheme 19) but in lower amounts.

A comparison of the potential yield of peroxy acid with the yield of adipic acid in the oxidation of 2-hydroxycyclohexanone at 323 K shows that about 50% of adipic acid (**9**) are formed according to Scheme 19. The second channel of the formation of adipic acid (**9**) simultaneously with adipic anhydride is the pericyclic rearrangement of hydroxyhydroperoxide **23** *via* the dioxetane (**26**) and oxirane (**27**) intermediates (Schemes 20 and 21).[6,8,20,43]

Scheme 19



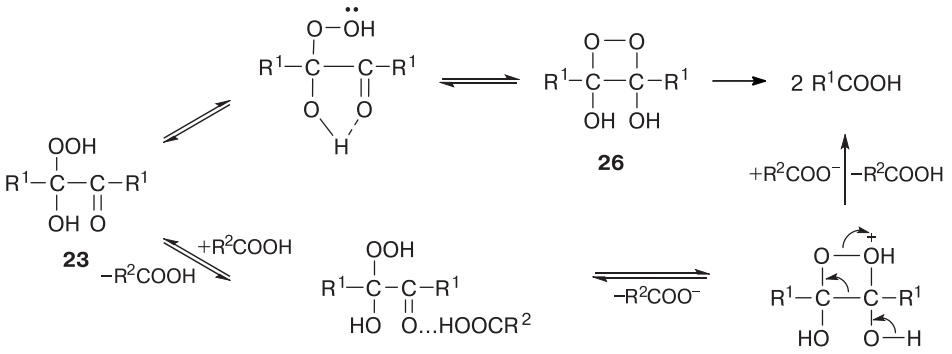
2-Hydroxycyclohexanone participates not only in radical-chain oxidation but also reacts with peroxide compounds. The effective rate constants for the decomposition of *tert*-butyl hydroperoxide at 423 K in the presence of equimolar amounts of cyclohexanol, cyclohexanone, and 2-hydroxycyclohexanone ($k^{eff}\times10^4$, s^{-1}) are 0.17, 0.20, and 10.0, respectively.[6,8,22] The reaction can include the addition of the peroxide compound to the carbonyl group of 2-hydroxycyclohexanone affording 6-oxohexanoic acid (**8**) (Scheme 22).[6,8,22]

When 2-hydroxycyclohexanone is introduced into methyl ethyl ketone oxidized at 396 K, the oxidation of the latter is almost completely retarded,[22] which was renewed after the quantitative transformation of 2-hydroxycyclohexanone into adipic anhydride and adipic acid (evidently, through hydroxyhydroperoxide **23**) and 6-oxohexanoic acid (**8**) (see Scheme 22), as well as into 6-hydroxyhexanoic acid (**7**) and ε-caprolactone. It is most probable that 6-hydroxyhexanoic acid (**7**) is a result of the homolytic decomposition of intermediate **28** (Scheme 23).

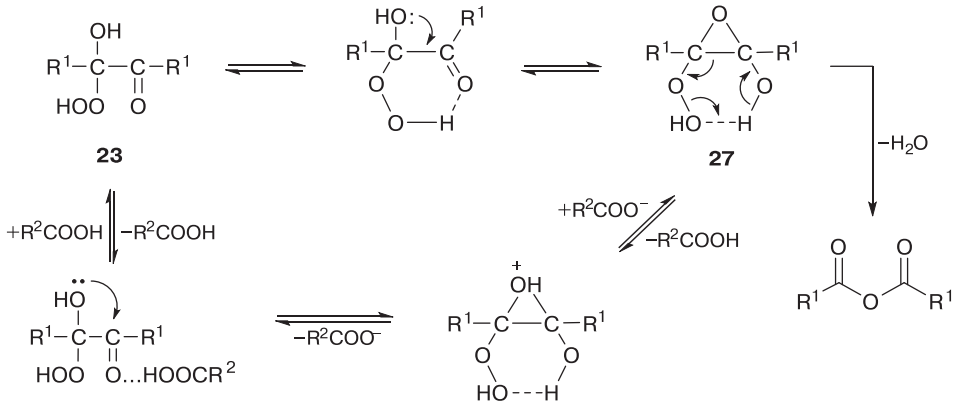
Cyclohexane-1,2-dione (**22**) is formed by both the free radical-induced decomposition of 2-hydroperoxycyclohexanone (**15**)[6,8,11,12,53] and the radical-chain oxidation of 2-hydroxycyclohexanone (see Schemes 18 and 19).[6,8,12,13,52] Routes of its further conversion are not clear. The problem is that cyclohexane-1,2-dione (**22**) exists predominantly in the monoenol form (2-hydroxycyclohex-2-enone (**29**)).[8,52] The liquid-phase oxidation of monoenol **29** in chlorobenzene at 373 K resulted in resin-like products and carbon oxides.[52] Indeed, it is difficult to imagine the formation of the known products of cyclohexane oxidation from two possible peroxide intermediates of oxidation of compound **29**, compounds **30** and **31**,[52] and the presence of the double bond assumes the possibility of polymerization processes to occur.

Meanwhile, cyclohexane-1,2-dione **22** and monoenol **29** can be involved in nonchain oxidation transformations.[8,52–55] Adipic anhydride (79.1%) and adipic acid

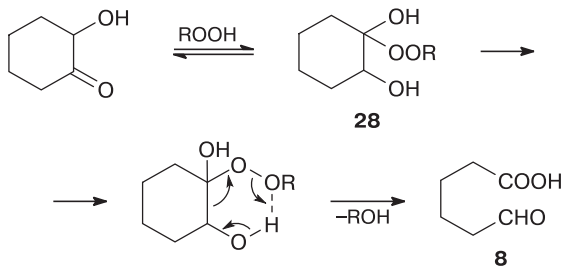
Scheme 20



Scheme 21

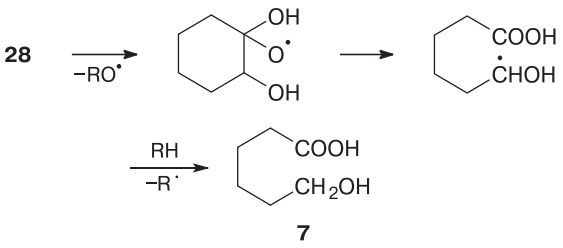


Scheme 22



R = H, alkyl, acyl

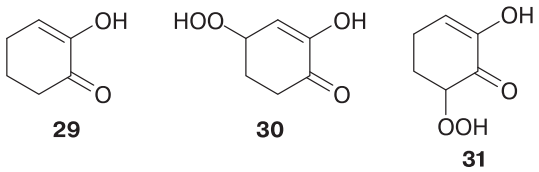
Scheme 23



(**9**) (6.3%) were found to be formed due to the oxidation of monoenol **29** by *tert*-butyl hydroperoxide.[53] It is shown for non-enolized hexadecane-8,9-dione (Fig. 3) that α-diketones are nearly quantitatively transformed with the carbon chain destruction in the presence of peroxide products of hydrocarbon oxidation (H_2O_2, hydroperoxides, and peroxy acids).[54,55] The nucleophilic addition of H_2O_2 to one of the carbonyl groups of α-diketone affords α-hydroperoxy-α-hydroxy ketone (analog of compound **23**), which is transformed, similarly to compound **23**, into anhydride or two acid molecules (see Schemes 20—22).[8,43]

In the case of hydroperoxides or peroxy acids, α-alkylperoxy-α-hydroxy and α-acylperoxy-α-hydroxy ketones, respectively, are formed.[8,43] They are transformed *via* Schemes 19 and 20.[8,43]

Thus, there are several parallel and consecutive-parallel channels of formation of caproic, 6-hydroxyhexanoic (**6**), 6-oxohexanoic (**8**), and adipic (**9**) acids, which



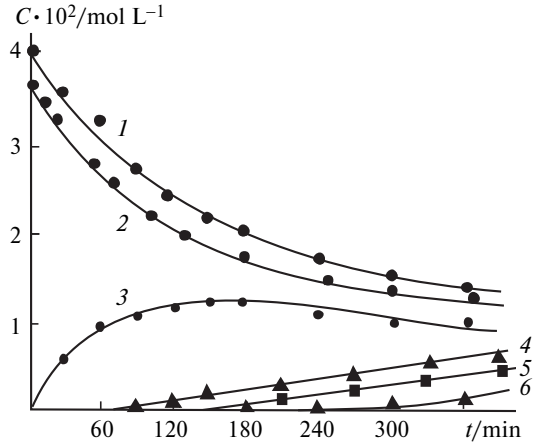


Fig. 3. Kinetics of the reaction of hexadecane-8,9-dione with *tert*-butyl hydroperoxide (296 K, cyclohexane). Consumption: *tert*-butyl hydroperoxide (*1*) and hexadecane-8,9-dione (*2*); accumulation: 9-*tert*-butylperoxy-9-oxy-8-hexadecanone (*3*), caprylic anhydride (*4*), caprylic acid (*5*), and *tert*-butyl peroxycaprylate (*6*).

