Spectroscopic Measurements. The UV absorption spectrum of the membrane was measured with a high-sensitive spectrophotometer (Shimazu UV2100). Flash photolysis measurement was carried out with a pulse and laser flash spectrophotometer equipped with a kinetic data processer (UNISOKU FR-2000). The laser flash was applied perpendicularly to the light path of the spectrophotometer, and the membrane was placed at the crossing of the laser flash and the light path and at 45° to both. The rapid absorption change was recorded with a contact-type photomultiplier to cancel the noise caused by scattered light. Rate parameters for nitrogen binding and dissociation were calculated by pseudo-first-order kinetics. The concentration of nitrogen in the membrane was calculated using the nitrogen solubility determined by gravimetric measurement.

Gravimetric and Permeation Measurements. The sorption amounts of nitrogen and oxygen in the polymer were measured gravimetrically by using an electromicrobalance (Cahn balance Model 2000) which was mounted in a high-pressure chamber made of stainless steel.[9] The chamber was placed in thermostatically controlled air.

Nitrogen and oxygen permeation coefficients for various upstream gas pressures were measured with a low-vacuum permeation apparatus in the chamber with stable thermostating (Rika Seiki K-315 N-03). The pressures on the upstream and the downstream sides were detected by using a Baratron absolute pressure gauge (MKS Instruments).

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Areas of "Macromolecular Complexes" from the Ministry of Education, Science and Culter, Japan.

Radical-Scavenging Reactions of Vitamin E and Its Model Compound, 2,2,5,7,8-Pentamethylchroman-6-ol, in a *tert*-Butylperoxyl Radical-Generating System[1]

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Contribution from the Tokyo Metropolitan Institute of Gerontology, 35-2 Sakaecho, Itabashiku, Tokyo 173, Japan, and the Faculty of Pharmaceutical Sciences and the Department of Reaction Chemistry, the Faculty of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyoku, Tokyo 113, Japan. *Received October 25, 1988*

Abstract: In a *tert*-butylperoxyl radical-generating system containing di-*tert*-butyl diperoxyoxalate (DBPO) and *tert*-butyl hydroperoxide (BOOH), vitamin E (α-tocopherol: **1**) is converted into 4a,5-epoxy-4a,5-dihydro-8a-hydroperoxy-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(8a*H*)-one (**2**) and 8a-(*tert*-butyldioxy)-4a,5-epoxy-4a,5-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(8a*H*)-one (**3**), and its model compound, 2,2,5,7,8-pentamethylchroman-6-ol (**4**), is converted into 4a,5-epoxy-4a,5-dihydro-8a-hydroperoxy-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one (**5**) and 8a-(*tert*-butyldioxy)-4a,5-epoxy-4a,5-dihydro-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one (**6**). The structures of these compounds were deduced on the basis of the spectral data and, in addition, that of **5** was confirmed by X-ray crystallography. The reactions did not proceed under degassed conditions, so the presence of molecular oxygen was suggested to be a requisite for them. In the system without DBPO, **4** gives **5** and **6** in low yields, and without BOOH, **4** gives its dimers (**7a** and **8a**) and trimer (**9a**). Further, it was observed that, in the presence of BOOH, **5** was derived from a hydroperoxide, 8a-hydroperoxy-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one (**10**), and was transformed into **6**. Accordingly, **10** and 8a-hydroperoxy-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(8a*H*)-one (**11**) may be intermediates of **5** and **2**, respectively, and **5** and **2** may be intermediates of **6** and **3**, respectively. A possible mechanism is shown for the reaction of **1** with the *tert*-butylperoxyl radical (BOO•) under the hydroperoxide-rich conditions. The reaction mechanism is discussed with respect to the chain-breaking reaction of **1** against lipid peroxidation.

Vitamin E, mainly (*R,R,R*)-α-tocopherol, is a naturally occurring radical scavenger and is considered to act as an efficient chain-breaking antioxidant against lipid peroxidation.[2] Vitamin E activity appears to be related to the retardation of some serious diseases and functional deteriorations,[3] such as cardiovascular diseases, cancer, and aging, which result at least partially from lipid peroxidation. The elucidation of its chain-breaking reactions is very important for the understanding of defense mechanisms in vivo and the development of new treatments against these deteriorative changes.

