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Reactivity of polyenes in solid-state autoxidation

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ABSTRACT: The reactivity of polyenes (β-carotene, canthaxanthin, lycopene and some retinyl polyenes as related compounds) in the solid state towards molecular oxygen at various temperatures and oxygen pressures was studied. The specimens were thin (*ca* 0.1 μm) amorphous films prepared by evaporation of one or two drops of appropriate solution on quickly rotating supports. The autoxidation was monitored by recording the changes in the electronic and infrared spectra of oxidizing films and was demonstrated to be a chain free-radical process with extremely high chain-initiation rates (10^{-5}–10^{-6} mol l^{-1} s^{-1}). For various polyenes the kinetic parameters of the initiation reaction were measured. In the films of several polyenes (retinyl acetate, retinal, methyl retinoate, β-carotene), the formation of free radicals proceeds in the absence of oxygen and the mechanism of the process was suggested. The observed ratios of the propagation and termination rate constants depend on the oxygen pressure, indicating the involvement of polyenyl radicals in the chain termination process. The observed trends are explained using the concepts of the stabilization energy of radicals, the reversibility of oxygen addition to polyenyls and morphological features of polyene films.

KEYWORDS: polyenes; solid-state autoxidation

INTRODUCTION

The behavior of linear polyenes in autoxidation reactions reveals some special features. The features of the liquid-phase autoxidation of polyenes were described in a previous paper.[1] The mechanism of the initial stage of the process was explained in terms of the isomerization of peroxy radicals and of the reversibility of the formation of polyenyl peroxy radicals. It was also shown that the reactivity of the polyenic compounds studied exceeds the reactivity of other related compounds by several orders of magnitude. This is a consequence of the weakness of the 'allylic' C—H bond (in the case of chain propagation through H atom abstraction) and the high stabilization energy of polyenyl radicals (in the case of propagation via peroxy radical addition to conjugated C═C bonds).[1]

The investigation of polyene autoxidation in the solid state was initiated by the observation that many polyenes of the vitamin A series and β-carotene in thin amorphous films on supports undergo autoxidation at extremely high rates. It was also shown that in the absence of oxygen there is no change in either the electronic or infrared spectra of the films during a considerable time. In the presence of O_2, fast oxidation of the polyenes occurs, resulting in corresponding changes in the electronic and IR spectra of the films.[2]

In this paper we present the results of a kinetic study of the solid-state autoxidation of some long-chain biologically active polyenes (β-carotene, canthaxanthin and lycopene) and related compounds with shorter polyene chains (retinyl acetate, methyl retinoate and retinal). The regularities of the solid-state autoxidation were found and explained using the main concepts of the reactivity of polyenes developed previously.[1]

EXPERIMENTAL

The experimental procedures of polyene purification and storage were described previously.[1,2] (All-*E*)-canthaxanthin (4,4′-diketo-β-carotene) was obtained by oxidation of (all-*E*)-β-carotene by an aqueous solution of $NaOCl_3$ at room temperature. The subsequent treatment and isolation were performed according to Ref. 3. (All-*E*)-lycopene (ψ,ψ'-carotene) was kindly supplied by Professor E. P. Feofilova (Institute of Microbiology, Russian Academy of Sciences) and was used without additional treatment. The inhibitors used were 2,6-di-*tert*-butyl-4-methylphenol and 2-*tert*-butyl-4-methoxyphenol. The purity of carotenoids and retinyl polyenes was checked by high-performance liquid chromatogra-

