Oxidation of ethers with dimethyldioxirane

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Oxidation of a series of *tert*-butyl ethers Bu^tOR (R = Me, Et, CH_2CH_2Cl, Pr^i, Bu^i), diethyl ether, diisopropyl ether, 1,2-dimethoxyethane, diisobutoxymethane, 1,4-dioxane, and tetrahydrofuran with dimethyldioxirane (DMDO) was studied. The reaction kinetics obeys the second-order equation $w = k[\mathrm{DMDO}][\mathrm{ether}]$. The rate constants in a range of 5—50 °C and the activation parameters of the reaction were determined. The solvent effect on the oxidation rate was studied. The oxidation products are the corresponding alcohols and carbonyl compounds. The competition between the nonradical (oxygen insertion) and radical mechanisms of the reaction is discussed. The reactions of the parent dioxirane and DMDO with a series of methyl ethers MeOR´ (R´ = Me, Et, CH_2CH_2F, Pr^i) were studied by the density functional theory (DFT). The (U)B3LYP-6-311G(d,p) method was employed to calculate the geometry and energies of the reactants and transition states. The data obtained indicate a possible increase in the probability of oxidation *via* the radical route and an increase in the activation barrier for the substrates containing electron-withdrawing substituents.

Key words: dimethyldioxirane, ethers, oxidation, kinetics, free radicals, *ab initio* calculations.

The chemistry of dioxiranes was under intense development for the last two decades.[1,2] A distinctive feature of these cyclic peroxides is a combination of high reactivity and selectivity of oxidation reactions.[3] The works concerning the oxidation of ethers with dioxiranes are few and, as rule, synthetic. For instance, the transformation of steroid ethers to the corresponding ketones was studied.[4] The oxidation of *O*-isopropylidene diol derivatives to 2-hydroxyketones and the oxidation of benzyl ethers were studied,[5,6] and a nonradical nature was postulated for these reactions. The oxidation of 1,3-dihydroisobenzofuran with dimethyldioxirane (DMDO) to 2-hydroxymethylbenzaldehyde was assumed[7] to involve radicals; however, the total composition of the products was not reported. The study[8] of the reaction products of dialkyl ethers with dioxiranes suggested the radical nature of this reaction, which has been developed further.[9,10] The study[10] of the products and kinetics of oxidation of ethers with DMDO concluded the competition of two processes: insertion of the oxygen atom at the C—H bond of the substrate and hydrogen atom abstraction followed by fast recombination of the radical pair that formed. The effect of oxygen on the yield of the products and conversion of the substrate were demonstrated for *para*-substituted analogs of 1-methoxy-1-phenylethane. Analysis of the kinetic data in the framework of the Hammett equation gives $\rho = -0.74 \pm 0.03$ (25 °C).[10] However, the mechanism of oxidation of different ethers was not studied systematically. We have previously[11,12] shown that C—H bonds of alkanes and alcohols are oxidized with DMDO *via* two parallel channels, nonradical and homolytic. The ratio of these processes was determined. In the present work, we studied the products and kinetics of the reactions of DMDO with aliphatic ethers **1—12** and the influence of different factors on the process to elucidate its mechanism.

Experimental

NMR spectra were recorded on a Bruker AM-300 spectrometer (Me_4Si as standard, solvents $(D_3C)CO$, $CDCl_3$, and CCl_4). Benzene or dimethylsulfone was used as reference for ^1H NMR estimations of the concentration.

Chromatographic analysis was carried out on a Chrom-5 instrument (column 3.7 m × 3 mm, SE-30 stationary phase) or on a Hewlett Packard 5890E SERIES II gas chromatograph (capillary column HP-5 (Crosslinked 5% PH ME Silicon) 30 m × 0.32 mm × 0.25 μm). *n*-Decane was used as internal standard.

GC-MS analysis was carried out on an HP 5890 Series II chromatograph (capillary column HP-5, *l* = 60 m) with an HP5972 mass-selective detector.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 10, pp. 2309—2318, October, 2005.

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Acetone (analytical grade) was purified by distillation. Dimethyldioxirane was synthesized according to a known procedure.[13] Identification and analysis of DMDO were carried out as described earlier.[3] Dioxirane was extracted in CCl_4 according to a known procedure.[14]

Synthesis of *tert*-butyl ethers. 2-Methoxy-2-methylpropane (**1**), 2-ethoxy-2-methylpropane (**2**), and 2-isopropoxy-2-methylpropane (**4**) were synthesized by a known procedure.[15] 2-(2-Chloroethoxy)-2-methylpropane (**3**) and 1-*tert*-butoxy-2-methylpropane (**5**) were synthesized similarly in 20 and 25% yields, respectively. 2-(2-Chloroethoxy)-2-methylpropane was washed with water to a minimum content of alcohols, dried with molecular sieves 4A, and distilled on a rectification column. The other ethers were washed 20—40 times with an equal amount of water to remove alcohols and then were refluxed for 12 h over metallic sodium and distilled. The purity of the resulting ethers was <99.9%.

2-Ethoxy-2-methylpropane (2). B.p. 72.5 °C, d^{25} 0.742 g cm^{-3}. ^{1}H NMR (acetone-d$_6$, 300 MHz), δ: 1.09 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.15 Hz); 1.16 (s, 9 H, CMe_3); 3.38 (q, 2 H, OCH_2, J = 7.15 Hz). ^{13}C NMR (acetone-d$_6$, 75 MHz), δ: 16.4 ($CH_2\underline{C}H_3$); 27.6 ($C\underline{C}H_3$); 56.7 (OCH_2); 72.1 (OC).

2-(2-Chloroethoxy)-2-methylpropane (3). B.p. 134.5 °C, d^{25} 0.946 g cm^{-3}. ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 1.18 (s, 9 H, CMe_3); 3.53—3.65 (m, 4 H, $OC\underline{H}_2C\underline{H}_2Cl$, J = 4.32 Hz). ^{13}C NMR (acetone-d$_6$, 75 MHz), δ: 27.4 (Me); 44.5 (CH_2Cl); 62.8 (OCH_2); 73.3 (OC).