Kinetic, spin trapping, and product analysis studies of lipid peroxidation show that the chain carrier is the peroxyl radical.[4-6] The accepted mechanism for chain breaking by **1** is outlined as follows:[7,8]

$$\mathrm{TOH} + \mathrm{LOO^{\bullet}} \rightarrow \mathrm{TO^{\bullet}} + \mathrm{LOOH}$$

$$\mathrm{TO^{\bullet}} + \mathrm{LOO^{\bullet}} \rightarrow \text{nonradical products}$$

where **1** is represented by TOH, the peroxyl radical by LOO•, the α-tocopheroxyl radical by TO•, and hydroperoxide **2** by LOOH. The reaction of **1** with the peroxyl radical is the rate-limiting step in the process.[2] Further understanding of the

† Tokyo Metropolitan Institute of Gerontology.
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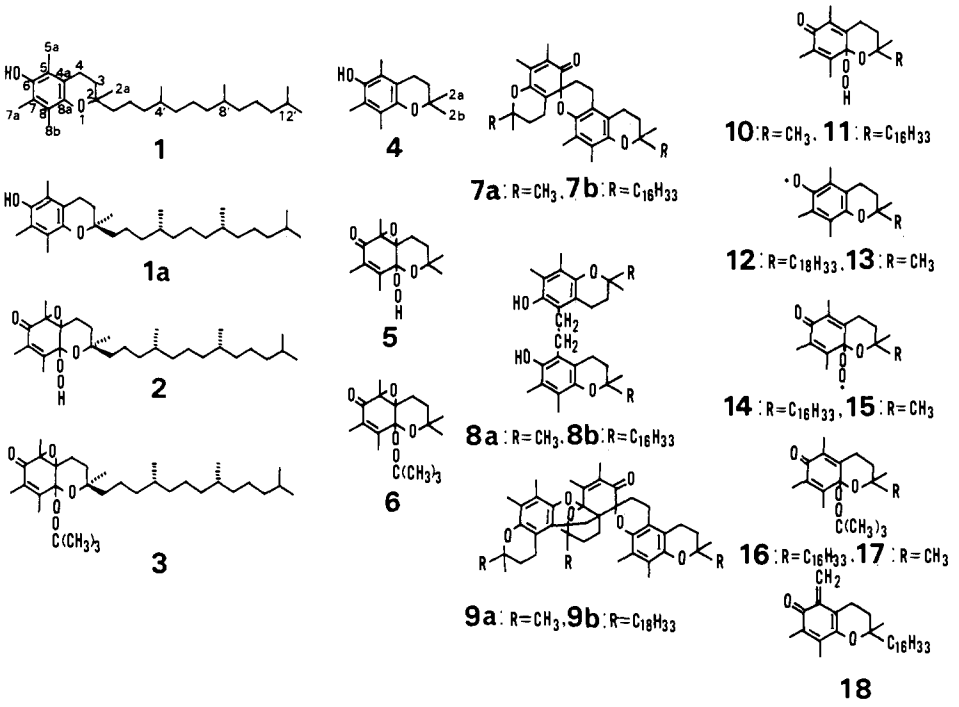


Figure 1. Molecular structures.

chain-breaking mechanism requires a knowledge of the products from this reaction.

Only one report, so far, has been published on the structural determination of reaction products from the reaction of **1** with the peroxyl radical. Mill and associates reported that **1** trapped the 1-cyano-1-methylethylperoxyl radical from 2,2′-azobis(isobutyronitrile) (AIBN) and also the 1-(*n*-butoxycarbonyl)-1-methylethylperoxyl radical from 2,2′-azobis((*n*-butoxycarbonyl)propane) (ABCP) to yield 8a-((1-cyano-1-methylethyl)dioxy)-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-chroman-6(8a*H*)-one and 8a-((1-(*n*-butoxycarbonyl)-1-methylethyl)dioxy)-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-chroman-6(8a*H*)-one, respectively.[9] Their conclusion, however, is somewhat open to question. Although they determined the structures of the products on the basis of the ultraviolet (UV) absorption at 236 nm and the convertibility into α-tocopherylquinone under acidic conditions, these data are ambiguous evidence for the assignment of the structures because several dienones with UV absorptions in the range 230–240 nm can be derived from **1** and converted into α-tocopherylquinone under acidic conditions.[10–12] The structures should be confirmed at least by ^{13}C nuclear magnetic resonance spectroscopy (NMR).

We report here the following findings: in a *tert*-butylperoxyl radical-generating system, **1** is converted into **2** and **3**; the model compound **4** is also converted into **5** and **6**; in addition, **5** is derived from **10** and can be converted into **6**. The structures of these compounds are shown in Figure 1. These results indicate the fate of **1** reacting with the peroxyl radical in hydroperoxide-rich circumstances.