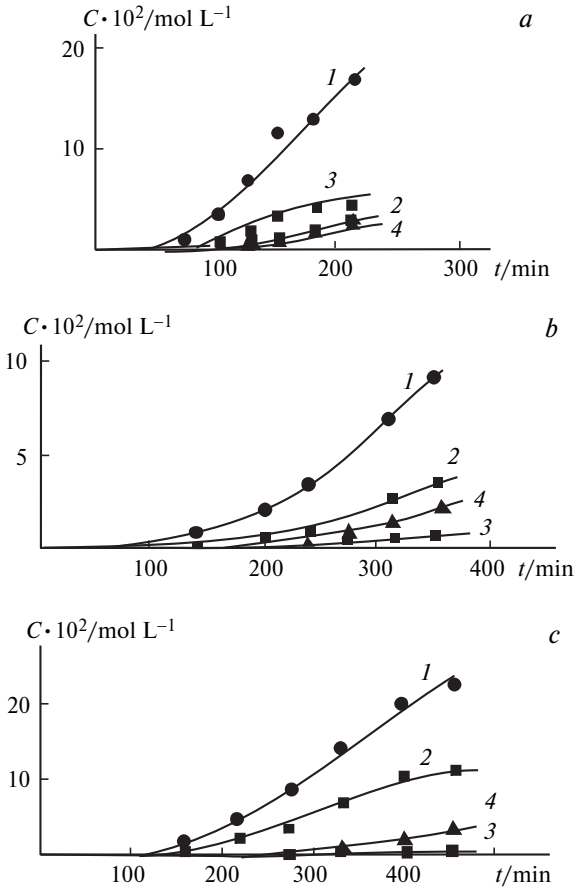


Fig. 4. Kinetic curves of accumulation of the following products of cyclohexanone oxidation (393 K, chlorobenzene): adipic (*1*), 6-oxohexanoic (*2*), 6-hydroxyhexanoic (*3*), and glutaric (*4*) acids in the presence of cobalt(II) naphthenate ($1.6 \cdot 10^{-3}$ mol L^{-1}) (*a*) and chromium(III) naphthenate ($1.6 \cdot 10^{-3}$ mol L^{-1})) (*b*) and without catalyst (*c*).

not always can be distinguished. Table 3 generalized the results of Figs 2 and 4 and the published data[15,19,22] on the influence of the conversion, oxidation conditions, and catalyst on the relative content of acids **6**, **8**, and **9**.

The data in Table 3 show that the relative content of 6-hydroxyhexanoic acid (**7**) decreases substantially on going from the oxidation of cyclohexane to cyclohexanone oxidation. This possibly evidences in favor of the formation of a considerable portion of compound **7** from cyclohexyloxyl radical **1** in the step of cyclohexyl hydroperoxide decomposition or during cyclohexanol oxidation. The second possibility is more preferable, because 1-hydroxycyclohexyloxyl radical **13** decomposes more readily with

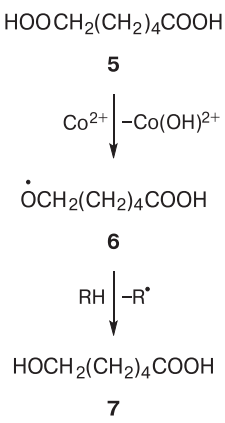
Table 3. Influence of the conversion and oxidation conditions on the relative content of 6-hydroxyhexanoic (**6**), 6-oxohexanoic (**8**), and adipic (**9**) acids (mol.% of their total content (Σ[RCOOH])) during the oxidation of cyclohexane, cyclohexanone, and 2-hydroxycyclohexanone

Substrate	Oxidation conditions	Σ[RCOOH]/mol L^{-1}						Reference
		0.05			0.10			
		6	**8**	**9**	**6**	**8**	**9**	
Cyclohexane	423 K	35.0	23.3	41.7	30.3	27.4	42.3	—
Cyclohexane	Cobalt(II) naphthenate (0.85 mmol L^{-1}), 423 K	41.1	21.0	37.9	29.3	20.9	49.8	—
Cyclohexanone	Chlorobenzene, 393 K	1.7	40.0	58.3	3.9	28.8	67.3	15
Cyclohexanone	Cobalt(II) naphthenate (1.6 mmol L^{-1}), chlorobenzene, 393 K	23.8	4.8	71.4	20.0	8.0	72.0	15
Cyclohexanone	Chromium(III) naphthenate (1.6 mmol L^{-1}), chlorobenzene, 393 K	2.0	25.5	72.5	4.1	24.5	71.4	19
2-Hydroxycyclohexanone*	Methyl ethyl ketone, 393 K	9.4	13.6	77.0	—	—	—	22
		(21.2)	(7.3)	(71.5)	—	—	—	22

* The relative contents of acids **6**, **8**, and **9** taking into account ε-caprolactone are given in parentheses.

C—C bond destruction than cyclohexyloxyl radical **1**,[8,42] and the formation of 6-hydroxyhexanoic acid (**7**) from radical **13** requires a less number of steps. It is noteworthy that the content of 6-hydroxyhexanoic acid (**7**) increases during cyclohexanone oxidation in the presence of the cobalt (but not chromium) catalyst (see Table 3). Since in the presence of the cobalt catalyst the yield of 6-oxohexanoic acid (**8**) decreases simultaneously with an increase in the content of 6-hydroxyhexanoic acid (**7**), it can be assumed that cobalt(II) naphthenate facilitates the homolytic decomposition of hemiperketal **17** with the formation of radical **13** and the transformation of 6-hydroperoxyhexanoic acid (**5**) to 6-hydroxyhexanoic acid (**7**) rather than to 6-oxohexanoic acid (**8**) (Scheme 24). Similar transformations (see Scheme 24) provide a higher yield of cyclohexanol over that of cyclohexanone in the industrial process of cyclohexane oxidation.[1,8,45]

Scheme 24



For non-catalyzed and catalyzed by cobalt(II) naphthenate cyclohexane oxidation, the relative content of 6-hydroxyhexanoic acid (**7**) decreases with the simultaneous increase in the relative content of adipic acid (**9**) with an increase in the oxidation depth (see Fig. 2, Table 3). This is a necessary but insufficient proof for a substantial value of the consecutive transformation of 6-hydroxyhexanoic acid (**7**) to 6-oxohexanoic (**8**) and adipic (**9**) acids. Oxidized cyclohexane (see Figs 1 and 2, *a*, *b*) contains adipic anhydride and monocyclohexyl adipinate. The latter is formed only during alcoholysis of adipic anhydride by cyclohexanol (see below)[24,25] and, hence, the content of ester reflect the amount of the formed adipic anhydride. As mentioned above, adipic anhydride is formed in parallel with adipic acid (**9**) in the course of the radical-chain oxidation of 2-hydroxycyclohexanone. In this case, the amount of adipic acid (**9**) is larger, as a rule, than the amount of adipic anhydride.[8,15—22] It follows from the data on the kinetics of accumulation of adipic acid (**9**) and monocyclohexyl adipinate (see Fig. 2) that a significant amount of adipic acid is formed from 2-hydroxycyclohexanone even at a low conversion of cyclohexane. This assumption is also confirmed by the estimation calculation of the relative rates of the reactions of the products of cyclohexane oxidation with cumylperoxyl radicals and *tert*-butylperoxyl radicals (Tables 4 and 5). The known kinetic data[56—58] were used in the calculation.