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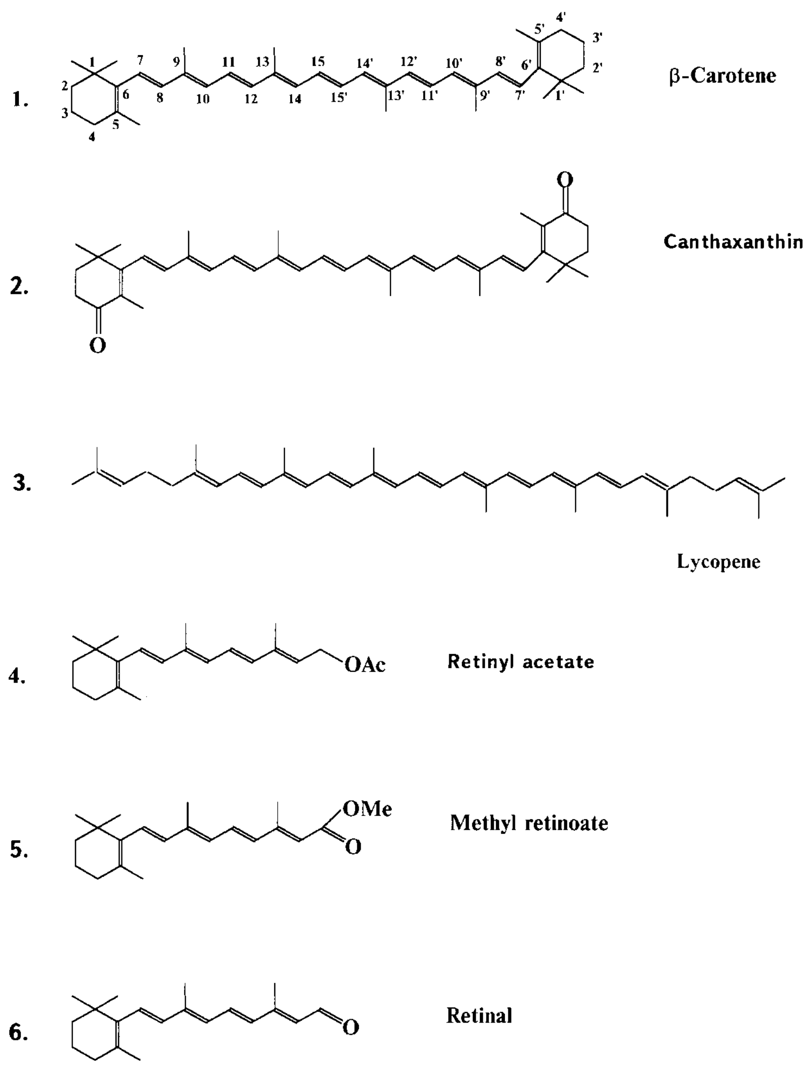


Scheme 1.

phy and was shown to be not less than 99%. Noncontrolled autoxidation was carefully avoided. All the polyenes were stored *in vacuo* [10^{-2}–10^{-3} Torr (1 Torr = 133.3 Pa)] at about $-15\,°C$. The solvents (benzene, *n*-hexane, $CHCl_3$) were purified by standard techniques and dried over sodium metal and calcium hydride (benzene and *n*-hexane) and Al_2O_3 ($CHCl_3$). After degassing, the dry solvents were vacuum condensed in glass tubes. The tubes were sealed at about 10^{-3} Torr. The solvents were saturated with argon before use by breaking off the tubes under an argon atmosphere.

Amorphous films of the polyenes were prepared in a dry argon atmosphere (in an argon box) by evaporation of one to two drops of the solution of a polyene on fast rotating quartz (for electronic spectra recording) or KRS-5 (for IR spectra recording) supports. The thickness of the films was estimated to be of about 0.1 μm.[4] Spectral techniques (electronic and IR) were used to investigate the kinetics and mechanism of autoxidation. The high molar absorption coefficients at the main absorption bands of the polyenes in the electronic spectra provides a convenient and precise spectroscopic technique for the investigation of the autoxidation process. A computer comparison showed that the main absorption bands of the starting compounds before autoxidation are identical with those at low (1–3%) degrees of conversion. Consequently, the spectra of primary autoxidation products do not superimpose on the main absorption bands of the polyenes.