Results

The *tert*-Butoxyl Radical-Induced Chain Decomposition of *tert*-Butyl Hydroperoxide: A *tert*-Butylperoxyl Radical-Generating System. It has been established that, according to the following reaction sequence, DBPO decomposes thermally to give the

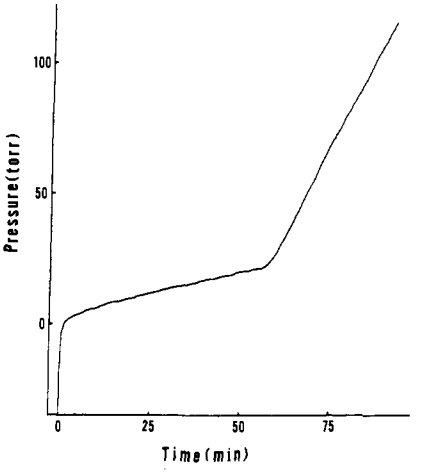
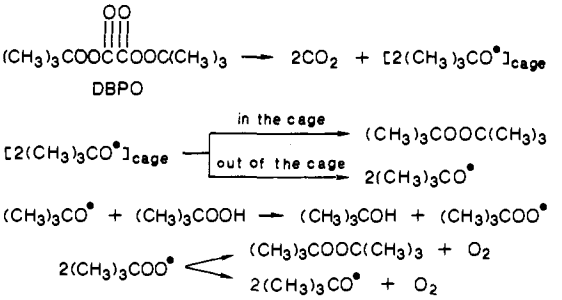


Figure 2. Effect of adding α-tocopherol on the change in pressure of the *tert*-butylperoxyl radical-generating system.

tert-butoxyl radical (BO•) and the BO• reacts with BOOH to give BOO•:[6,13,14]



When BO• cannot react with any species, it undergoes β-scission to afford acetone and the methyl radical:

$$(CH_3)_3CO^{\bullet} \rightarrow (CH_3)_2C{=}O + {}^{\bullet}CH_3$$

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Table I. Reactions of α-Tocopherol and Its Model Compound in the *tert*-Butylperoxyl Radical-Generating Systems

	reaction system,[a] molar ratio					reactn	recovery, %		yield,[b] %								
run	1	4	DBPO	BOOH	gas phase	time, h	1	4	2a	2b	3a	3b	5	6	7a	8a	9a
1	1		0.50	20	air	5	nd[c]		14	14	tr[d]	tr					
2	1		0.50	20	air	40	nd		tr	tr	10	10					
3		1	0.25	20	air	5		17					31	7	nd	nd	nd
4		1	0.50	20	air	5		nd					46	12	nd	nd	nd
5		1	0.50	20	air	48		nd					tr	47	nd	nd	nd
6		1	0	20	air	22		75					12	tr	nd	nd	nd
7		1	0	20	degas	22		80					nd	tr	nd	nd	nd
8		1	0.50	20	degas	5		53					nd	2	nd	nd	nd
9		1	0.36	0	air	5		58					nd	nd	6	7	13

[a] Benzene was used as a solvent. [b] Mole % to each theoretical yield based on starting material. [c] Not detectable. [d] Trace.

The quantitative generation of BOO• in the system was confirmed by the gas-chromatographic findings that carbon dioxide and *tert*-butyl alcohol were quantitatively produced and no acetone was detected.

In the presence of a radical scavenger (AOH), BOO• is trapped before it undergoes the bimolecular interaction

$$n(CH_3)_3COO^{\bullet} + AOH \rightarrow \text{stable products}$$

where n is the stoichiometric number of radicals trapped by a molecule of the radical scavenger.

Figure 2 shows an example of the DBPO-induced radical-chain decomposition of BOOH in the presence of **1**. A mixture of DBPO, BOOH, and **1** in benzene was placed in an ampule, which was connected to a pressure transducer. The ampule was immersed into a water bath at 37 °C at time 0. As the temperature increased at the initial stage, the pressure was rapidly increased. The temperature was equilibrated within less than 1 min, and then the pressure was constantly increased due to the evolution of carbon dioxide from DBPO. While **1** trapped BOO•, only carbon dioxide was evolved; the absence of molecular oxygen was confirmed by gas chromatography. This stage corresponds to an induction period. However, when **1** had been depleted, the pressure was rapidly increased by the evolution of both molecular oxygen and carbon dioxide. In the absence of **1**, BOOH was decomposed by a chain mechanism and molecular oxygen was evolved at a constant rate without an induction period (data not shown). These results indicate that, in the presence of **1**, all of BOO• generated is trapped without the bimolecular interaction.