The oxidation rate of the *i*th organic compound is determined by the equation $W_i = k_{pi}^{ov}[C_i][RO_2^{\bullet}]$, and the oxidation rate of the *i*th organic compound referred to the rate of cyclohexane oxidation is determined by the equation $W_i/W_{ch} = k_{pi}^{ov}[C_i]/k_{pch}^{ov}[C_{ch}]$, where k_{pi}^{ov} and k_{pch}^{ov} are the overall rate constants of chain propagation of the *i*th compound and cyclohexane, respectively (L mol^{-1} s^{-1}); C_i and C_{ch} are the concentrations of the product and cyclohexane (mol L^{-1}).

The data on k_{pi}^{ov} for cyclohexane and some products of its oxidation in the reactions with cumyl- and *tert*-butylperoxyl radicals are available (see Tables 4 and 5). For 6-oxohexanoic acid (**8**), k_{pi}^{ov} was accepted equal to that of butanal.[58] For 6-hydroxyhexanoic acid (**7**), data on k_{pi}^{ov} in the reactions with the indicated radicals are lacking.[57] It is known that at 403 K the partial constants for the reactions of the secondary hexadecylperoxyl radical with the α-CH bonds of octan-2-ol and decanol are equal to 20.7 and 15.1 L mol^{-1} s^{-1}, respectively.[57] Based on these data, we estimated the ratio of overall rate constants of the reactions for the primary and secondary alcohols to be equal to $2 \cdot 15.1/1 \cdot 20.7 = 1.46$. The k_{pi}^{ov} value equal

Table 4. Relative rates of the reactions of the products formed upon cyclohexane oxidation (423 K, Δ[RH] = 0.6 mol L^{-1}) with cumylperoxyl radical at 358 K without catalyst and catalyzed by cobalt(II) naphthenate

Product	k^{ov}_{pi} /L mol^{-1} s^{-1}	Without catalyst		Co^{II} naphthenate	
		C_i/mol L^{-1}	W_i/W_{ch}	C_i/ mol L^{-1}	W_i/W_{ch}
Cyclohexane	0.21[56]	7.40	1	7.40	1
Cyclohexanol	6.50[56]	0.21	0.88	0.30	1.25
Cyclohexanone	0.58[56]	0.34	0.13	0.24	0.09
2-Hydroxycyclohexanone	41.70[51]	0.011	0.30	0.010	0.27

Note. Here and in Table 5, k^{ov}_{pi} is the overall rate constant of chain propagation of the product, C_i is the concentration of the product, and W_i and W_{ch} are the oxidation rates of the product and cyclohexane, respectively.

Table 5. Relative rates of the reactions of the products formed upon cyclohexane oxidation (Δ[RH] = 0.6 mol L^{-1}) with *tert*-butylperoxyl radical without catalyst and catalyzed by cobalt(II) naphthenate

Product	T/K	k^{ov}_{pi} /L mol^{-1} s^{-1}	Without catalyst		Co^{II} naphthenate	
			C_i/mol L^{-1}	W_i/W_{ch}	C_i/mol L^{-1}	W_i/W_{ch}
Cyclohexane	333	0.046[a]	7.4	1	7.4	1
	423	2.2[a] [57]		1		1
Cyclohexanol	333	0.43[40]	0.21	0.260	0.300	0.380
Cyclohexanone	333	0.22[40]	0.34	0.220	0.240	0.160
6-Hydroxyhexanoic acid (**7**)	333	0.63	0.014	0.026	0.016	0.029
6-Oxohexanoic acid (**8**)	333	2.19[b]	0.01	0.064	0.007	0.046
	423	69.2[b]		0.043		0.030

[a] Calculated from the published data: log$A$ = 10.4, E = 81 500 J mol^{-1}.[57]
[b] Calculated from the published data: log$A$ = 3.7, E = 15 050 J mol^{-1} for butanal.[58]

to 1.46k_{pi}^{ov} for cyclohexanol was used to estimate the rate of oxidation of 6-hydroxyhexanoic acid (**7**).

An analysis of the data in Tables 4 and 5 shows that for non-catalyzed and catalyzed by cobalt naphthenate cyclohexane oxidation (conversion of cyclohexane (Δ[RH]) = = 0.6 mol L^{-1} (~6 mol.%)) the oxidation rate of 2-hydroxycyclohexanone, which is presented in the reaction medium, is by an order of magnitude higher than the oxidation rates of 6-hydroxy- and 6-oxohexanoic acids (see Tables 4 and 5). Therefore, the main amount of adipic acid is formed from 2-hydroxycyclohexanone during cyclohexane oxidation.

The contribution of the radical-chain oxidation of 6-hydroxy- (**7**) and 6-oxohexanoic (**8**) acids to the formation of adipic (**9**) acid during cyclohexane oxidation remains insufficiently clear. They are accumulated in parallel in the course of the oxidation of cyclohexanone (see Fig. 4)[15,19] and 2-hydroxycyclohexanone[22] as for the oxidation of cyclohexane (see Fig. 2). Based on the studies of the liquid-phase oxidation of 6-oxohexanoic acid (**8**) in chlorobenzene, the authors[59] concluded that in cyclohexanone oxidation they are the final products rather than the intermediates. The reason for the low oxidizability of 6-oxohexanoic acid (**8**) in the model experiment[59] is insufficiently clear. This can partially be explained by the fact that the carboxyl groups of 6-oxohexanoic acid (**8**) solvate peroxyl radicals and thus decrease their reactivity.[10] It is known that the rate of caprylic aldehyde oxidation in acetic acid is by eight times lower than that in a chlorobenzene solution.[60]

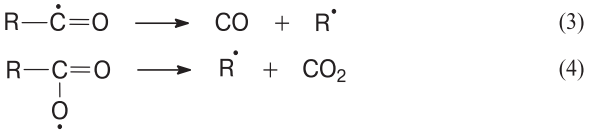
Therefore, the contribution of various channels of formation of bifunctional acids C_6 should depend on the depth of cyclohexane oxidation.[42] The main amount of adipic acid (**9**) is formed in the steps following the formation of 2-hydroxycyclohexanone.[6,8,13–22,43]

Formation of formic, valeric, and bifunctional C_5 acids

As already mentioned, a significant number of carboxyl-containing compounds with the number of carbon atoms less than six is formed under the industrial conditions of cyclohexane oxidation (see Fig. 1). In the model experiments of cyclohexane oxidation, a considerable part of these compounds is not formed in appreciable amounts (see Fig. 2). This is explained, first, by the fact that recurrent cyclohexane (about 90%) containing a series of oxygen-containing compounds, including those with the number of carbon atoms less than six, is used in the industrial process. Therefore, in this section we consider only the carboxyl-containing compounds that were found among the products of oxidation of cyclohexanol and cyclohexanone.

Theoretically there are many channels of formation of valeric and bifunctional C_5 acids in the course of cyclohexane oxidation. Among them we can mention the multistep destructive transformations of radicals **1**, **13**, **18**, and **24**, including oxidative transformations of aldehyde, carboxyl, and anhydride groups.[1–4,8,11,29–31,42,61] The cyclohexanone oxidation at the C(3)—H bonds[11] and C(2)—H and C(6)—H bonds[62] was proposed to explain the formation of glutaric acid upon cyclohexanone oxidation. The formation of carboxylic C_5 acids assumes carbon chain shortening due to decarbonylation and decarboxylation reactions (Scheme 25), as well as due to the elimination of formaldehyde or formic acid molecules (see below Scheme 26).