Thermostated quartz cells were used for recording electronic spectra. A support with the film was placed in the cell in an argon atmosphere (in an argon box). The cell was set in the sample compartment of the spectrophotometer and connected to a vacuum line and a manostat for oxygen feeding. After evacuation of the cell, the spectra of the film were recorded *in vacuo* and then in an oxygen atmosphere at a given oxygen pressure and temperature. For recording transmission IR spectra, a vacuum cell with KRS-5 windows was used. Multiple attenuated total reflection (ATR) spectra were obtained

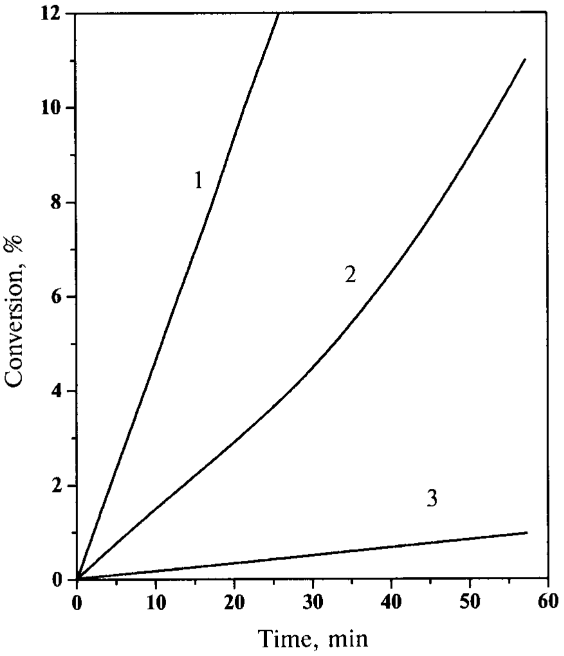


Figure 1. Plots of methyl retinoate consumption at 60 °C: (1) at oxygen pressure 760 Torr without additive; (2) with added 0.05 mol kg^{-1} of 2-*tert*-butyl-4-methoxyphenol at oxygen pressure 760 Torr; (3) under Ar atmosphere (760 Torr)

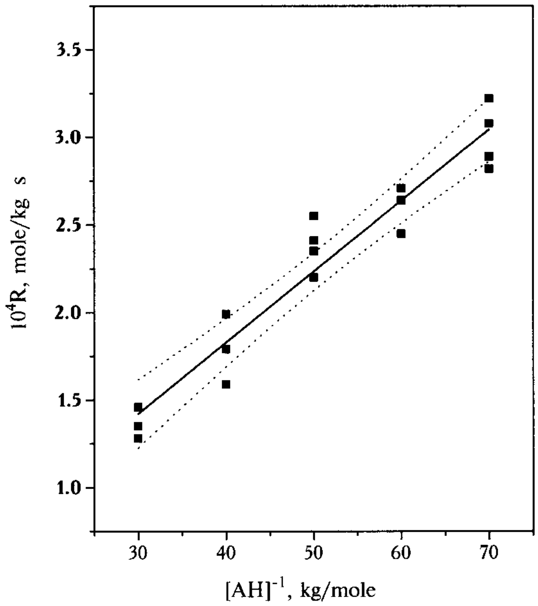


Figure 2. Dependence of retinyl acetate autoxidation rate in films at 20 °C and oxygen pressure 150 Torr (total pressure 760 Torr) according to Eqn. 2. Inhibitor: 2-*tert*-butyl-4-methoxyphenol. The full line corresponds to the least-squares fit $R = \{(0.2 \pm 0.15) + (0.04 \pm 0.02)/[AH]\} \times 10^{-4}$ mole l^{-1} s^{-1}; the dotted lines show the 0.95 confidence limit

using an ATR unit with KRS-5 reflection elements (49 × 25 × 3.5 mm, 14 reflections, 45° facets). The ATR IR spectra were recorded by exposing the films to air in the spectrometer sample compartment. UV–visible spectra vere recorded on a Specord M40 spectrophotometer and IR spectra on a Specord M80 spectrophotometer (Carl Zeiss, Jena, Germany).

The conversion of the polyenes during their autoxidation was determined by monitoring the decrease in the optical densities of the absorption bands of their electronic spectra. The kinetic data were evaluated from the initial slopes of the polyene consumption curves. The compounds investigated are shown in Scheme 1.