Products from a Vitamin E Model Compound, 2,2,5,7,8-Pentamethylchroman-6-ol, in the *tert*-Butylperoxyl Radical-Generating System. In the *tert*-butylperoxyl radical-generating system containing DBPO and BOOH, **4** was converted into **5** and **6** (Table I). The structures of **5** and **6** were determined as described below. The elemental analysis data indicate that the molecular formula of **5** is $C_{14}H_{20}O_5$, corresponding to that of **4** with three additional oxygen atoms. The UV, infrared (IR), and NMR spectra reveal that the molecular skeleton of the carbon atoms in **5** is the same as that of **4** and that **5** has both an epoxide ring and a hydroperoxy group, the three oxygen atoms of which correspond to the additional oxygen atoms (the structural assignment of the spectral data is given in Table II in the supplementary material: see the paragraph at the end of the paper). Accordingly, **5** is expected to be epoxydihydrohydroperoxy-2,2,5,7,8-pentamethylchromanone. By X-ray crystallographic analysis, the structure of **5** was conclusively proved to be 4a,5-epoxy-4a,5-dihydro-8a-hydroperoxy-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one.[1] Figure 3 shows the X-ray crystal structure of **5**. In the asymmetric unit of a crystal of **5**, there are two crystallographically independent molecules, **5a** and **5b**, which differ in the conformation of their two hydroperoxy groups (parts a and b of Figure 3). It can be seen from the figure that the stereochemical relationship is trans between the epoxy and hydroperoxy groups in **5**. The crystallographic data of **5** are given in the Experimental Section.

The elemental analysis and spectral data show that **6** has a *tert*-butyldioxy group and that its structure without the *tert*-butyldioxy group coincides with that of **5** without a hydroperoxy group (see the Experimental Section and Table II in the supplementary material). Accordingly, **6** is determined to be 8a-(*tert*-butyldioxy)-4a,5-dihydro-2,2,5,7,8-pentamethylchroman-6-(8a*H*)-one.

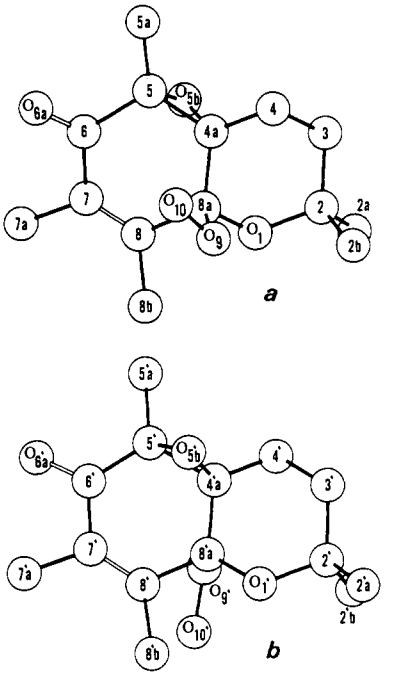

Figure 3. X-ray crystal structures of (a) **5a** and (b) **5b**.

Factors and Intermediates for the Formation of the Reaction Products. The reaction conditions for the formation of **5** and **6** were examined (Table I). The reaction system, which was composed of **4**, DBPO, and BOOH (molar ratio 1.0:0.50:20) in benzene, was heated at 50 °C for 5 h under air to give **5** and **6** in 46% and 12% yields, respectively (run 4), and under degassed conditions to give only **6** in very low yield (run 8). On long heating under air, **6** was produced in a 47% yield and **5** was only slightly detected (run 5). By an insufficient addition of DBPO, the reaction was retarded (run 3). When DBPO was omitted from the reaction system, small amounts of **5** and **6** were obtained under air (run 6), and virtually no products were obtained under degassed conditions (run 7). When BOOH was omitted, the dimers (**7a** and **8a**) and trimer (**9a**) of **4** were obtained (run 9); their structures are shown in Figure 1 (the structure of **9a** was recently revised by Yamauchi et al.[15]). In this case, the recovery of the starting material **4** was rather higher. This may be accounted for by the β-scission of BO• generated in the system.

Time course studies were undertaken on the formation of the reaction products observed by ^{1}H NMR spectroscopy (the time course data are shown in Figure 6 in the supplementary material). Compound **5** was detected in the reaction mixture 30 min after the onset of the reaction, both **5** and **6** were formed after 5 h, and only **6** was found after 28 h. This suggests that **5** is a possible