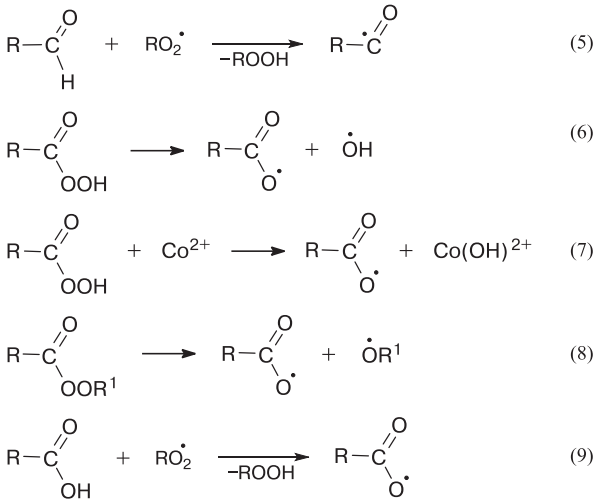
Scheme 25



Acyl radicals formed by the homolytic decay of 2-oxoperoxides (see Schemes 17 and 19) and radical-chain oxidation of aldehyde groups (Scheme 26, reaction (5)) undergo decarbonylation,[1,8,11,42] whereas acyloxyl radicals formed by the homolytic or catalytic decomposition of

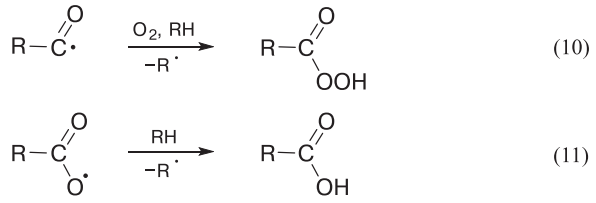
peroxy acid (Scheme 26, reactions (6) and (7)),[1,8,11,42] homolytic decay of peroxy esters (Scheme 26, reaction (8)),[8,63,64] and by hydrogen atom detachment from carboxyl groups by peroxyl radicals (Scheme 26, reaction (9)) undergo decarboxylation.[11]

Scheme 26



An alternative to reaction (3) in Scheme 25 is the reaction of the acyl radical with oxygen and substrate to form peroxy acids (Scheme 27, reaction (10)), and the reaction with the substrate to give carboxylic acid (Scheme 27, reaction (11)) is an alternative to reaction (4) in Scheme 25.[6,8,11]

Scheme 27



The occurrence of the reactions shown in Scheme 25 is favored by the temperature increase and stability of radical R$^{\bullet}$, whereas the reactions shown in Scheme 27 are facilitated by the presence of a reactive solvent. Based on the introduction of ^{14}C(1),^{14}C(6)-labeled adipic acid into oxidized cyclohexanone, the authors[65] concluded that less than 1% adipic acid underwent tandem oxidation—decarboxylation under the experimental conditions. The amount of CO formed by cyclohexanone oxidation is substantially lower than that of CO_2.[11] This indicates that the acyl radicals of oxidized ketone are more prone to the reactions of type (10) (see Scheme 27) leading to peracyl radicals and then to peroxy acids. The problems of decarbonylation and decarboxylation are considered more comprehensively and in more detail in the monograph[11] and review.[8]

A principal possibility of formation of some amounts of valeric and bifunctional C_5 acids in the steps of transformation of cyclohexyloxyl and 1-hydroxycyclohexyloxyl radicals cannot be excluded. However, the main attention should be given to the channels of forming these acids from 2-oxocyclohexyl radical and 6-oxohexanoic acid (**8**) generated mainly in the steps following the oxidation of cyclohexanone. The proposed mechanisms should be consistent with the following experimental data.

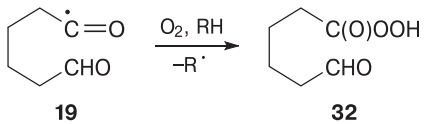
(1) When cyclohexanone ^{14}C- or ^{13}C-labeled at the carbonyl groups is oxidized (373 K, cobalt acetate, acetic acid), 91% labeled glutaric acid are formed.[61]

(2) Up to 58% active carbon dioxide (of its total content) is evolved in the initial steps of oxidation (393 K) of cyclohexanone ^{14}C-labeled at the CO group, and the fraction of $^{14}CO_2$ decreases to 43% with an increase in the reaction depth.[11]

It follows from the last assertion that the carbon chain shortening during cyclohexanone oxidation with carbon dioxide evolution proceeds *via* more than one channel. If the carbonyl carbon atom of cyclohexanone almost is not "lost" upon the formation of glutaric acid, then this carbon atom should eliminate upon the formation of other oxidation products with the number of carbon atoms less than six.

According to the most popular concepts, 2-oxocyclohexyloxyl radical **18** decomposes with carbon chain destruction and formation of 1,6-dioxohexyl (**19**) or 5,6-dioxohexyl (**20**) radicals (see Scheme 17). Under the conditions of cyclohexanone oxidation, radical **19** is transformed, most probably, into 6-oxoperoxyhexanoic acid (**32**) (Scheme 28).

Scheme 28

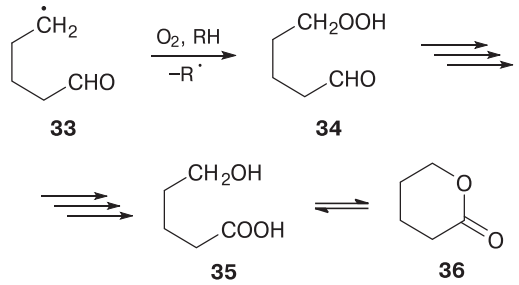


19 **32**

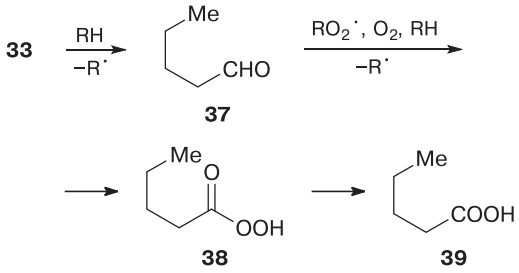
The shortening of the chain of 1,6-dioxohexyl radical **19** can be resulted from either its direct decarbonylation (reaction of type (3) in Scheme 25), or the homolytic decomposition of peroxy acid **32** at the O—O bond followed by the decarboxylation of the acyloxyl radical (reactions of type (6) or (7) in Scheme 26 and type (4) in Scheme 25). The 5-oxopentyl radical (**33**) formed in both cases can successively react with the substrate and oxygen to form 5-oxopentyl hydroperoxide (**34**) (Scheme 29). The subsequent multistep transformations of peroxide **34** can lead to 5-hydroxypentanoic acid (**35**) and then to δ-valerolactone (**36**) (see Scheme 29).

The competitive reaction of radical **33** with the substrate affords valeric aldehyde (**37**), whose radical-chain

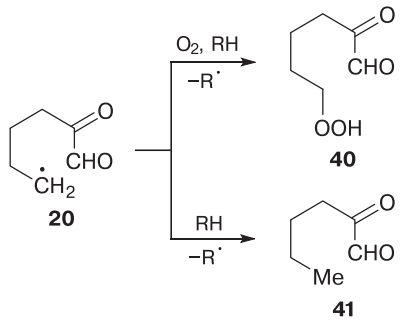
Scheme 29



Scheme 30



Scheme 31



oxidation results in peroxy acid **38** and then in valeric acid (**39**) (Scheme 30).

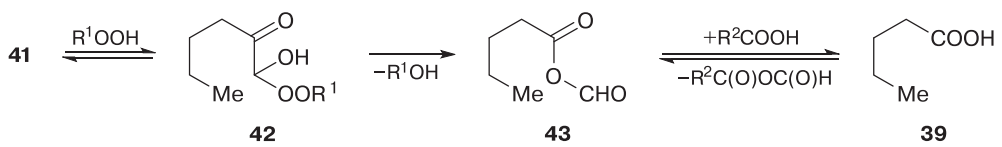
5,6-Dioxohexyl radical **20**, as well as radical **19**, can either successively react with oxygen and substrate to give 6-hydroperoxy-2-oxohexanal (**40**), or can detach hydrogen from the substrate to form 2-oxohexanal (**41**) (Scheme 31).