2-Isopropoxy-2-methylpropane (4). B.p. 87.6 °C, d^{25} 0.737 g cm^{-3}. ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 1.05 (d, 6 H, $CHMe_2$, J = 6.15 Hz); 1.14 (s, 9 H, CMe_3); 3.74 (m, 1 H, $C\underline{H}Me_2$, J = 6.15 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz), δ: 25.0 ($CH\underline{C}H_3$); 28.3 ($C\underline{C}H_3$); 63.4 (OCH); 73.0 (OC).

1-*tert*-Butoxy-2-methylpropane (5). B.p. 111.5 °C, d^{20} 0.755 g cm^{-3}. ^{1}H NMR (acetone-d$_6$, 300 MHz), δ: 0.88 (d, 6 H, $CHMe_2$, J = 6.7 Hz); 1.15 (s, 9 H, CMe_3); 1.61—1.76 (m, 1 H, $CH_2C\underline{H}Me_2$); 3.09 (d, 2 H, OCH_2, J = 6.4 Hz). ^{13}C NMR (acetone-d$_6$, 75 MHz), δ: 19.6 ($CH\underline{C}H_3$); 27.6 ($C\underline{C}H_3$); 29.6 ($CH_2\underline{C}HMe_2$); 68.5 (OCH_2); 72.1 (OC).

Dioxane (**6**), 1,2-dimethoxyethane (**7**), diisobutoxymethane (**8**), ethoxyethane (**9**), 2-isopropoxypropane (**10**), and tetrahydrofuran (**11**) were dried above metallic sodium and distilled under argon. 1,3-Dioxolan-2-one (**12**) was distilled under reduced pressure.

Procedure of kinetic experiments. The reaction kinetics was studied from the consumption of dioxirane. The change in the DMDO concentration during the reaction was monitored spectrophotometrically at λ_{max} = 335 nm (ε = 13.5 L mol^{-1} cm^{-1}) on a Specord M-40 instrument. A solution of ether was placed in a quartz cell, and the temperature of the cell was maintained at a specific level in the cell chamber of the spectrophotometer at 7—50 °C. A required amount of a solution of DMDO was rapidly added, oxygen (1.5 min) or argon was passed through the solution if necessary, and the change in absorbance was monitored. The initial concentrations of DMDO and ethers **1—12** were varied within $(0.7—6.5) \cdot 10^{-2}$ and $(4.0—60.0) \cdot 10^{-2}$ mol L^{-1}, respectively. Acetone, CCl_4, or $Me_2CO—CCl_4$ and $Me_2CO—Bu^tOH$ mixtures were used as solvents.

Analysis of products. A solution of DMDO in 3 mL of acetone (0.07 mol L^{-1}, 0.21 mmol) was placed in a flat-bottom flask (10 mL) equipped with a magnetic stirrer. The solution was saturated with oxygen filling with oxygen the gas volume of the flask. Substrate **1—12** (2.1 mmol) was added with stirring, the flask was tightly closed with a ground stopper, and the solution was left to stir (T = 25 °C). After a time period necessary for the reaction to occur by 95% (according to the kinetic data), a standard solution of *n*-decane was added, and the resulting mixture was analyzed. The products were identified by GC-MS. The obtained mass spectra agree well with those in the NIST library (1999). Quantitative analysis was carried out on an HP 5890E Series II chromatograph.

The products of 2-ethoxy-2-methylpropane (**2**) oxidation with dimethyldioxirane were also studied by ^{1}H NMR in a $CCl_4—CD_2Cl_2$ solution. A solution of DMDO in 2 mL of CCl_4 (0.1 mol L^{-1}, 0.2 mmol) was placed in a flat-bottom flask (10 mL) equipped with a magnetic stirrer and saturated with oxygen filling the flask volume with oxygen. A solution (0.2 mL) of 2-ethoxy-2-methylpropane (1 mol L^{-1}, 0.2 mmol) in CCl_4 was added with stirring, the flask was tightly closed with a ground stopper, and the solution was left to stir for 36 h (T = 25 °C). The resulting solution (sample of 0.4 mL) was placed in a tube to record NMR spectra, a solution (0.15 mL) of benzene (0.11 mol L^{-1}) in CD_2Cl_2 (standard for quantitative analysis) was added, and the ^{1}H NMR spectrum was recorded. The products were identified by the characteristic signals of Me groups. No signal of the aldehyde proton was observed.

Solutions of the products were analyzed for a content of peroxides by the iodometric method.

Quantum chemical calculations. Density functional theory (DFT) calculations were performed using a combination of the three-parameter hybrid exchange Becke functional (B3)[16,17] with the Lee—Yang—Parr correlation functional (LYP),[18] which is designated hereinafter as B3LYP. The standard two- and three-exponential 6-31G** and 6-311G** basis sets[19] were used. All geometric parameters for molecules, intermediates, and transition states were optimized without symmetry restraints. The nature of optimized structures was confirmed by analysis of the eigenvalues of the Hessian matrix, being the matrix of the second derivatives of the energy by the coordinates, which were calculated analytically.[20] The calculated energies were corrected for the zero-point vibration energies taken without a scaling factor. All calculations were performed using the Gaussian 98 program package.[21]

Results and Discussion

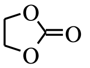
Reaction products. The oxidation products of ethers with dimethyldioxirane are presented in Table 1.

Acyclic ethers are transformed by DMDO into semiacetals, which decompose rapidly to the corresponding alcohols and carbonyl compounds (Scheme 1).

Cyclic ethers are oxidized to the corresponding hydroxy derivatives (Scheme 2), which are further transformed into lactones.

In the most cases, the yields of the products based on the DMDO consumed are lower than 100%, which is due to their subsequent oxidation with dioxirane. Under the studied conditions, compound **12** is not oxidized by DMDO.