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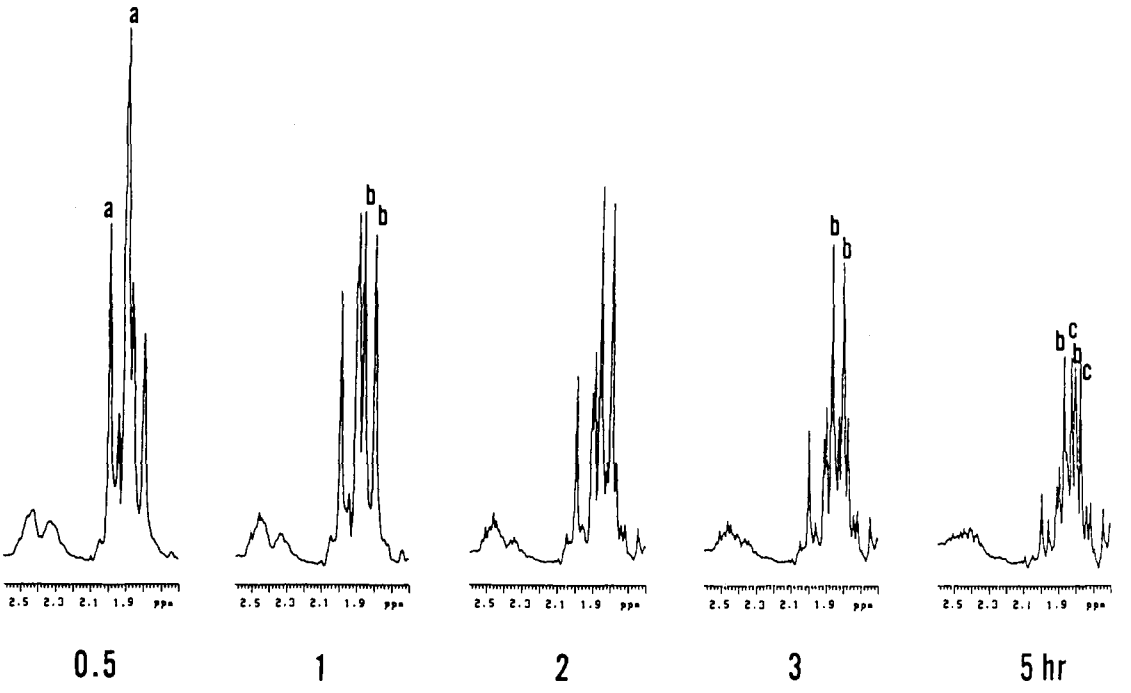

Figure 4. Time course of the alteration in the ^1H NMR signals of the reaction mixture from **10** in the range from 1.6 to 2.6 ppm. Signals a are assigned to the protons of methyl groups attached to sp^2 carbon atoms in **10**, signals b to those in **5**, and signals c to those in **6**.

precursor of **6**. The intermediacy of **5** was proved from the observation that, when allowed to stand at 50 °C for 20 h in benzene containing a 30-fold molar amount of BOOH, **5** was almost quantitatively transformed into **6**.

It appears that, in the initial step of the reaction, there is some intermediate(s) that is converted into **5**, because two ^1H NMR signals which cannot be assigned to hydrogen atoms in **5** and 6 were observed immediately after the onset of the reaction (Figure 6 in the supplementary material). The peak height of the signals remained unchanged as long as **4** existed in the reaction mixture and reduced gradually after **4** had been consumed. The signals disappeared within 5 h. The structure of the intermediate was tentatively identified on the basis of the ^1H NMR chemical shifts of the compounds related to **4**. Compound **10** was found to exhibit the signals identical with the above ones; the chemical shifts are 1.89, 1.91, and 1.99 ppm due to the 5a-, 7a-, and 8b-methyl groups in **10** in a mixture of benzene-d_6 and BOOH (12:1 v/v). Furthermore, when the reaction system containing **10** instead of **4** was heated at 50 °C for 5 h, both **5** and **6** were detected by ^1H NMR spectroscopy in the reaction mixture (Figure 4) and were found to be produced in 21% and 15% yields, respectively. In this case, signals a (due to **10**) disappeared after heating for 3 h and signals c (due to **6**) began to appear after heating for 2 h. In addition, the electron spin resonance (ESR) spectrum indicated that, on heating at 50 °C for 1 h, the reaction mixture contained the α-tocopheroxyl radical (**12**).[16] The 2,2,5,7,8-pentamethylchroman-6-oxyl radical (**13**) was also derived from **4** under similar conditions.[16] No radicals were found in the mixtures that had been heated for 5 h. Probably, **1** and **4**, and hence **12** and **13** also, were consumed within 5 h; this is consistent with the finding that no **4** was recovered at 5 h after the onset of the reaction (Table I, run 4).

In the system without BOOH, presumably BO•, which had been derived from DBPO, abstracted the phenolic hydrogen from **4** (or **1**). As a result, **13** (or **12**) was formed, which did not react with BO• but dimerized and trimerized (Table I, run 9).

Products from α-Tocopherol in the *tert*-Butylperoxyl Radical-Generating System. When a mixture of (*R,R,R*)-α-tocopherol (**1a**), DBPO, and BOOH in benzene was heated at 50 °C for 5 h, products **2a**, **2b**, **3a**, and **3b** were obtained. As shown in Table I (runs 1 and 2), the yields of **2** and **3** were rather low. Although

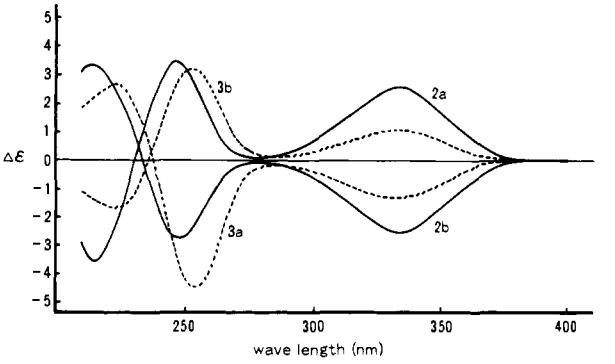

Figure 5. Circular dichroism spectra of **2a**, **2b**, **3a**, and **3b**.