The further transformations of compounds **40** and **41** (as α-dicarbonyl compounds) can be related to the reactions with hydroperoxides, H_2O_2, and peroxy acids (see above). In the case of oxidation of compound **40** with hydroperoxides, α-hydroxy-α-peroxy ketone **42** is formed and decomposes *via* the pericyclic mechanism (see Scheme 21) to mixed anhydride of formic and valeric acids **43**. The transacylation of the latter with carboxylic acids results in valeric acid **39** (Scheme 32).

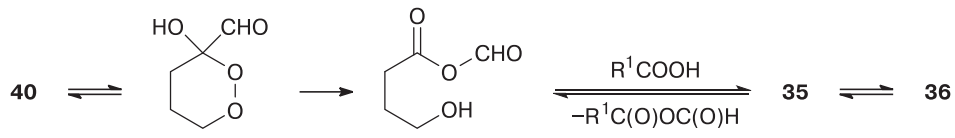
In the case of 6-hydroperoxy-2-oxohexanal (**40**), the intramolecular version of hydroperoxide group addition (Scheme 33) is possible along with the intermolecular version (see Scheme 32).

It is known that 5-hydroxycarboxylic acids (unlike 6-hydroxycarboxylic[66]) are fairly readily transformed into stable δ-lactones. For example, the conversion of δ-caprolactone into the hydroxy acid under reflux with a double volume of water for 1 h is only 35%.[66] Therefore, it should be expected that the equilibrium of the ring closure of 5-hydroxypentanoic acid **35** to δ-valerolactone in a hydrocarbon medium is shifted to the left. Obviously, that is why, no free hydroxy acid **35** was observed in the products of oxidation of cyclohexane and its oxygen-containing derivatives. Data on the oxidizability of δ-valerolactone under the radical-chain process conditions are lacking. 4-Oxobutanoic acid, succinic acid, and succinic anhydride were found among the products of autooxidation of γ-butyrolactone at 419 K.[67] According to the published data,[65] at 393 K ε-caprolactone is not oxidized in the absence of initiating additives. The data on the relative reactivity (compared to that of the CH bond of cyclohexane) of the CH bonds in cyclohexanol, cyclohexanone, cyclohexyl acetate, and methyl hexanoate in the reactions with *tert*-butylperoxyl radicals are presented in Fig. 5.[5,37,40,68,69] If assuming that the same regularities should be fulfilled for lactone oxidation as for the oxidation

Scheme 32



Scheme 33



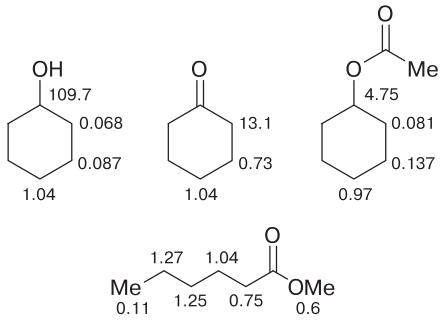
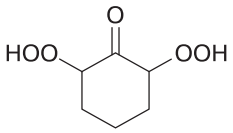


Fig. 5. Relative reactivity of the C—H bonds in cyclohexanol, cyclohexanone, cyclohexyl acetate (all at 333 K), and methyl hexanoate (at 373 K) in the reactions with *tert*-butylperoxyl radicals compared to the reactivity of the C—H bonds in cyclohexane.

of esters, then these data indicate indeed the lower oxidizability of lactones not only compared to cyclohexanone but also to cyclohexane. At 333 K, the overall constant for the reaction of a cyclohexyl acetate with *tert*-butylperoxyl radical is by 1.5 times lower than the corresponding value for cyclohexane.[5] Therefore, the question about the possibility of transforming δ-valerolactone into glutaric acid under the conditions of cyclohexane oxidation remains unanswered.

As already mentioned, the schemes including the formation of 2,5-dihydroperoxycyclohexanone (**44**)[62] and oxidation of ketone at the β-CH bonds[11] were proposed to explain the routes of glutaric acid formation during cyclohexanone oxidation.

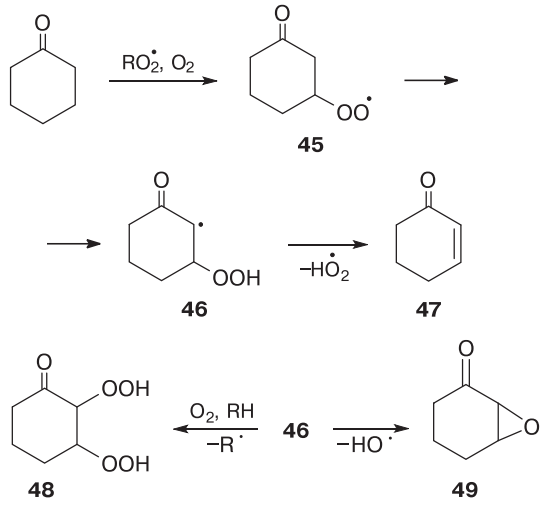


44

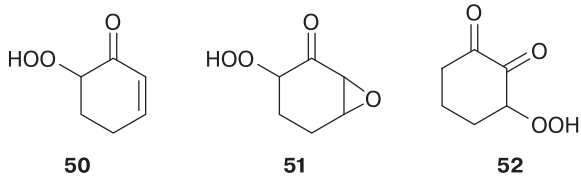
Although the formation of compound **44** due to intramolecular chain transfer along the reaction cycle including the carbonyl group (proved for the oxidation of dibenzyl ketone[70]) is real, its transformation into acids C_5 will inevitably result in the "loss" of the carbon atom of the carbonyl group. Therefore, this approach is inappropriate for the channel of glutaric acid formation to be significant (see above). The oxidation of cyclohexanone at the β-CH bonds (positions 3 and 5) does not lead, as it was accepted earlier, to 3-hydroperoxycyclohexanone. 2-Oxo-5-hydroperoxycyclohexyl radical **46** resulted from the intramolecular isomerization of 3-oxocyclohexylperoxyl radical **45** is transformed into 2-cyclohexenone (**47**), 2,3-dihydroperoxycyclohexanone (**48**), and 2,3-epoxycyclohexanone (**49**) (Scheme 34).[6,40]

According to the available data on the reactivity of the cyclohexane derivatives (systematized in the review[5]) and Scheme 34, it is most probable that the further oxidation

Scheme 34



of compounds **47** and **49** will proceed at position 5 to give hydroperoxides **50** and **51**, respectively. At the same time, the decomposition of dihydroperoxide **48** induced by peroxyl radicals can afford diketohydroperoxide **52**.



It is doubtless that of peroxides **50**, **51**, and **52** only compound **52** can be transformed into 5-oxopentanoic and glutaric acids with retention of the carbon atom of the carbonyl group. Since the reactivity of the β-CH bonds of cyclohexanone is lower than that of the CH bonds of cyclohexane (see Fig. 5) and the fraction of diperoxy ketone **48** in the overall content of compounds **47**, **48**, and **49** does not exceed 14%, the considered channel of glutaric acid formation can hardly be the main one.

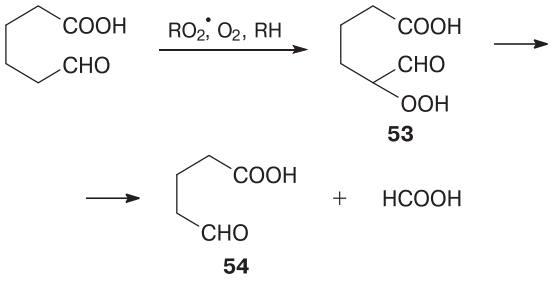
The radical-chain oxidation of 6-oxohexanoic acid (**8**) at the C(5)—H bonds with the formation of 5-hydroperoxy-6-oxohexanoic acid (**53**) can be an important source of 5-oxopentanoic and glutaric acids. The decay of acid **53** *via* the dioxetane mechanism (see Scheme 14) leads to formic and 5-oxopentanoic (**54**) acids (Scheme 35). This reaction was used to explain the formation of formic and 5-oxopentanoic acids found upon the oxidation of cyclohexane (see Fig. 1), cyclohexanol, and cyclohexanone (Table 6).