Table 1. Oxidation products of ethers with dimethyldioxirane in acetone at 25 °C and the ratio of reactants [ether] : [DMDO] = 10 : 1

Ether	Products	Yield[a] (%)
Bu^tOMe (**1**)[b]	2-Methylpropan-2-ol	60
Bu^tOEt (**2**)	2-Methylpropan-2-ol	99
	Ethanal	97
$Bu^tO(CH_2)_2Cl$ (**3**)[b]	2-Methylpropan-2-ol	41
	2-Chloroethanal	12
	Chloroacetic acid	3
Bu^tOPr^i (**4**)[c]	2-Methylpropan-2-ol	97
	Acetone	97
Bu^tOBu^i (**5**)	2-Methylpropan-2-ol	98
	2-Methylpropanal	96
1,4-Dioxane (**6**)	1,4-Dioxan-2-ol	11
	1,4-Dioxan-2-one	44
$MeO(CH_2)_2OMe$ (**7**)[b]	Methanol	32
	2-Methoxyethanal	4
	Methoxyacetic acid	3
$Bu^iOCH_2OBu^i$ (**8**)	2-Methylpropan-1-ol	96
	2-Methylpropanal	96
Et_2O (**9**)	Ethanol	99
	Ethanal	99
Pr^iOPr^i (**10**)[c]	Propan-2-ol	98
	Acetone	99
Tetrahydrofuran (**11**)	Tetrahydrofuran-2-ol	96
 (**12**)[d]	Not oxidized	—

[a] Based on the consumed dioxirane.
[b] The reaction was carried out in oxygen.
[c] Solvent CCl_4.
[d] 50 °C, solvent CCl_4—acetone (5 : 1).

Reaction kinetics. The reaction kinetics was studied under the condition that $[DMDO]_0 \ll [RH]_0$, where $[DMDO]_0$ and $[RH]_0$ are the initial concentrations of dimethyldioxirane and the substrate, respectively. For ethers **2**, **4—6**, and **9—11** and acetal **8**, the kinetic curves are described by the first order equation with a high correlation coefficient (0.98—0.999) (Fig. 1). The apparent first-order rate constants were calculated from the anamorphoses of the kinetic curves

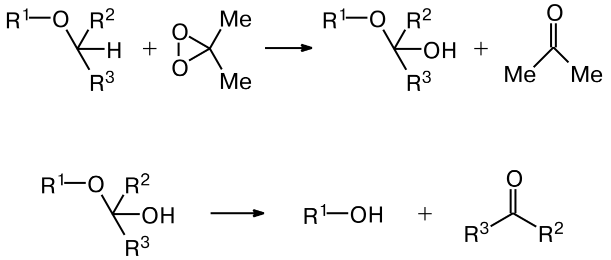
$$k_{app} = k \cdot [RH]^n,$$

where k is the apparent rate constant, and n is the reaction order with respect to ether. The plot of k_{app} *vs.* ether concentration is linear and takes the following form:

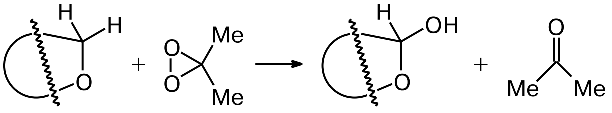
$$k_{app} = k \cdot [RH] + k_d,$$

which indicates two channels of DMDO consumption: the reaction with ether (k) and thermal decomposition (k_d) (Fig. 2). It follows from the plot in Fig. 2 that $k_d = (2 \pm 6) \cdot 10^{-6}\ s^{-1}$; at this temperature, the rate constant of DMDO decomposition is $7 \cdot 10^{-7}\ s^{-1}$.[12] The resulting k_d value is in good accord with the thermolysis constant of dioxirane in acetone.[12]

Scheme 1



Scheme 2



The rate constant k_{app} is independent of the oxygen content in the reaction mixture and DMDO concentration. The kinetic equation of the reaction has the following form:

$$d[DMDO]/dt = k \cdot [DMDO] \cdot [RH] + k_d \cdot [DMDO].$$

The temperature plot of the rate constant in an interval of 5—55 °C was studied and the activation parameters for the ethers were determined (Table 2). The $\Delta H^{\neq}{}_{298}$, $\Delta S^{\neq}{}_{298}$, and $\Delta G^{\neq}{}_{298}$ values were calculated by the Eyring equation.[22] The resulting parameters indicate that the oxidation can proceed *via* a concerted mechanism with the simultaneous cleavage of several bonds in the molecules

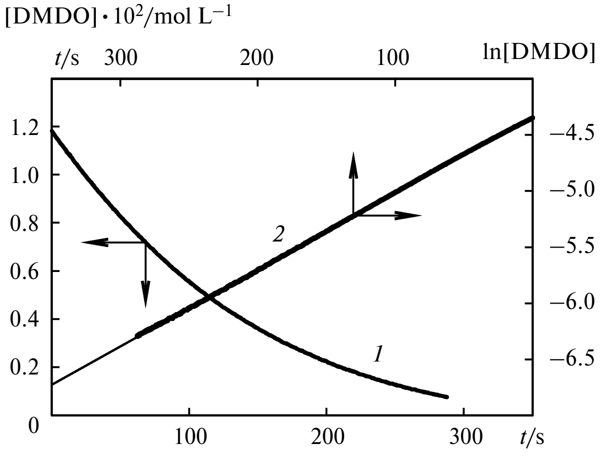


Fig. 1. Kinetic curve of DMDO consumption in the reaction with 2-isopropoxypropane (**10**) (*1*) and its semilogarithmic anamorphosis (*2*) ($[\mathbf{10}]_0 = 0.968\ mol\ L^{-1}$, 37 °C).

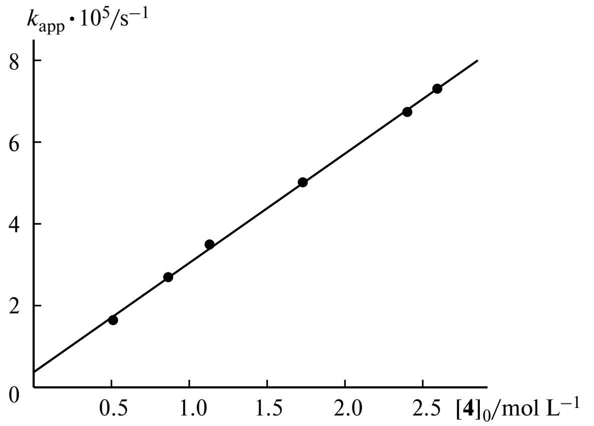


Fig. 2. Apparent rate constant of DMDO consumption (k_{app}) *vs.* concentration of 2-isopropoxy-2-methylpropane (**4**) (solvent acetone, 15 °C).