RESULTS AND DISCUSSION

Kinetics of solid-state autoxidation

The autoxidation of polyenes in thin amorphous films proceeds at very high rates without any induction period. The inhibition of the substrate consumption by low concentrations of common chain-breaking antioxidants (2,6-di-*tert*-butyl-4-methylphenol and 2-*tert*-butyl-4-methoxyphenol) indicates a free-radical chain mechanism of the process.[5] The rates of oxidation were calculated from the values of the initial slope of kinetic curves. To describe the data obtained, the usual scheme of non-initiated autoxidation[5] was used (see also Ref. 1). According to the scheme, the overall rate of the process in the absence of an initiator is given by the following equation:

$$R = R_0 + (k_p/k_t^{1/2})_{obsd}[RH]R_0^{1/2} \tag{1}$$

where R is the overall rate of polyene autoxidation, (k_p/

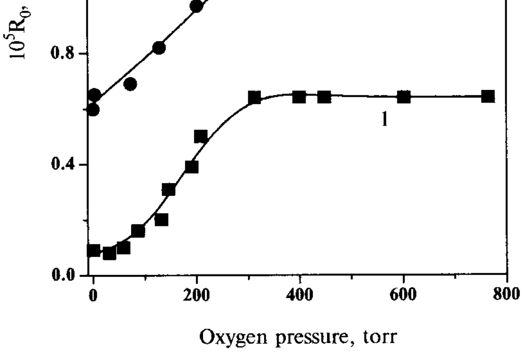


Figure 3. Dependence of R_0 in β-carotene films on oxygen pressure at different temperatures: (1) 25 °C; (2) 35 °C

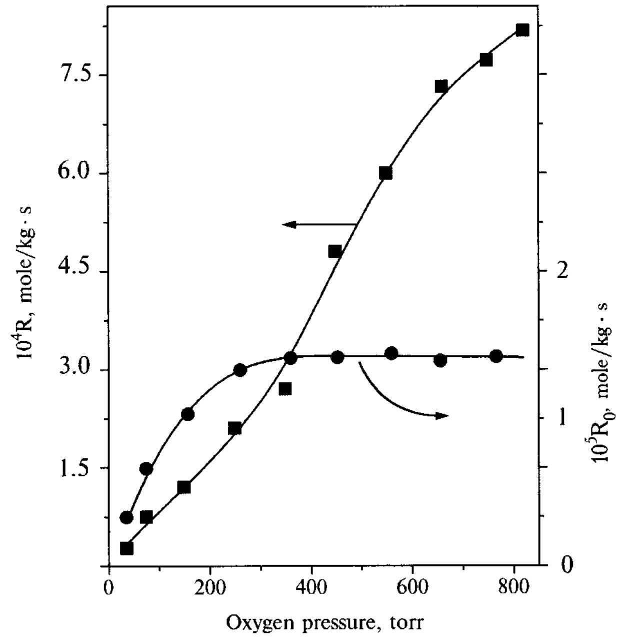


Figure 4. Dependences of the autoxidation and initiation rates in retinal films on oxygen pressure at 25 °C

$k_t^{1/2})_{obsd}$ is the observed ratio of the propagation (k_p) and termination (k_t) rate constants, [RH] is the polyene concentration in a film (mol kg^{-1}) and R_0 is the initiation rate (rate of free radical formation).

In the presence of a chain-breaking inhibitor, the rate of the autoxidation fits the equation

$$R = R_0 + (k_p/k_{inh})[RH]R_0/f[AH] \qquad (2)$$

where k_{inh} is the rate constant of chain termination by inhibitor, f is the inhibition coefficient and [AH] is the inhibitor concentration.