If accepting that the overall rate constant for the reaction of acid **8** with *tert*-butylperoxyl radicals (k^{ov}_p) at 333 K is 2.19 L mol^{-1} (see Table 5) and the partial rate constant (k^H_p) of the reaction of the same radical with the C(5)—H bonds of acid **8** is equal to k^H_p for the C(2)—H bond of cyclohexanone (k^H_p = 0.05 L mol^{-1} s^{-1}),[5] then the con-

Table 6. Absorbed oxygen and contents of selected products in oxidized cyclohexanol and cyclohexanone[42]

Parameter	Concentration/mol L^{-1}	
	Cyclohexanol	Cyclohexanone
Absorbed oxygen	$82.1 \cdot 10^{-3}$	$44.6 \cdot 10^{-3}$
Formic acid	$2.1 \cdot 10^{-3}$	$3.25 \cdot 10^{-3}$
Cyclohexyl formate	$2.38 \cdot 10^{-3}$	—
Glutaric acid	$0.58 \cdot 10^{-3}$	$0.41 \cdot 10^{-3}$
5-Oxopentanoic acid	$1.25 \cdot 10^{-3}$	$1.31 \cdot 10^{-3}$
Adipic acid	$7.52 \cdot 10^{-3}$	$3.32 \cdot 10^{-3}$
Mono- and dicyclohexyl adipinates	$0.97 \cdot 10^{-3}$	—
6-Oxohexanoic acid	$0.82 \cdot 10^{-3}$	$1.4 \cdot 10^{-3}$

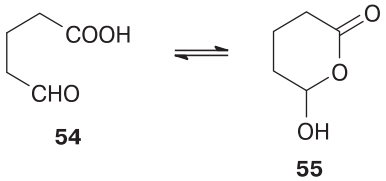
Scheme 35



tribution of the reaction of the *tert*-butylperoxyl radical with the C(5)—H bonds of acid **8** will be 4.6% of the overall transformation of the oxo acid. The contribution of the reactions shown in Scheme 35 (due to a decrease in selectivity) should increase on going to more reactive secondary peroxyl radicals and at higher temperatures.

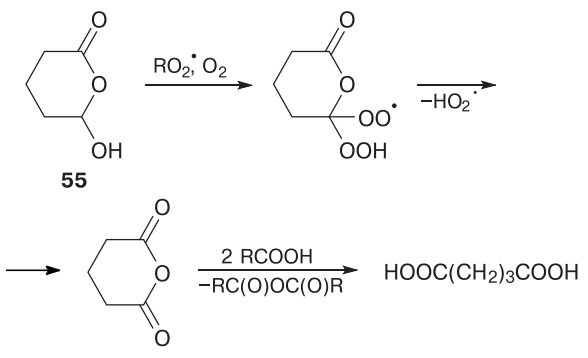
It could be expected that 5-oxopentanoic acid would be oxidized, in turn, *via* Scheme 35 to form formic and 4-oxobutanoic acids. However, the last compound was not found in the oxidation products of cyclohexane, cyclohexanol, and cyclohexanone.[41] This was explained by the reversible ring closure of oxo acid **54** leading to 6-hydroxytetrahydro-2*H*-pyran-2-one (**55**) (Scheme 36).[41]

Scheme 36



This ring closure (ring-chain tautomerism) is well known for 4- and 5-oxocarboxylic acids.[71] The ring closure of oxo acid **54** to compound **55** is accompanied by a change in the reactivity of a series of CH bonds in the reactions with peroxyl radicals. As a result of reaction **54** → **55**, the aldehyde group is transformed into the hemiacylal group (see Scheme 36). This decreases the reactivity of the whole molecule (see Fig. 5 and Table 5) with the CH bonds responsible for formic acid formation *via* Scheme 35 being the most deactivated. It is necessary to take into account that the C(4)—H bonds of oxo acid **54** become the C(5)—H bonds of compound **55**. The oxidation rate of a mixture of compounds **54** and **55** formed according to Scheme 36 should be lower than the oxidation rate of individual oxo acid **54** taken in the concentration equal to the sum of concentrations of compounds **54** and **55** in the mixture due to a decrease in the effective concentration of aldehyde groups. The oxidation of hydroxylactone **55** should proceed more selectively than the oxidation of oxo acid **54** because of the aforementioned deactivation of the C(5)—H bonds. The oxidation of compound **54** can result in glutaric acid *via* the reactions similar to those presented in Scheme 30. Published data on the reactivity and mechanisms of transformation of compound **55** under the radical-chain process conditions are lacking. Based on the data presented above, we can expect that the C(6)—H bond should predominantly undergo oxidation and its reactivity should be close to that of the C(1)—H bond of cyclohexanol or even somewhat higher than it (see Fig. 5). It is substantial that compound **55** will be oxidized more easily than δ-valerolactone. The result of the radical-chain transformations of pyranone **55** can be glutaraldehyde and then glutaric acid (Scheme 37).

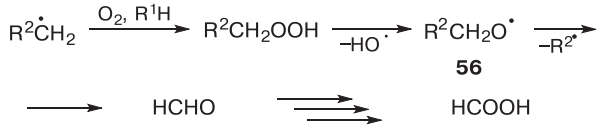
Scheme 37



The channel proposed for the formation of glutaric acid does not contradict the known experimental data. In particular, according to the kinetic studies (see Fig. 4), glutaric acid is formed, most likely, from 6-oxohexanoic acid (**8**) (see Fig. 4). The higher yield of formic acid in the oxidation of cyclohexanone compared to that for cyclohexanol oxidation correlates well with an increase in the content of 6-oxohexanoic acid (**8**) on going from the oxidized alcohol to oxidized ketone (see Table 6). The routes proposed for glutaric acid formation make it possible to completely retain in its structure the carbon atom of the carbonyl group of cyclohexanone and are consistent with the data of the kinetic study, which assumed that glutaric and valeric acids are formed from different precursors.[11,65,72]

The channels of formation of formic acid or its mixed anhydrides presented in Schemes 32, 33, and 35 have some advantages over those proposed in the monograph.[1] The mechanisms presented earlier[1] include either the successive decarboxylation of monocarboxylic acids, or radical-chain transformations of the initially formed carbon-centered radicals followed by the fragmentation of oxyl radical **56** (Scheme 38). They are characterized by the multistep formation of formic acid from monocarboxylic acids and imply its consecutive rather than parallel accumulation as it is observed experimentally (see Fig. 1).

Scheme 38

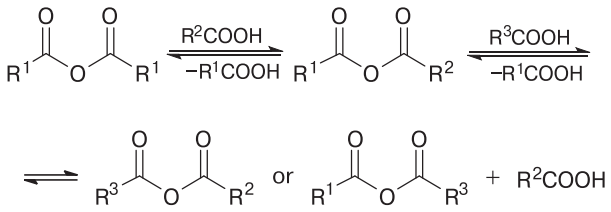


The role of carboxylic acid anhydrides in cyclohexane oxidation

In the course of cyclohexane oxidation, carboxylic acid anhydrides (predominantly of adipic acid) are formed in the step of radical-chain oxidation of 2-hydroxycyclohexanone (see Schemes 18 and 21), 1,2-cyclohexane-1,2-dione (see above), and other 1,2-dicarbonyl compounds with hydrogen peroxide and peroxy acids (see Schemes 32 and 33), as well as possibly by the oxidation of hydroxylactones (see Scheme 37) and lactones. When the reaction medium contains mono- and dicarboxylic acids, the fast transacylation of adipic and other anhydrides with carboxylic acids occurs and results in mixed anhydrides containing residues of all carboxylic acids present in the oxidation products[6,8,23–25,41,43,55] (Scheme 39).