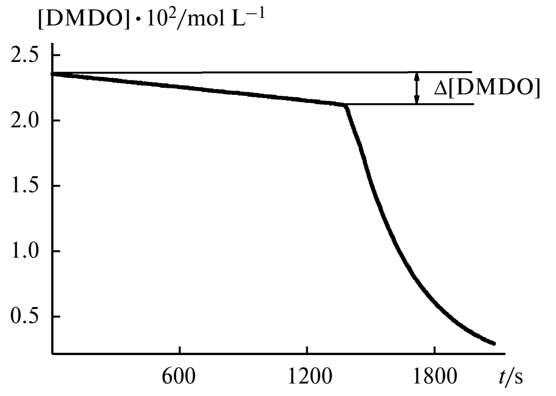


Fig. 3. Kinetic curve of DMDO consumption in the presence of 2-(2-chloroethoxy)-2-methylpropane (**3**) ($[\mathbf{3}]_0$ = 0.94 mol L^{-1}, $[O_2]_0$ = 0.011 mol L^{-1}, 15 °C).

to form new bonds, as it should occur according to the mechanism of oxygen atom insertion at the C—H bond of an ether molecule. However, these data are insufficient to prove the "insertion" mechanism.

Ethers **1**, **3**, and **7** are oxidized with an induction period (Fig. 3). Saturation of the initial solutions with oxygen leads to a prolonged induction period. On the other hand, when the initial O_2 concentration was decreased by bubbling with an inert gas, the induction period decreased too. Before the kinetic curve inflection, the rate of DMDO consumption remains the same as that in the runs where the oxygen dissolved in the solution was present during the whole experiment. The variation of the concentrations of ethers and DMDO at a constant initial concentration of oxygen does not substantially change Δ[DMDO]. The apparent rate constants in the region before acceleration increase proportionally to the ether concentration. A similar phenomenon has been observed earlier[11,12] for the oxidation of alkanes, alcohols, and ketones. The high rate of DMDO consumption after the end of the induction period was found to be caused by the involvement of DMDO in a chain radical process, which is induced by free radicals.[9,11,12,23—25] Since the rate constant of the reaction $R^{\cdot} + O_2$ is rather high ($(1—5) \cdot 10^9$ L mol^{-1} s^{-1}),[26] the sharp acceleration of the reaction can be due to the complete consumption of oxygen. In the system under study, oxygen is an efficient inhibitor of the chain radical process. According to the inhibitor theory, the rate of O_2 consumption is proportional to the initiation rate (except for the contribution of hidden radical processes), and the amount of the consumed inhibitor (oxygen) makes it possible to determine the efficiency of initiation. In the previous studies,[11,12] we determined the efficiency of free radical generation in the reactions of DMDO through the $[O_2]_0$/Δ[DMDO] ratio. The data on

Table 2. Kinetic parameters for the oxidation of ethers with dimethyldioxirane in acetone

Ether	k[a] · 10^4 /L mol^{-1} s^{-1}	E_a /kcal mol^{-1}	log$A$	$\Delta H^{\neq}_{298}$ /kcal mol^{-1}	$-\Delta S^{\neq}_{298}$ /cal K^{-1} mol^{-1}	$\Delta G^{\neq}_{298}$ /kcal mol^{-1}
2-Methoxy-2-methylpropane[b]	1.1±0.1	17.8±1.2	9.1±0.8	17±1	18.8±1.2	22±2
2-Ethoxy-2-methylpropane	19±2	16.6±0.9	9.5±0.9	16.0±0.9	17.3±1.7	21±2
2-(2-Chloroethoxy)-2-methylpropane[b]	0.78±0.02[c]	—	—	—	—	—
2-Isopropoxy-2-methylpropane	0.66±0.05	13.3±0.7	5.6±0.5	12.7±0.7	35±3	23±3
1-*tert*-Butoxy-2-methylpropane	13±3	11.6±0.8	5.6±0.8	10.9±0.8	35±4	21±3
Diisobutoxymethane	6.2±0.3	13.7±0.9	6.9±0.7	13.1±0.9	29±2	22±2
2-Isopropoxypropane	30±2	12.0±0.7	6.3±0.3	11.4±0.7	31.9±1.1	21±2
Ethoxyethane	17.8±0.7	12.6±0.8	6.5±0.7	12.0±0.8	31±3	21±3
1,4-Dioxane	1.56±0.14	16.8±0.7	8.5±0.6	16.2±0.7	22±2	23±3
1,2-Dimethoxyethane[b]	3.0±0.1	14.5±0.4	7.1±0.3	13.9±0.5	27.9±1.1	22.2±1.8
Tetrahydrofuran	37±2[c]	—	—	—	—	—

[a] 25 °C.

[b] The rate constants were obtained from the initial regions of the kinetic curves of DMDO consumption; the solution was saturated with oxygen prior to experiment.

[c] At 15 °C.

Table 3. Ratio of the initial concentration of O_2 ($[O_2]_0$) to the amount of DMDO consumed in the reaction with ethers at different temperatures

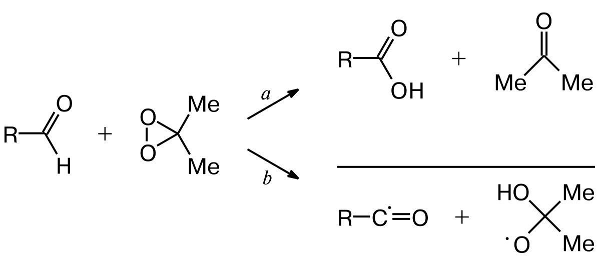
Ether	T/°C	$[O_2]_0/\Delta[\mathrm{DMDO}]$*
1,2-Dimethoxyethane	45.2	0.24±0.03
	50.8	0.24±0.03
	54.8	0.24±0.03
2-Methoxy-2-methylpropane	24.5	0.57±0.05
	30.0	0.48±0.05
	35.9	0.44±0.05
	40.2	0.28±0.04
	49.7	0.27±0.03
2-(2-Chloroethoxy)-2-methylpropane	15.0	0.95±0.05

* The amount of dimethyldioxirane consumed during the induction period (see Fig. 3).

the ratio of the initial oxygen concentration to the amount of consumed DMDO in the reactions with ethers are given in Table 3.