the formation of the remaining products was observed by ^1H NMR spectroscopy, they were unable to be isolated and identified. Their mass (MS) spectra reveal that the molecular weights of **2a** and **2b** and of **3a** and **3b** are 478 and 534, respectively. The compounds were identified on the basis of analysis of their spectral data and of comparison of the spectral data with the spectral data of **5** and **6** (the structural assignment of the spectral data is given in Table II in the supplementary material). Compounds **2a** and **2b** are shown to be a pair of diastereoisomers of 4a,5-epoxy-4a,5-dihydro-8a-hydroperoxy-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(8a*H*)-one. Compounds **3a** and **3b** are found to be a pair of diastereoisomers of 8a-(*tert*-butyldioxy)-4a,5-epoxy-4a,5-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(8a*H*)-one. The UV and IR absorption bands and NMR signals of **2** without the isoprenoid side chain correspond to those of **5**, and the bands and signals of **3** without the isoprenoid side chain correspond to those of **6**. It is obvious that the configurations of the epoxy and hydroperoxy groups in **2** are responsible for the structural difference between **2a** and **2b** and that the configurations of the epoxy and *tert*-butyldioxy groups in **3** are responsible for the structural difference between **3a** and **3b**. As shown in Figure 5, not only the circular dichroism (CD) curves of **2a** and **2b** but also those of **3a** and **3b** are mirror images, although they are not perfectly symmetric. Hence, **2a** and **2b**, as well as **3a** and **3b**, may be nearly antipodal to each other. This is explainable, considering that while only their ring moieties, except the carbon atoms at the 2 positions, are antipodes, the *R* configuration of the carbon atoms at the 2, 4, and 8 positions is

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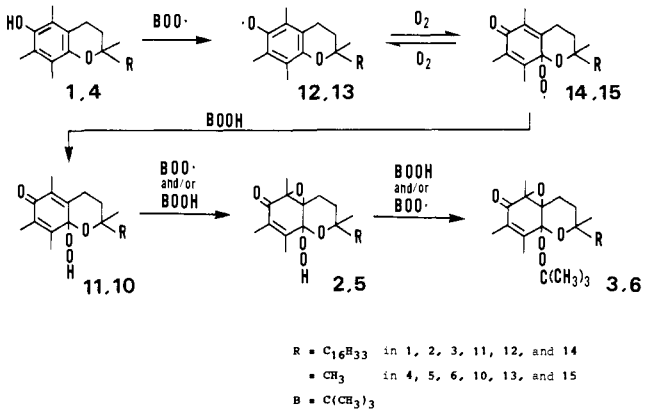
Scheme I. Possible Reaction Pathways for the Formation of Reaction Products



still retained (see Figure 1). The profile of the CD curve of **2a** is similar to that of **3b**, and the profile of **2b** is similar to that of **3a**. Furthermore, the product analysis indicated that no isomers of **5** and **6** were present, and X-ray crystallographic analysis indicated a trans configuration of the epoxy group at C_{4a} and C_5 and the hydroperoxy group at C_{8a} in **5**. These results suggest that the relative configurations are trans between the epoxy and hydroperoxy groups in **2** and between the epoxy and *tert*-butyldioxy groups in **3** and that the configurations of the ring moieties in **2a** and **3b** are similar, being reverse to those in **2b** and **3a**.

Discussion

Scheme I shows the possible reaction pathways for the interactions between **1** and BOO•. Initially, **1** reacts with BOO• to give **12** and BOOH. Under aerobic conditions, **12** interacts reversibly with molecular oxygen to form **14**. In the presence of a high concentration of BOOH, **14** abstracts the hydroperoxidic hydrogen to afford hydroperoxide **11**. Further, **11** is epoxidized by either another BOO• and/or BOOH to produce **2**. On attack of either BOO• and/or BOOH on **2**, a hydroperoxy group in **2** is replaced by a *tert*-butyldioxy group to yield the end product **3**. Compounds **5** and **6** can be produced from **4** in the same manner.

This series of reactions is considered to be initiated by hydrogen abstraction from **1** or **4**. The hydrogen abstraction in the complete system must be performed by BOO•, since the evolution of only carbon dioxide without accompanying molecular oxygen was found before depletion of **1** (Figure 2). In the absence of BOOH, BO• can also abstract a phenolic hydrogen atom from **1** or **4** so that **1** gives **7b**, **8b**, and **9b** or **4** gives **7a**, **8a**, and **9a** (Table I, run 9).