The main dependences found are shown in Figs. 1–4 and in Tables 1 and 2. According to these dependences, the solid-state autoxidation of polyenes is a non-branching chain process [Figs. 1 and 2, Eqns 1 and 2]. The most impressive feature is the high rate of free radical formation (initiation) both in an oxygen atmosphere and in the absence of oxygen (in argon or *in vacuo*). Three types of R_0 change with oxygen pressure were found: (a) linear growth (Fig. 3); (b) non-linear growth when R_0 eventually reaches a limiting constant value (Figs. 3 and 4); and (c) the independence of R_0 of P_{O2} [for retinyl acetate $R_0 = (8.6 \pm 2.1) \times 10^{-6}$ mol kg^{-1} s^{-1} at P_{O2} from 0 to 720 Torr at 20 °C]. It is essential that the overall rate of autoxidation increases with increase in oxygen pressure when R_0 is constant (Fig. 4). As follows from Fig. 2–4, the main contribution to the rate of free radical formation at low P_{O2} values is due to the rate of thermal reaction (R_{01}) without participation of O_2. It is interesting to compare the rate of the reaction in solution and in amorphous films. For example, for retinyl acetate in chlorobenzene solution at 45 °C R_{01} increases linearly with $[RH]^2$ (at [RH] <0.15 mol l^{-1}) and $k_{01} \approx 3.7 \times 10^{-7}$ l mol^{-1} s^{-1}. Extrapolating the solution value of R_{01} to the concentration of polyene in the film (3.05 mol kg^{-1} or about 2.5 mol l^{-1}), one obtains at 45 °C $R_{01} = 1.9 \times 10^{-6}$ mol l^{-1} s^{-1}. In a solid film at the same temperature (from the data in Table 1) $R_{01} = 4.6 \times 10^{-3}$ mole kg^{-1} s^{-1}. This value is about 2000 times higher than that in a hypothetically analogous solution. Moreover, the rate of free radical formation in solid films is much higher than that in solution, both in the absence and in the presence of O_2. For β-carotene autoxidation in solution[6] the following expression was found: $R_0 = 3.7 \times$

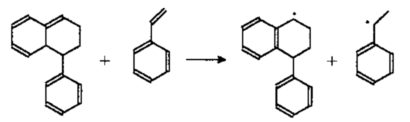
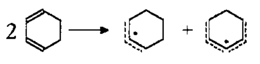
Table 1. Rates and Arrhenius parameters of thermal initiation of polyene autoxidation in solid films

Polyene	Temperature (°C)	Oxygen pressure (Torr)	$R_0 \times 10^5$ at 25 °C (mol kg^{-1} s^{-1})	Log *A*	E_0 (kJ mol^{-1})
β-Carotene	25	750	0.68	—	—
Retinyl acetate	11–25	720	3.3	29.4 ± 0.3	193 ± 12
Retinyl palmitate	25	720	0.1	—	—
Methyl retinoate	48–60	760	0.011	19.0 ± 1.8	148 ± 11
Retinal	25–45	150	1.03	−1.88 ± 0.24	17.8 ± 1.4

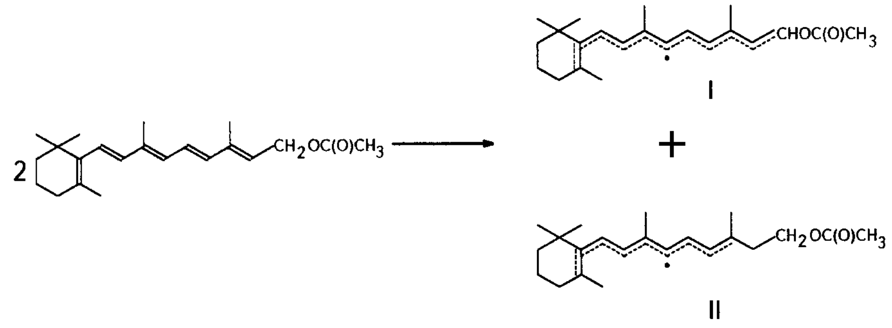
Table 2. Kinetic parameters of solid-state autoxidation of polyenes

Polyene	Temperature (°C)	$R \times 10^4$ at 25 °C (mol kg^{-1} s^{-1})	Log *A*	*E* (kJ mol^{-1})	$(k_p/k_t^{1/2})_{obsd}$ at 25 °C $(kg\ mol^{-1}\ s^{-1})^{1/2}$
β-Carotene	12–25	0.58	3.1 ± 0.5	37.7 ± 3.0	0.03
	28–48		9.9 ± 0.5	76.7 ± 2.9	
Canthaxanthin	35–45	6.0×10^{-6}	23.0 ± 2.0	161.0 ± 15.0	—
Lycopene	25	0.54	—	—	—
Retinyl acetate	25	8.6	—	—	0.063
Methyl retinoate	48–60	0.0046	19.6 ± 3.9	147.7 ± 2.4	0.00044
Retinal	25–45	0.85	3.1 ± 0.1	41.1 ± 9.8	0.0066

Table 3. Heats of reaction (01) and stabilization energies of radicals generated[a]