However, since the products of the reactions of ethers with DMDO undergo further oxidation in some cases, the stoichiometric ratio DMDO : O_2 can differ from unity. The oxidation products of ether **1** showed no methanal or products of its transformation as, *e.g.*, for the oxidation of methanol[11] with DMDO. This indicates the further oxidation of methanal. The authors of the single study[27] of the oxidation of aldehydes with DMDO found that the free radical processes contribute substantially to the reaction. In the case of ether **1**, the source of free radicals is, most likely, the reaction of DMDO with methanal. A similar situation is observed for the oxidation of ethers **3** and **7**: acids were found in the reaction products, and the overall yield of the oxidation products was lower than those of the reactions of other ethers. These facts can be explained assuming a side reaction (Scheme 3).

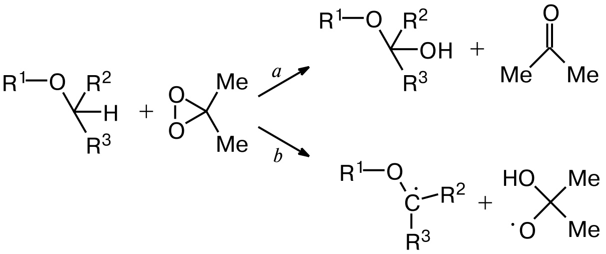
Scheme 3



The H atom abstraction from an aldehyde molecule produces carbon-centered radicals, which react rapidly with oxygen to result in a chain of transformations characteristic of radical oxidation of aldehydes in the presence of oxygen.[28—30] The oxidation products of aldehydes formed from ethers **1**, **3**, and **7** are volatiles hardly detectable by standard analytical methods. This explains a disadvantage of the reaction products for the calculation of the material balance. The preliminary results showed a considerable contribution of radical processes to the reactions of aldehydes with DMDO.

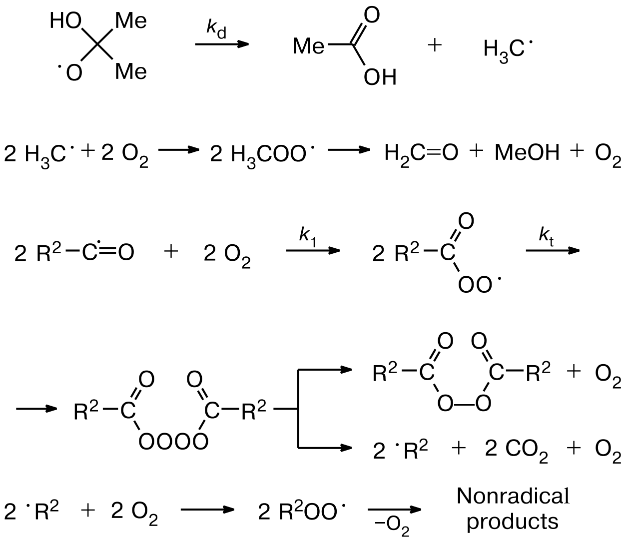
The reactions of the most part of ethers under study with DMDO involve no radical processes (Scheme 4, route *a*). The exceptions are the ethers containing electron-withdrawing substituents for which route *b* occurs, probably, in part (see Scheme 4). This assumption is based on the fact that no radical formation was observed for the oxidation of alcohols of similar structure with DMDO. In addition, in the case of ethers, whose oxidation affords no aldehydes (for instance, compounds **4**, **6**, and **10**), no effect of O_2 was observed on the kinetics and composition of the reaction products.

Scheme 4



Stoichiometry of O_2 consumption can be estimated with allowance for the oxidation reaction *via* route *a* (see Scheme 4) followed by the decomposition of semiacetal to aldehyde and alcohol. The further oxidation of aldehyde results in the formation of radicals *via* route *b* (see

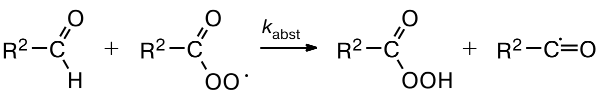
Scheme 5



Scheme 3) and their transformation *via* the chain-radical oxidation scheme[28,29,31] (Scheme 5).

At deeper steps of oxidation and a low concentration of O_2, chain termination can occur by the recombination of acyl radicals.[31] Let us estimate the contribution of chain propagation (H atom abstraction from an aldehyde molecule by the $R^2C(O)OO^{\bullet}$ radical) (Scheme 6).

Scheme 6



Applying the quasi-stationary approximation, for the concentrations of acyl and acyl peroxide radicals (k_1 = 10^8—10^9 L mol^{-1} s^{-1})[31] we obtain

$$d[R^2C(O)OO^{\bullet}]/dt = k_{ox}[DMDO][Ald] - k_t[R^2C(O)OO^{\bullet}]^2 = 0,$$

where [Ald] is the aldehyde concentration under the experimental conditions (~10^{-2}—10^{-3} mol L^{-1}), and k_{ox} is the rate constant of the reaction of DMDO with aldehyde (according to our preliminary data, it equals ~10^{-2}—10^{-3} L mol^{-1} s^{-1}). Since k_t for acyl peroxide radicals with sterically unhindered aliphatic substituents is[29] (3.4—10.4)·10^7 L mol^{-1} s^{-1}, the stationary concentration of the $R^2C(O)OO^{\bullet}$ radicals can be calculated. Under the experimental conditions, this concentration is about ~10^{-7} mol L^{-1} and, therefore, the ratio of the recombination rate of the acyl peroxide radicals and the rate of their reaction with aldehyde is

$$w_t/w_{abst} = (k_t^{1/2} \cdot k_{ox}^{1/2} \cdot [DMDO]^{1/2})/(k_{abst}[Ald]^{1/2}) \approx 10—5$$
$$(k_{abst} = (1.1—3.9) \cdot 10^2 \text{ L mol}^{-1} \text{ s}^{-1}).$$

Therefore, H atom abstraction from the aldehyde molecule by the $R^2C(O)OO^{\bullet}$ radical can be neglected in this case. This conclusion agrees with the results of analysis of the products: no formation of peracids was found. The reaction of the oxyl radical with aldehyde can also be neglected because of the low concentration of the latter and the rate of destruction[32] of this radical, which prevails over the rate of H atom abstraction from the aldehyde molecule by 10^3—10^2 times.