There may be an equilibrium between **12** and **14** (or **13** and **15**) in the presence of molecular oxygen. However, if no efficient hydrogen donors, such as hydroperoxides, exist, **14** cannot be converted into **11**. This is consistent with the finding that, in benzene, no detectable reaction occurred between molecular oxygen and **12**, the latter having been derived from the reaction of **1** with BO•.[17]

The epoxide formations did not proceed under anaerobic conditions. Presumably, the conversion of **12** into **14** is the process of oxygen addition in the overall reaction pathway. Under degassed conditions, however, a very small amount of **6** was obtained (Table I, run 8). Since there is a possibility that molecular oxygen is evolved from the decomposition of some products in the reaction systems, the molecular oxygen might be involved in the formation of **3** and **6**.

The intermediacy of **11** and **10** was deduced from the fact that, when **10** instead of **4** was added into the reaction system, **5** and **6** were formed. However, **10** was also converted into **5** and **6** in benzene containing only BOOH; in addition, it has been reported that BOOH can act without any catalyst as an epoxidizing agent.[18]

Accordingly, BOOH may epoxidize **11** and **10** in a polar fashion, while BOO• may epoxidize them through a radical coupling.

The last step is supported from the findings that **5** was almost quantitatively transformed into **6**, appeared prior to the formation of **6**, and decreased as **6** increased. It is possible that BOOH, BOO•, or both may be responsible for the substitution of a *tert*-butyldioxy group for a hydroperoxy group.

The reaction of **1** with BOO• is thought to be a model for the reaction of **1** with the peroxyl radical, as occurs in chain-breaking action during lipid peroxidation. It should be pointed out, however, that a high concentration of BOOH was added into the present reaction system. Thus, we believe the formation of **2** shows the fate of **1** in radical-scavenging reactions against lipid peroxidation in hydroperoxide-rich circumstances.

Under the conditions that the concentration of the hydroperoxide is much lower, the reverse step from **14** to **12** must be more important. In such cases, **12** may react with another BOO• to form a BOO• adduct **16**. As a result, a molecule of **1** scavenges two molecules of BOO•, consistent with the kinetic observation that a stoichiometric number of 2 was estimated for **1** in the initial propagation of autoxidation of olefins.[2,19] So far, however, **16** has not been obtained. In addition, under the conditions without BOOH, **4** gave the dimers **7a** and **8a** and trimer **9a**, which were unaccompanied by **17** (Table I, run 9). Presumably, **16** and **17** might decompose to **12** and **13**, respectively, with release of molecular oxygen. This is supported by the findings that both **10** (the 8a-hydroperoxide of **4**) and bis(2,2,5,7,8-pentamethyl-6-oxo-6,8a-dihydrochroman-8a-yl) peroxide (the 8a-dioxy dimer of **4**) decomposed to **4** and molecular oxygen.[20] Further, **12** might dismutate into **1** and quinone methide **18**, the latter being converted into dimers **7b** and **8b** and trimer **9b**.[21]

In conclusion, when **1** acts as an antioxidant against lipid peroxidation in hydrophobic environments, its fate depends on the amounts of hydroperoxides and oxygen radicals in the reaction systems; **1** may be converted into the epoxyhydroperoxide **2** under hydroperoxide-rich conditions as in this study, while **1** may give the dimers, the trimer, the peroxyl radical adducts, and some reversionary **1** under hydroperoxide-poor conditions. Furthermore, as the concentration of oxygen radicals and hence of **12** increases, there will be a greater chance for regeneration of **1** by reaction with reducing agents such as ascorbic acid.[19]

Experimental Section

General. All melting points were determined with a Yanagimoto MP-52 melting point measuring apparatus (Yanagimoto Seisakusho, Kyoto, Japan) and are uncorrected. IR spectra were measured on a JASCO IR-2 spectrometer (Japan Spectroscopic Company, Tokyo, Japan), UV spectra on a Cary 118C spectrometer (Varian Associates, Palo Alto, CA), CD spectra on a JASCO J-500A spectrometer, and MS spectra on a Hitachi M-80B spectrometer (Hitachi Seisakusho, Katsuta, Japan). ESR spectra were taken on a Varian E-109 spectrometer (*X* band) with an E-233 large access cylindrical cavity. ^1H and ^{13}C NMR spectra were recorded on Varian XL-200 and XL-300 (for the spectra of compounds **2** and **3**) and VXR-400S (for time course experiments) spectrometers using tetramethylsilane (TMS) as internal standard ($\delta_{TMS} = 0$ for ^1H or ^{13}C); for ^{13}C NMR measurements, the DEPT and, in part, INEPT pulse sequences were used. High-performance liquid chromatography (HPLC) was conducted on a Varian 8200 high-performance liquid chromatograph (Varian Associates, Walnut Creek, CA). Gas chromatography was performed on a Shimazu GC-6A gas chromatograph (Shimazu Seisakusho, Kyoto, Japan) equipped with a Carbowax 20M column (3 mm × 7 m; for the analysis of *tert*-butyl alcohol and acetone) or a molecular sieve 13× column (3 mm × 4 m; for the analysis of carbon dioxide and molecular oxygen) (Gasukuro Kogyo Inc., Tokyo, Japan). (*R,R,R*)-α-Tocopherol was purified, by HPLC, from a mixture of the isomers obtained from Sigma Chemical Company (St. Louis, MO). Compound **4** was synthesized by the method of Nilsson et al.,[22]