No.	Reaction	ΣE_s (R_i) kJ mol^{-1}	ΔH_{01} (kJ mol^{-1})	Ref.
1	$2C_2H_4 \rightarrow CH_3CH_2^\bullet + CH_2 = CH^\bullet$	18	269.5	11
2	$C_2H_4 + c\text{-}C_5H_8 \rightarrow C_2H_5^\bullet + c\text{-}C_5H_7^\bullet$	112.2	188.0	12
3	$2\ c\text{-}C_5H_8 \rightarrow c\text{-}C_5H_9^\bullet + c\text{-}C_5H_7^\bullet$	132.8	199.8	13, 14
4		162.6	111.7	15
5		216.2	92.0	16
6	2 (Retinyl acetate) → I + **II** (Scheme 2)	293.6	−14.0	This work

[a] The values of ΣE_s (R_i) and ΔH_{01} were calculated using data from Refs. 10–16.



Scheme 2. Thermal formation of radicals from retinyl acetate

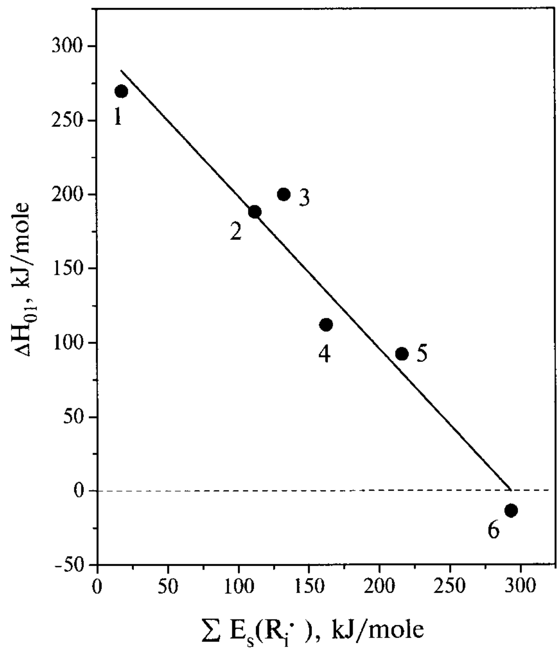


Figure 5. Relationship between the heat of reaction (01) and the sum of the stabilization energies of the radicals formed. The numbers adjacent to the points are the numbers of reactions in Table 3. The straight line corresponds to Eqn. 4

10^{12}[RH][O_2]exp[(−107.5 kJ mol^{-1})/RT]. Extrapolating the data to the conditions of film oxidation (35 °C, P_{O2} = 750 Torr, [RH] = 1.55 mol l^{-1}) one obtains $R_0 = 3.3 \times 10^{-8}$ and 3.3×10^{-9} mole l^{-1} s^{-1} at O_2 concentrations of 10^{-2} and 10^{-3} mole l^{-1}, respectively. This is 300 and 3000 times less than the rate of free radical formation in the films [the thermal initiation reaction (Fig. 3) was not taken into account]. In the absence of oxygen the formation of free radicals proceeds in films of retinyl acetate, methyl retinoate, retinal and β-carotene. Because in solutions of retinyl acetate at high concentrations $R_{01} \approx [RH]^2$, one may suppose that at these concentrations in solution and also in amorphous films of the polyene, free radicals are formed by the following reaction:

$$2RH \rightarrow R^\bullet + R'^\bullet \qquad (01)$$

Several reactions of free radical formation by disproportionation of two unsaturated molecules are known. These reactions along with their corresponding ΔH_{01} values are given in Table 3. For retinyl acetate, we consider the reaction shown in Scheme 2. The heat of the reaction was estimated using the equation

$$\begin{aligned}\Delta H_{01} = {} & D(\text{R---H}) + D^{\pi}(\text{C=C}) - E_s(\text{II}) \\ & -D(> \text{CH---H}) \qquad (3)\end{aligned}$$