Thus, six O_2 molecules are required to oxidize two aldehyde molecules *via* route *b* (see Scheme 3), and three O_2 molecules are formed due to the recombination of peroxide radicals (see Scheme 5). Therefore, the $3[O_2]_0/2\Delta[DMDO]$ ratio characterizes the escape of radicals into the bulk (Δ[DMDO] is the amount of dioxirane consumed during the induction period). However, aldehyde oxidation is preceded by the reaction with ether and, hence, the following correlation should be taken into account:

$$\{3/[4 \cdot (1 + 2\varpi_{Ald})]\} \cdot ([O_2]_0/\Delta[DMDO]),$$

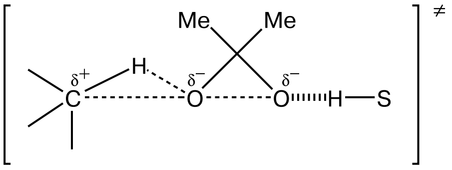
where ϖ_{Ald} is the yield of aldehyde based on the consumed dioxirane in the inhibited process. However, a possibility of radical formation in the reaction of DMDO with ether (see Scheme 4, route *b*), as that found for the oxidation of alcohols with DMDO,[11] cannot be excluded completely. This is related to the fact that the approach proposed earlier[12] does not allow one to determine which initiation reactions are involved in each particular case. Taking into account the results of studying the oxidation products, we can propose that the initiation reaction is the oxidation of aldehyde with dioxirane.

In the case of ethers **2**, **5**, and **9—11** and acetal **8**, the rate of ether oxidation, under the reaction conditions, exceeds the reaction rate of DMDO with the oxidation products (aldehydes or alcohols). When the oxidation rates of the product and ether are comparable (compounds **6** and **3**) or the reaction rate with the product is much higher (compounds **1** and **7**), the deeper oxidation products are observed (see Table 1).

To check the above assumption about the reaction mechanism, we studied the interaction of ether **2** with DMDO at an equivalent ratio of reactants in more detail. In this case, the kinetic curve of DMDO consumption has a break, whose time of appearance depends on the oxygen concentration in the system, unlike the kinetic curves observed in a ≤10-fold excess of the substrate. Analysis of the composition of the reaction mixture after the complete consumption of dioxirane in an oxygen-saturated solution showed equal amounts of acetic acid, 2-methylpropan-2-ol, and the starting ether, which also differs from the composition of oxidation products of this ether in excess substrate. Thus, the rate of the main reaction (ether + DMDO) decreases with a decrease in the ether concentration, and the side reaction, aldehyde oxidation, begins to contribute substantially to the overall process. In this case, aldehyde is completely consumed to the acid.

Therefore, the low rate of ether oxidation can be a reason for the appearance of side reactions, such as the further oxidation of the products that formed, due to which free radicals and the products of deeper oxidation appear in the system under study. In some cases, the process can be directed to the formation of only the primary oxidation products by the variation of the initial ether concentration. Increasing this concentration, one can achieve such a rate of the primary reaction that it will be predominant.

Solvent effect on the oxidation rate. The oxidation of the C—H bond with dioxiranes was proposed[33—36] to proceed *via* a highly ordered transition state (TS).



S—H is solvent molecule

Solvents capable of forming a hydrogen bond stabilize the negative charge on the oxygen atom, thus facilitating substrate oxidation.[36]

Analysis of the data obtained (Table 4) shows a weak increase in the rate constant of oxidation of ethers **2**, **5**, and **10** with DMDO in the presence of Bu^{t}OH compared to solvents for which the effect of the hydrogen bond is less pronounced (acetone, CCl_4).

Structure of substrate and its reactivity. Based on the partial rate constants, we can arrange the substrates in the following series of reactivity: **6** < **3** ≈ **4** ≈ **1** ≈ **7** < **8** < **5** < **9** < < **2** < **11** < **10**. The low reactivity of ether **4** compared to other ethers containing the tertiary C—H bond in the α-position to the oxygen atom is caused, probably, by steric hindrance of the oxidized bond and a high sensitivity of DMDO to steric factors.[1,2] An increase in the number of oxygen atoms near the reaction center of an ether molecule decreases the rate of substrate oxidation in the order **6** ≈ **7** ≈ 1,3-dioxocycloalkanes[37,38] < ethers. Ethers are oxidized by an order of magnitude more slowly than alcohols,[10,11] which is related, most likely, to a lower σ value for the substituents at the reaction center and to an increase in steric hindrance in the case of ethers due to the replacement of the OH group by OR.

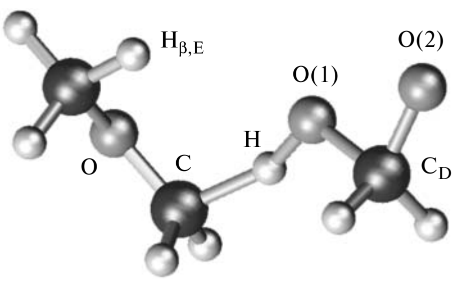
Quantum chemical calculations. We performed quantum chemical calculations for several model systems. The geometry of the reactants, products, and transition states and the activation energies for the oxidation of methoxymethane, methoxyethane, 2-methoxypropane, and 1-fluoro-2-methoxyethane with the parent dioxirane (DO), *viz.*, CH_2O_2 (in the case of methoxymethane with dimethyldioxirane as well), were calculated.

