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Autoxidation of linoleic acid in a strong magnetic field (9.4 T)

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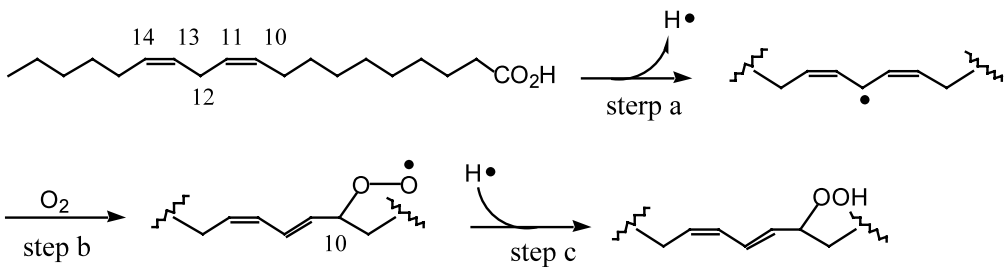
Abstract—Autoxidation of linoleic acid in a strong magnetic field (9.4 T) has been studied. Formation of the hydroperoxides has been monitored by the $Fe(SCN)_3$ method, showing that the magnetic field accelerates the autoxidation of linoleic acid.

Concerns about magnetic effects on biological systems are growing since the chances for mankind to be exposed to moderate or strong magnetic fields, e.g. linear motor cars and MRI, are increasing. Living organisms are functioned by a series of chemical reactions and, therefore, basic knowledge of the magnetic effects on fundamental chemical reactions may be required for understanding the effect of a magnetic field on human health.

In our studies on the effects of a magnetic field on chemical reactions, superconductive NMR instruments (400 MHz) have been used. They can produce a strong and extremely stable magnetic field (9.4 T). We have recently reported that a butyltin hydride reduction of halides, supposedly a radical reaction, is accelerated by a strong magnetic field (9.4 T).[1]

We were interested to see if autoxidation of linoleic acid, an essential constituent of mammalian lipids, would be affected by the magnetic field, because the oxidation is known to proceed via radical reactions. The autoxidation course of linoleic acid is shown in Scheme 1.[2] The hydroperoxides are formed by abstraction of a hydrogen atom from the doubly allylic methylene group and addition of oxygen to the allyl radical, followed by addition of a hydrogen to the peroxide radical. The present report deals with a comparative study of linoleic acid autoxidation in the presence or absence of a 9.4 T magnetic field.

Linoleic acid (250 μmol) was dissolved in ethanol (2.5 mL) and the solution was added to 0.1 M phosphate buffer (pH 7.0). The total volume of the mixture was adjusted to 25.0 mL. A 0.5 mL portion of this mixture (1.00×10^{-2} M for linoleic acid) was placed in a 0.5 mm NMR tube (this sample was designated $S_{9.4T}$), which was then set in the probe of a 400 MHz NMR spectrometer (Bruker ARX-400). Prior to insertion of the sample tube, the temperature (37°C) of the probe was measured by a thermocouple (Yokogawa 2455). Throughout the reaction, the spinner and transmitter for a lock signal were turned off to avoid effects other than that of the magnetic field. The other four 0.5 mL portions of the mixture (S_{0T}) were put in NMR tubes,



Scheme 1.

Keywords: autoxidation; linoleic acid; unsaturated fatty acid; magnetic field.

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Table 1. Autoxidation[a] of linoleic acid in the presence and absence of 9.4 T magnetic field

Exp. no.	1	2	3	4	5	6	7	8	9	10
LA[b] (μM)	9.90	10.0	10.4	10.0	10.5	10.0	10.4	10.5	9.90	9.80
A (9.4 T)[c]	0.56	0.69	0.63	0.67	0.58	0.65	0.56	0.70	0.65	0.72
A' (0 T)[d]	0.53	0.56	0.56	0.53	0.55	0.58	0.54	0.63	0.54	0.59
A/A'	1.06	1.23	1.13	1.26	1.05	1.12	1.04	1.11	1.20	1.22