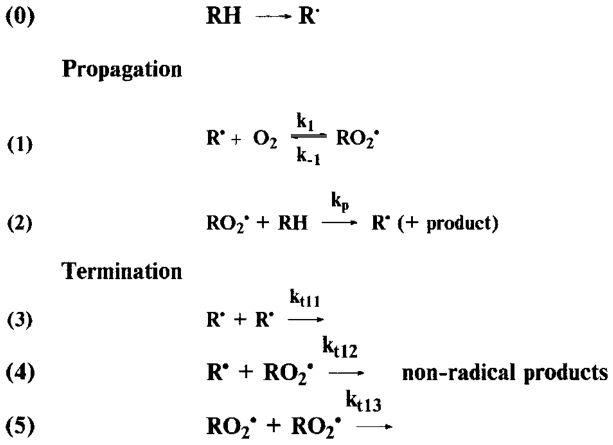
where D(R— H) = 286 kJ mol^{-1},[7] D^{π}(C=C) = 245 kJ mol^{-1},[8] E_s(II) ≈ 140 kJ mol^{-1}, from interpolation between $E_s \approx 152$ kJ mol^{-1} for pentaenyl (I)[1] and $E_s \approx 130$ kJ mol^{-1} for heptatrienyl,[9] D(>CH—H) = 405 kJ mol^{-1} (Ref. 10) and $\Delta H_{01} \approx -14$ kJ mol^{-1}. The result may be regarded as approximate but it is obvious from Table 3 and Fig. 5 that the endothermicity of the reaction (01) decreases with increasing stabilization energy of the radicals generated. For retinyl acetate the reaction may be regarded as at least thermoneutral or even exothermic. The data in Table 3 fit the equation

$$\begin{aligned}\Delta H_{01} = {} & (302 \pm 20) - (1.03 \pm 0.11)\Sigma E_s(\mathrm{R}_i^{\bullet}), \\ r = {} & 0.954 \qquad (4)\end{aligned}$$

where $E_s(R_i^{\bullet})$ is the stabilization energy of radical $\mathrm{R}_i^{\bullet}$.[1,10]

It is difficult to propose a mechanism for the thermal initiation reaction of the other polyenes studied. However, with regard to β-carotene it is reasonable to consider the possibility of thermal initiation of autoxidation through the biradical state. The thermal formation of biradicals from this polyene has been proposed and the Arrhenius parameters of the process have been evaluated.[17] If the two radical parts of a biradical react independently of each other, the overall rate of thermal initiation may be calculated from the data in Ref. 17 and equals about 10^{-7} mol l^{-1} s^{-1} for 15–15′ biradical and about 10^{-6} mol l^{-1} s^{-1} for 13–14 biradical at 35 °C. Our experimental value of R_0 is higher, 6×10^{-6} mol l^{-1} s^{-1} (Fig. 3). There may be two main reasons for the discrepancy. First, in the amorphous state of such a long molecule there is a probability of partial twisting around one of its double bonds. The twisting may be forced by the strains arising during the formation of a film at the instantaneous evaporation of a polyene solution drop on the quickly rotating support. As a result, the activation barrier separating *trans* from *cis* isomers may be considerably reduced, leading to an increased rate of biradical formation. Second, it is not excluded that the generation of free radicals in amorphous films of β-carotene occurs without mediation of the biradical state. However, more experimental evidence is needed to elucidate the real mechanism of thermal free radical formation in amorphous films of polyenes.

Effect of the reversibility of peroxy radical formation on the autoxidation kinetics



Scheme 3. Simplest mechanism of autoxidation

The increase in R with increase in oxygen pressure at constant R_0 (Fig. 4) should be regarded as a consequence of the involvement of carbon radicals in the chain termination reactions (Scheme 3). As a result, the dependence of the autoxidation rate on the oxygen pressure is complicated and does not reach a constant value with increasing P_{O_2} (Fig. 4). Consequently, in the range of the oxygen pressures studied (up to 820 Torr), reaction (5) does not play a role in the termination process which is confined to reactions (3) and (4) (Scheme 3). In this case the overall reaction rate may be described by the equation

$$R = k_1 k_p K_1[\mathrm{O}_2][\mathrm{RH}]R_0{}^{1/2}/[\alpha(\alpha k_{t11} + \beta k_{t12})]^{1/2} \qquad (5)$$

where $\alpha = k_1 + k_p K_1[\mathrm{RH}]$, $\beta = k_1 K_1[\mathrm{O}_2]$ and $K_1 = k_1/K_{-1}$.