In the case of reaction systems possibly involving radical (biradical) intermediates, the problem appears for choosing an adequate method for quantum chemical calculations. The standard calculation schemes based on the use of restricted wave functions for closed shells (restricted Hartree—Fock or Kohn—Sham methods) are inappropriate in such situations. It has previously[39] been shown that the wave functions calculated[40—43] for the transition state of the reactions of dioxiranes with alkanes, aldehydes, and alcohols have singlet-triplet instability, *i.e.*, there is another unrestricted solution of the Schrödinger (or Kohn—Sham) equation with nonequivalent α and β orbital manifolds, which is lower in energy. Calculation methods that take into account the multiconfigurational character of the wave function are necessary for the adequate description of systems of biradical nature. However, similar computations are computationally intensive and time-consuming. The DFT calculations of (bi)radicals using the hybrid B3LYP functional in the unrestricted variant (UB3LYP) with broken α—β-symmetry were shown[44,45] to give results, whose quality is comparable with the state-of-the-art multi-reference coupled cluster calculations (MR-AQCC). In this work, we used the UB3LYP method to calculate the reactions of dioxiranes with ethers. Generally, in calculations of singlet biradicals in the framework of the unrestricted hybrid DFT methods, such as UB3LYP, fairly strong spin contamination is inevitable: the $<S^2>$ value can be considerably higher than zero, which indicates a significant radical character of the molecular wave function. It is known[46] that the thermochemical and geometric parameters calculated by the hybrid DFT methods are less prone to the influence of spin contamination than those obtained by the HF, MP2, CC, and other methods.

The detailed UB3LYP/6-311G(d,p) study of the potential surface energy of a dioxirane—methoxymethane system revealed the first order saddle point (Fig. 4), which was attributed to the transition state of the reaction. The geometry of this saddle point (TS-1, see Fig. 4) is similar to the structure of the transition state described earlier for

Table 4. Effect of the solvent nature on the rate constant of oxidation of ethers with dimethyldioxirane (k/L mol^{-1} s^{-1})

Ether	Solvent	T/°C	$k \cdot 10^4$
2-Ethoxy-2-methylpropane	CCl_4	6.7	1.9±0.1
	Acetone	6.7	3.0±0.2
	Acetone—Bu^{t}OH (1 : 1)	6.7	6.6±0.2
1-*tert*-Butoxy-2-methylpropane	CCl_4	4.8	1.5±0.1
	Acetone	4.8	3.0±0.1
	Acetone—Bu^{t}OH (1 : 1)	4.8	3.6±0.1
2-Isopropoxypropane	CCl_4	4.8	5.7±0.1
	Acetone	4.8	6.8±0.1
	Acetone—Bu^{t}OH (1 : 1)	4.8	7.8±0.1



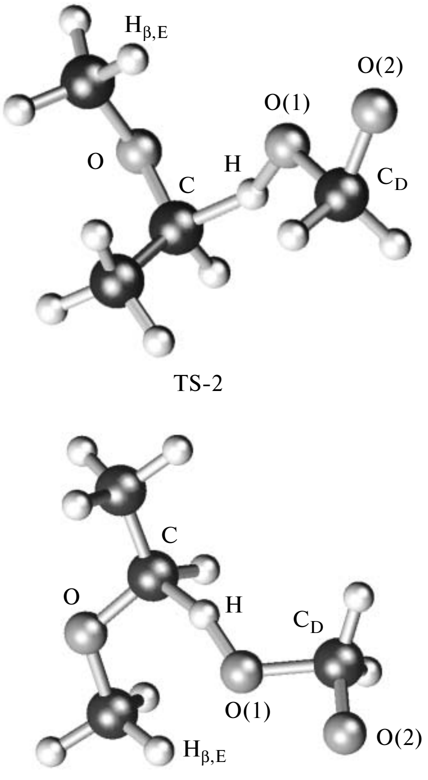
TS-1

Fig. 4. Transition state TS-1 for the oxidation of methoxymethane with dioxirane calculated by the UB3LYP/6-311G** method.

Table 5. Calculated activation barriers* (kcal mol^{-1}) to the oxidation of ethers with DO and DMDO

Transition state	Basis set	B3LYP		UB3LYP	
		DO	DMDO	DO	DMDO
MeOMe					
TS-1	6-31G**	20.7	25.1	—	—
	6-311G**	18.3	22.0	14.5	17.1
MeOEt					
TS-2	6-31G**	17.6	20.7	—	—
	6-311G**	15.7	18.1	13.5	—
TS-3	6-31G**	16.7	20.7	—	—
	6-311G**	14.7	18.1	12.7	—
$MeOCH_2CH_2F$					
TS-4	6-31G**	21.3	26.3	—	—
	6-311G**	19.7	—	14.3	—
TS-5	6-31G**	18.8	22.7	—	—
	6-311G**	16.7	—	13.5	—
TS-6	6-31G**	19.7	24.1	—	—
	6-311G**	17.5	—	13.7	—
$MeOPr^i$					
TS-7	6-31G**	15.0	17.1	—	—
	6-311G**	13.5	—	12.2	—

* Relative to the reactants, including ΔZPVE.



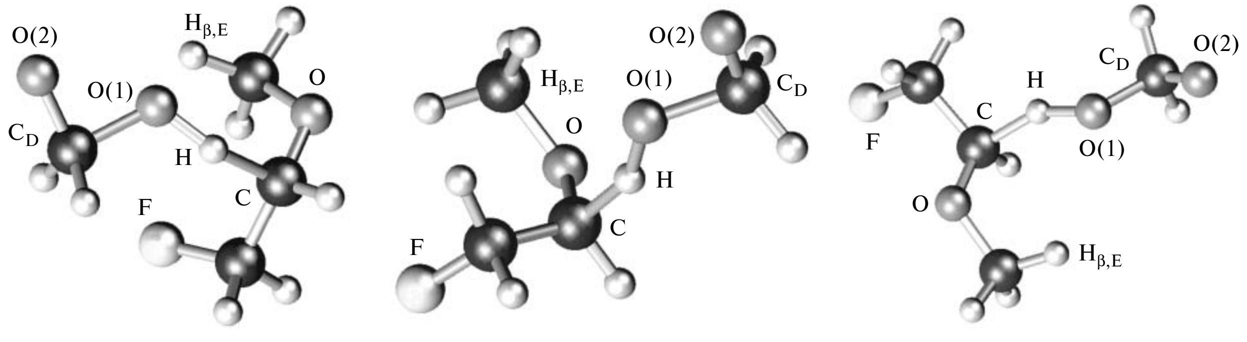
TS-2

TS-3

Fig. 5. Transition states TS-2 and TS-3 for the oxidation of methoxyethane with dioxirane calculated by the UB3LYP/6-311G** method.