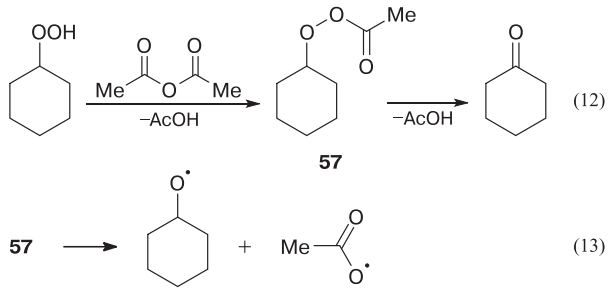
Being highly reactive, mixed carboxylic acid anhydrides react with water, alcohols, and hydroperoxides that are present in the reaction mixture.[8,23,43] The reaction of

Scheme 39



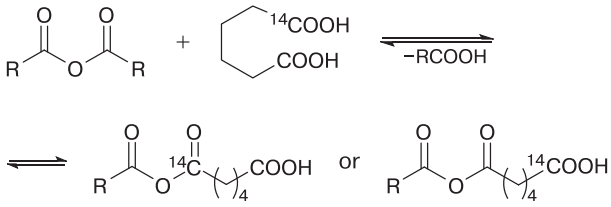
cyclohexyl hydroperoxide with acetic anhydride at 373 K affords cyclohexyl peroxyacetate (**57**) decaying *via* the pericyclic mechanism to cyclohexanone and acetic acid (Scheme 40, reaction (12)) or *via* the homolytic route (about 15%) to form cyclohexyloxyl and acetyloxyl radicals (Scheme 40, reaction (13)).[6,63]

Scheme 40



If ^{14}C-labeled dicarboxylic acid is formed due to the oxidation of cyclohexanone ^{14}C-labeled at the carbonyl group, then its transacylation can equiprobably afford the anhydride ^{14}C-labeled at the functional group and non-labeled anhydride (Scheme 41).

Scheme 41

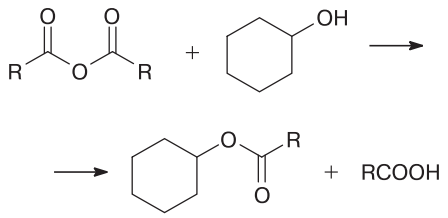


When a mixture of these anhydrides enters successively into reactions (12) and (13) (see Scheme 40) and reaction (8) (see Scheme 26), then the decarboxylation of the corresponding acyloxyl radicals would give close amounts of ^{14}C-labeled and non-labeled carbon dioxide, as it was observed in the experiment.[11]

The most important channel of consumption of mixed anhydrides during cyclohexane oxidation is their reactions with cyclohexanol resulting in cyclohexyl esters of all

compounds containing carboxyl groups, including mono- and dicarboxylic acids[6,8,23,41,43,55] (Scheme 42).

Scheme 42



It was assumed[8,23] that the alcoholysis of mixed carboxylic acid anhydrides formed according to Scheme 39 equiprobably form esters of carboxylic acids present in the structure of mixed anhydrides. However, according to the data in Fig. 1, the ratio of concentrations of cyclohexyl formate and formic acid is fourfold higher than the ratio of concentrations of monocyclohexyl adipinate and adipic acid.[41] The phenomenon observed is well consistent with the known properties of mixed anhydrides of formic and acetic acid, whose alcoholysis predominantly affords formates.[73—76]

The kinetic parameters of the reaction of valeric anhydride with cyclohexanol in the presence of formic acid (*o*-dichlorobenzene, 333—373 K)[25] (Scheme 43) and without formic acid[77] were obtained. It was found that formic acid exerted no catalytic effect on the reactions shown in Scheme 31. The temperature dependences of the reaction rate constants are described by the following equations[25]:

$$\ln k_1 = (9.6\pm0.4) - (22\,300\pm300)/(RT),$$

$$\ln k_1 = (8.9\pm0.4) - (44\,400\pm900)/(RT),$$

$$\ln k_{-1} = (-0.7\pm0.1) - (22\,400\pm400)/(RT),$$

$$\ln k_2 = (24.3\pm1.0) - (89\,300\pm800)/(RT),$$

$$\ln k_2' = (14.6\pm2.1) - (69\,100\pm1200)/(RT),$$

$$\ln k_3 = (15.2\pm1.2) - (69\,500\pm800)/(RT).$$

A comparison of the values of constants k_2 and k_2' confirms the predominant formation of formates during alcoholysis of mixed anhydrides of formic acid.

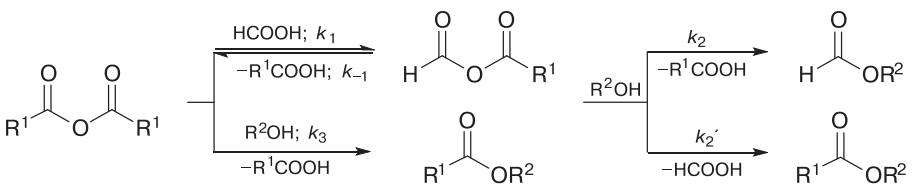
The data necessary for the quantitative estimation of the role of the alternative channel of formation of cyclohexyl esters of mono- and dicarboxylic acids (esterification reaction) were obtained by studying the kinetics of the reactions of cyclohexanol with formic, caproic, and adipic acids (*o*-dichlorobenzene, 423—463 K).[24]

It is shown for the industrial process of cyclohexane oxidation (see Fig. 1) that the rates of formation of all cyclohexyl esters *via* esterification reactions are significantly lower than the alcoholysis rates of mixed anhydrides.[24] For cyclohexyl formate, this rate is more than 25 000 times lower than the rate of its formation by alcoholysis of mixed anhydrides of formic acid. The contribution of esterification to the formation of mono- and dicyclohexyl adipinates is somewhat higher than the contribution to the formation of cyclohexyl formate, but even in this case it does not exceed 0.2%.[24] Since the esterification reaction is reversible, under certain conditions it can decrease the content of cyclohexyl esters formed upon the alcoholysis of carboxylic acid anhydrides.[24]

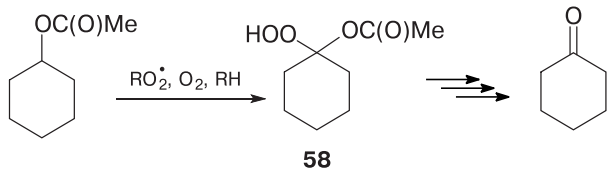
The routes of further transformation of cyclohexyl esters in the medium of oxidized cyclohexane remain insufficiently clear. The decreased reactivity of the alcohol moiety of cyclohexyl acetate and acyl group of methyl hexanoate compared to that of cyclohexane indicates that at the low conversion of cyclohexane cyclohexyl esters of mono- and dicarboxylic acids (probably, except for cyclohexyl formate) can conventionally be considered to be the final products. The partial rate constant for the reaction of the C(1)—H bond of the cyclohexyl moiety of cyclohexyl acetate with the *tert*-butylperoxyl radical is by five times higher than that for the CH bond of cyclohexane (see Fig. 5). Therefore, the C(1)—H bond will be oxidized first. The formed 1-acetoxycyclohexyl hydroperoxide (**58**) is probably capable of transforming into cyclohexanone[68,78] (Scheme 44).

Quantitative data on the oxidizability of the acyl moiety of formic acid esters are scarce. The oxidizability parameters are known[79] for the initiated oxidation (348 K, chlorobenzene) of cholesterol and its esters, being ($k_p(2k_t)^{-0.5}\cdot10^3$, $L^{0.5}$ $mol^{-0.5}$ $s^{-0.5}$) 5.36 for cholesterol, 6.35 for formate **59a**, 4.45 for acetate **59b**, 3.40 for propionate **59c**, 4.07 for butyrate **59d**, and 5.20 for pelargonate **59e**. If accepting that the rate constants of chain termination (k_t) are equal for all cholesterol esters, then the data presented indicate a higher reactivity of compound **59a** in

Scheme 43

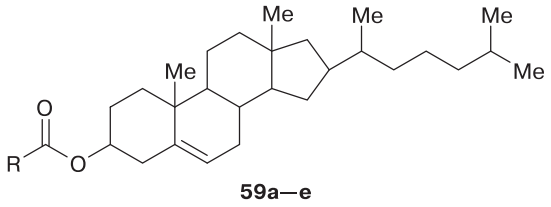


Scheme 44



58

the reactions with peroxyl radicals compared to other cholesterol esters.