[a] For the experimental conditions, see text. Autoxidation (at 37°C) was stopped at 10 h, and the concentration of the peroxides was expressed as the absorbance at 500 nm after $Fe(SCN)_3$ coloration.
[b] LA, linoleic acid.
[c] Absorbance of the sample in a 9.4 T magnetic field.
[d] Absorbance of the sample without a magnetic field. The average value of four experiments. Standard deviations were from 0.01 to 0.02.

which were covered with aluminum foil to shield them from light, and they were immersed in a water bath, the temperature of which had been set at 37°C by use of the same thermocouple. After 3 h, the reaction mixtures ($S_{9.4T}$ and S_{0T}) were taken out of the tubes, and 100 μL portions of the respective mixtures were added to 75% ethanol containing a mixture of 30% aqueous NH_4SCN (100 μL) and 20 mM $FeCl_2$ in 3.5% hydrochloric acid (100 μL). The concentration of $Fe(SCN)_3$, which is proportional to the amount of the hydroperoxides,[3] was expressed as the absorbance at 500 nm on a spectrophotometer. The same procedure was carried out using a freshly prepared mixture until the reaction time reached 5 h, and the hydroperoxide concentration was determined. These operations were repeated, changing the reaction times from 3 to 20 h. The results are summarized in Fig. 1.

It is obvious that the autoxidation rate of $S_{9.4T}$ is greater than that of S_{0T}. The 9.4 T magnetic field apparently accelerates the autoxidation of linoleic acid. It is also noticeable that the difference between S_{0T} and $S_{9.4T}$ becomes distinct after 10 h reaction time. Therefore, in further experiments, autoxidation was interrupted after 10 h, and the absorbance at 500 nm after

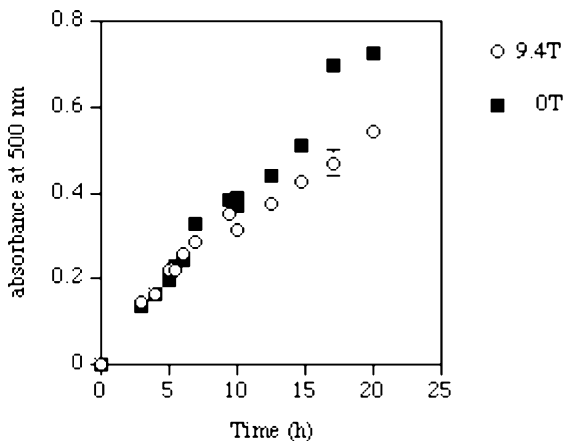

Figure 1. The reaction course of the autoxidation of linoleic acid in the presence (■) ($S_{9.4T}$) and absence (○) (S_{0T}) of a 9.4 T magnetic field. The absorbance at 500 nm of S_{0T} is an average of four experiments performed at 37°C.

$Fe(SCN)_3$ coloration was determined for $S_{9.4T}$ and S_{0T}. The results are summarized in Table 1.

In all the experiments, the concentration of the hydroperoxides determined by the $Fe(SCN)_3$ method was larger for the 9.4 T sample than for the 0 T one, supporting the experimental results shown in Fig. 1. The average ratio of A (9.4 T) versus A' (0 T) was 1.14±0.08, indicating that the autoxidation ratio of linoleic acid (10 μM) at 37°C was increased by 14±8% after 10 h.

The same (concentration, temperature, and reaction time) experiments were repeated on another 400 MHz NMR instrument (JEOL AL400). Again, the increased ratio under the 9.4 T magnetic field was observed: A (9.4 T)/A' (0 T) = 1.15±0.09 (ten experiments).

Difference in the reaction rates between $S_{9.4T}$ and S_{0T} was, however, not observed in 1.4 T (JEOL PMX-60) and 0.4 T (a neodymium magnet) magnetic fields.

Interpretation of the increased rate of the autoxidation in a 9.4 T magnetic field has been difficult so far. There are three possible substitution positions for the hydroperoxy group (C-10, -12, and -14: see Scheme 1), and *cis* and *trans* isomers are feasible for the respective hydroperoxides. The hydroperoxides are unstable and they tend to decompose into complex mixtures including short-chain aldehydes.

We are presuming that one of the radical reactions (steps a–c in Scheme 1) is activated by a 9.4 T magnetic field on the basis of our finding that the tributyltin hydride reduction of phenylalkyl halides is accelerated by the magnetic field,[1] although the mechanism of the acceleration is not clear.

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