the TS of the reaction of dioxirane with a C—H bond,[40] which was calculated by the B3LYP method for closed shells (RB3LYP) and assigned to the TS of the concerted insertion of an oxygen atom. However, in this case, $<S^2> = 0.436$, *i.e.*, TS-1 has a pronounced biradical character. The transition state found by the RB3LYP method has singlet-triplet instability and, as shown earlier[39] for isobutane oxidation, does not describe the experimentally observed regularities. On going from methoxymethane to 2-methoxypropane, differences between the geometric parameters of the TS and the energies calculated by the RB3LYP and UB3LYP methods decrease. This indicates a decrease in the probability that the reaction proceeds *via* the radical mechanism. The conformation of ether exerts no substantial effect on the energy barrier to its oxidation (Table 5, Fig. 5).

The effect of electronegative substituents was studied for 1-fluoro-2-methoxyethane. The introduction of a fluorine atom into an ether molecule (Tables 5 and 6, Fig. 6) destabilizes the carbocationic center in the substrate molecule in the transition state and increases the activation barrier. The parameters calculated by the B3LYP and UB3LYP methods differ significantly. Electronegative



TS-4 TS-5 TS-6

Fig. 6. Transition states TS-4, TS-5, and TS-6 for the oxidation of 1-fluoro-2-methoxyethane with dioxirane calculated by the UB3LYP/6-311G** method.

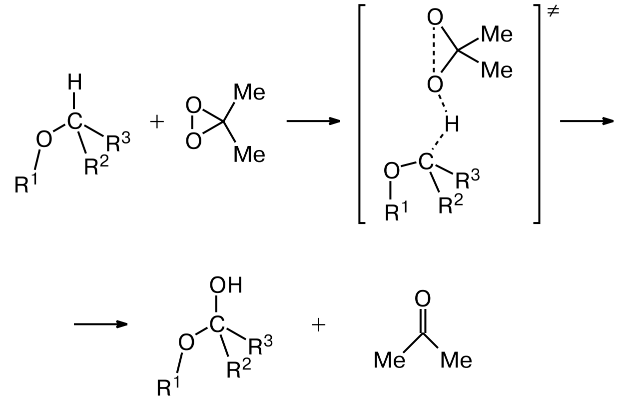
Table 6. Geometric parameters for the transitions states of oxidation of methyl ethers with dioxirane (distances (*r*) and angles (ω))

Transition state	Calculation method	*r*/Å						ω/deg	
		C—H	H...O(1)	O(1)—O(2)	C_D—O(1)	C_D—O(2)	$H_{\beta,E}$—O(1)	C—H—O(1)	H...O(1)—C—O(2)
MeOMe									
TS-1a	B3LYP/6-311G**	1.371	1.129	1.982	1.456	1.321	2.533	149.5	168.2
	UB3LYP/6-311G**	1.219	1.332	1.921	1.410	1.362	2.735	166.8	176.6
TS-1b	B3LYP/6-31G**	1.451	1.086	2.016	1.494	1.323	2.452	137.8	163.9
MeOEt									
TS-2a	B3LYP/6-311G**	1.317	1.175	1.944	1.446	1.326	2.576	157.9	174.0
	UB3LYP/6-311G**	1.214	1.347	1.894	1.411	1.359	2.661	167.2	177.2
TS-3a	B3LYP/6-311G**	1.321	1.168	1.948	1.444	1.327	2.566	161.7	174.3
	UB3LYP/6-311G**	1.212	1.347	1.888	1.410	1.359	2.720	171.1	177.3
$MeOPr^i$									
TS-7a	B3LYP/6-311G**	1.285	1.213	1.912	1.437	1.332	2.552	165.0	176.2
	UB3LYP/6-311G**	1.210	1.356	1.871	1.411	1.357	2.615	170.8	177.5
$MeOCH_2CH_2F$									
TS-4a	B3LYP/6-311G**	1.430	1.093	2.009	1.466	1.319	2.467	149.2	162.9
	UB3LYP/6-311G**	1.239	1.294	1.944	1.416	1.364	2.772	175.5	174.5
TS-5a	B3LYP/6-311G**	1.353	1.141	1.973	1.462	1.322	2.707	154.3	176.4
	UB3LYP/6-311G**	1.219	1.334	1.908	1.414	1.362	2.842	169.3	180.0
TS-6a	B3LYP/6-311G**	1.386	1.117	1.988	1.456	1.322	2.570	153.7	170.6
	UB3LYP/6-311G**	1.220	1.329	1.908	1.411	1.362	2.919	174.5	178.8

substituents should increase the probability of the reaction to proceed *via* the radical route.

The data obtained on the oxidation products, kinetics of the process, and solvent effect on the process rate can be rationalized in the framework of a mechanism that assumes the nonradical or hidden radical oxidation of the α-C—H bond of an ether molecule (Scheme 7).

Scheme 7



However, it cannot be excluded that some ethers containing electron-withdrawing substituents (for instance, compound **3**) can exhibit a competition between the nonradical and homolytic mechanisms, which assumes hydrogen atom abstraction from an ether molecule by dioxirane.

This work was financially supported by the Russian Science Support Foundation and the Division of Chemistry and Materials Science of the Russian Academy of Sciences (Program of Fundamental Research "Theoretical and Experimental Study of the Chemical Bond Nature an Mechanisms of the Most Important Chemical Reactions and Processes").

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Received March 18, 2005;
in revised form June 25, 2005