The dependence of the observed rate constant ratio on

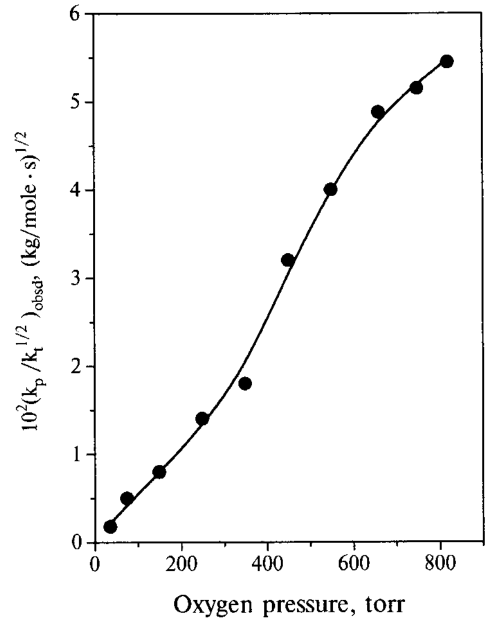


Figure 6. Dependence of the observed rate constant ratio on the oxygen pressure for the autoxidation of retinal films

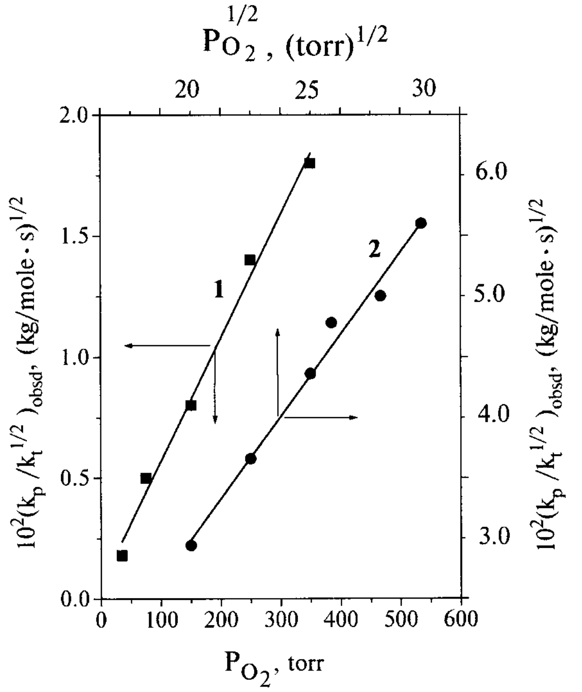


Figure 7. Linear relationships according to Eqns 6 (1) and 7 (2)

the oxygen pressure is shown in Fig. 6. At low P_{O_2}, when the only termination reaction is reaction (3),

$$(k_p/k_t^{1/2})_{obsd} = \frac{k_1 k_p K_1[O_2]}{(k_1 + k_p K_1[RH])k_{t11}^{1/2}} \tag{6}$$

At higher P_{O_2} values the termination reaction (4) becomes the prevailing one and

$$(k_p/k_t^{1/2})_{obsd} = \frac{k_p(k_1 K_1[O_2])^{1/2}}{\{k_{t12}(k_1 + k_p K_1[RH])\}^{1/2}} \tag{7}$$

As follows from these equations, the linear dependence of $(k_p/k_t^{1/2})_{obsd}$ on P_{O_2} should change with increase in the oxygen pressure to a linear dependence on $P_{O_2}^{1/2}$. This change was observed for retinal film autoxidation (Fig. 7). In the range of P_{O_2} from 40 to 350 Torr,

$$(k_p/k_t^{1/2})_{obsd} = (5.36 \pm 0.22) \times 10^{-5} P_{O_2}, \quad r = 0.987 \tag{8}$$

and at higher oxygen pressures (450–820 Torr),

$$(k_p/k_t^{1/2})_{obsd} = [(-3.68 \pm 0.19) + (0.33 \pm 0.32)] \times 10^{-2} P_{O_2}^{1/2}, \quad r = 0.986 \tag{9}$$

The result may be regarded as an evidence for a high carbon radical concentration in autoxidizing polyene films due to the reversibility of reaction (1) (see also Ref. 1).

Acknowledgements

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