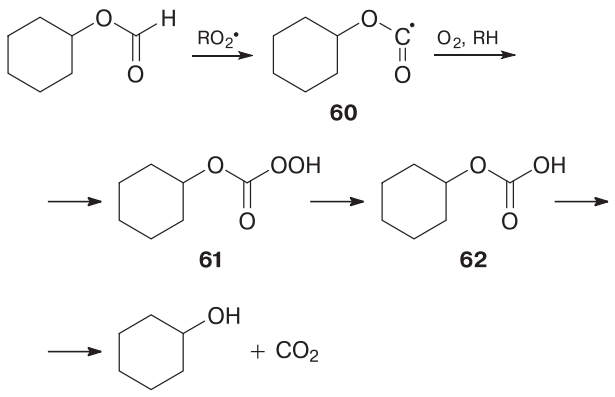


59a—e

59: R = H (**a**), Me (**b**), Pr (**c**), Bu (**d**), $Me(CH_2)_7$ (**e**)

Taking into account the deactivating effect of the electron-withdrawing acyl group on the reactivity of the alkoxyl moiety of ester compared to that of alcohol[5,78] (*cf.* the data for cyclohexanol and cyclohexyl acetate, Fig. 5), it can be assumed that the formyl group (being more electron-withdrawing) should deactivate ester to a higher extent than the acetyl group does. Therefore, we may conclude that the higher reactivity of formate **59a** compared to other cholesterol esters is caused by the possibility of oxidation of the CH bond of the formyl group (Scheme 45). Acyl radical **60** formed due to the hydrogen atom detachment from this bond can either undergo decarbonylation (decarboxylation), or can be transformed into peroxy acid **61** upon the reaction with oxygen and RH. Compound **61** can undergo thermal or catalytic decomposition[80] or can withdraw active oxygen, for example, by oxidizing carbonyl compounds and producing monocyclohexyl carbonate (**62**) and then cyclohexanol (see Scheme 45).

Scheme 45



The experimental data presented in the review were obtained using the procedures systematized in the reviews[81—84] that allow one to eliminate, to a significant extent, the distorting influence of peroxide and other labile compounds on the results of analytical determination of oxidation products.

Conclusion

Under the conditions of cyclohexane oxidation at 423 K, mono- and bifunctional carboxylic acids are formed due to multistep consecutive-parallel transformations. All of them assume the destruction of the cyclohexane ring that can proceed *via* radical and nonradical mechanisms. The initial molecular product, cyclohexyl hydroperoxide, decomposes *via* the homolytic and nonradical route to cyclohexanol and cyclohexanone. Cyclohexyl hydroperoxide is transformed into cyclohexanol *via* cyclohexyloxyl radical **1**, which is partially isomerized with carbon chain destruction to 6-oxohexyl radical **2**. Cyclohexanol and cyclohexanone are substantially more reactive than cyclohexane and are already involved in the initial radical-chain and nonchain oxidation transformations to form 1-hydroxy-1-hydroperoxy- (**11**) and 1-hydroxy-1-cyclohexylperoxycyclohexane (**12**). The homolytic decomposition of these peroxides gives 1-hydroxycyclohexyloxyl radical **13**, which can isomerize to 5-carboxypentyl radical **14**. Radicals **2** and **14** are the main sources of caproic and 6-hydroxyhexanoic (**7**) acids formed in the course of cyclohexane oxidation. The role of radical **14** should increase with an increase in the depth of cyclohexane conversion. Its precursor, radical **12**, is more readily formed and undergoes destruction than less oxidized radical **1**. The probability of consecutive transformation of 6-hydroxyhexanoic acid (**7**) and, hence, radicals **2** and **14** into 6-oxohexanoic (**8**) and adipic (**9**) acids seems to be low. This process is multistep and, therefore, assumes the successive accumulation rather than parallel accumulation of these acids as it is observed for the oxidation of cyclohexane. Attempts to decrease the number of steps by using intramolecular transformations have no basis, because these transformations are poorly probable in the case of seven-membered (and larger) reaction cycles.

2-Hydroperoxycyclohexanone (**15**) is formed by the radical-chain oxidation of cyclohexanone, and its decomposition gives predominantly 2-hydroxycyclohexanone. It is known that transformations of compound **15** with carbon chain destruction can proceed either *via* the pericyclic mechanism, or with the formation of 6-oxohexanoic acid (**8**) *via* the radical route (through 2-oxohexyloxyl radical **18**) to form 1,6-dioxohexyl (**19**) and 5,6-dioxohexyl (**20**) radicals. The formation of 6-oxohexanoic acid (**8**) is possible by the oxidation of 2-hydroxycyclohexanone with peroxide compounds (hydroperoxides, H_2O_2, and peroxy acids). 6-Oxohexanoic (**8**) and adipic (**9**) acids can be

obtained from radical **19** due to multistep transformations in a medium of oxidized cyclohexane.

The main channel of adipic acid (**9**) formation during cyclohexane oxidation is related to the radical-chain oxidation of 2-hydroxycyclohexanone, whose reactivity is considerably higher than those of cyclohexanol and cyclohexanone. The initial oxidation product, 2-hydroxy-2-hydroperoxycyclohexanone (**23**), decomposes *via* the nonradical route to form adipic acid (**9**), adipic anhydride, and cyclohexane-1,2-dione. The homolytic transformations of compound **23** afford adipic acid and cyclohexane-1,2-dione. Anhydrides of carboxylic acids are resulted from the oxidation of cyclohexane-1,2-dione and other α-dicarbonyl compounds (for example, radical **20**).

The formation of valeric and bifunctional C_5 acids assumes the carbon chain shortening due to the reactions of decarboxylation, decarbonylation, and formic acid elimination. Valeric (**39**) and 5-hydroxypentanoic (**35**) acids can be generated from radicals **2**, **14**, **19**, and **20** and also from the 1-oxo-5-carboxypentyl radical formed by the homolytic decomposition of 2-hydroxy-2-hydroperoxycyclohexanone **23**. Evidently, the higher the degree of oxidation of the radical, the lesser number of steps is required to obtain the indicated acids. The possibility of intramolecular transformations appears for the 1,5-bifunctional compounds unlike the 1,6-bifunctional ones. For example, 5-hydroxyhexanoic acid (**35**) is probably transformed completely into δ-valerolactone under the cyclohexane oxidation conditions. The reactivity of the latter is substantially lower than that of the hydroxy acid. Therefore, the possibility of δ-valerolactone to be transformed into 5-oxohexanoic and glutaric acids remains insufficiently clear.

The schemes of formation of 5-oxohexanoic and formic acids *via* the radical-chain oxidation of 6-oxohexanoic acid (**8**) at the C(5)—H bonds were proposed. The ring closure of 5-oxohexanoic acid (**35**) to 6-hydroxytetrahydro-2*H*-pyran-2-one (**55**) (ring-chain tautomerism) is possible. Pyranone **55** is more reactive than δ-valerolactone, and its radical-chain oxidation can result in glutaric anhydride and then glutaric acid. This scheme corresponds to the experimental data on the nearly entire "retention" of the carbon atom of the carbonyl group in glutaric acid. Formic acid can also be a result of the oxidation of the transformation products of radical **20** with peroxide compounds.

Mixed anhydrides containing residues of all carboxylic acids present in the reaction medium are formed by the transacylation of the initially formed anhydrides (mainly adipic anhydride) with carboxylic acids. The reactions of mixed anhydrides with hydroperoxides formed upon oxidation of cyclohexane, for example, with cyclohexyl hydroperoxide, afford peroxy esters, which give cyclohexanone *via* the pericyclic rearrangement. The homolytic decomposition of peroxy esters is accompanied by decarboxylation. The alcoholysis of mixed anhydrides with cyclohexanol affords 100% of all cyclohexyl esters of mono- and dicarboxylic acids. The higher yield of cyclohexyl formate is caused by a specific feature of alcoholysis of mixed formic acid anhydrides.

Cyclohexyl esters of mono- and dicarboxylic acids (except for cyclohexyl formate) are oxidized at the C(1)—H bond of the alkoxyl group is more slowly than cyclohexanol and cyclohexanone. The formation of cyclohexanone is also possible in this case. The oxidation of cyclohexyl formate at the CH bond of the acyl group should result in cyclohexanol.

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