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its dimer **7a** by that of Schudel et al.,[23] dimer **8a** by that of Skinner and Alaupovic,[24] and trimer **9a** by that of Lloyd et al.[25] Compound **10** was prepared from the reaction of **4** with singlet oxygen.[20] Di-*tert*-butyl diperoxyoxalate was prepared by the method of Bartlett et al.[13] *tert*-Butyl hydroperoxide was obtained from Nippon Oil and Fats Co. (Tokyo) and was distilled under 24 Torr at 42 °C before use. Its purity was confirmed to be more than 98% by an iodometric methods. All other chemicals were obtained from commercial sources.

X-ray Crystallography. A single crystal of **5** was subjected to X-ray diffraction analysis. The intensities of 985 reflections were measured above the $2\sigma(I)$ level using graphite monochromated Cu Kα radiation. The maximum value of 2θ reached in intensity measurement was 120°. The structure was solved by the direct method and refined by the method of block-diagonal least squares to an R value of 0.098. There are two crystallographically independent molecules, **5a** and **5b**, in an asymmetric unit. Parts a and b of Figure 3 illustrate the structures of **5a** and **5b**, respectively, the perspective views of which were drawn by the PLUTO program.[26] The numbers of carbon and oxygen atoms in **5b** are indicated as primes, so that atom $O_{10'}$ in **5b** corresponds to atom O_{10} in **5a**. All the hydrogen atoms except those in the hydroperoxy groups ($O_{10}H$ and $O_{10'}H$) were included in the refinement for the assumption of isotropic thermal vibrations. The crystal data of **5** are given below: space group $P2_1/a$, $Z = 8$, crystal system monoclinic, $a = 14.138$ (8) Å, $b = 17.867$ (11) Å, $c = 11.439$ (7) Å, $\beta = 101.50°$ (6)°, $U = 2832$ Å^3. Additional crystallographic data are available as supplementary material.

Electron Spin Resonance Measurements. A mixture of **1** (21 mg, 49 μmol), DBPO (5.6 mg, 24 μmol), and BOOH (100 μL, 1.0 mmol) in benzene (1.0 mL) was heated in an ESR sample tube at 50 °C for 1 h. The ESR spectra then were taken at 50 °C. Next the mixture was cooled to room temperature and degassed by the freeze–thaw method under about 10^{-2} Torr. The ESR spectra of the degassed samples were taken at room temperature.[16,27] The ESR spectrum of a radical derived from **4** was also observed after the same workup.

Time Course Experiments on the Formation of the Reaction Products by ^{1}H NMR Spectroscopy. (A) Conversion of 4 into 5 and 6. A mixture of **4** (5.5 mg, 25 μmol), DBPO (2.8 mg, 12 μmol), and BOOH (50 μL, 0.50 mmol) in benzene-d_6 (0.60 mL) was placed in a NMR sample tube. The tube was heated at 50 °C within the NMR cavity. The ^{1}H NMR spectra were taken at 0.5, 1, 2, 3, 5, and 28 h after the onset of heating. Under the above conditions, the ^{1}H NMR chemical shifts of hydrogen atoms in the 7a- and 8b-methyl groups of **5** are 1.80 and 1.86 ppm, respectively, and in the 7a- and 8b-methyl groups of **6** are 1.77 and 1.82 ppm, respectively.

(B) Conversion of 10 into 5 and 6. The mixture of **10** (5.6 mg, 22 μmol), DBPO (2.5 mg, 11 μmol), and BOOH (50 μL, 0.50 mmol) in benzene-d_6 (0.60 mL) was heated at 50 °C. The ^{1}H NMR spectra were taken at 0.5, 1, 2, 3, and 5 h after the onset of heating and showed the signals of 5a-, 7a-, and 8b-methyl groups in **10** at 1.89, 1.91, and 1.99 ppm. The yields of **5** and **6** were 21% and 15%, respectively, on heating for 5 h, as estimated by ^{1}H NMR spectroscopy.

Generation of the *tert*-Butylperoxyl Radical. According to the method reported previously,[28] the quantitative generation of BOO• in the system used was confirmed. A mixture of DBPO (21 mg, 90 μmol) and BOOH (100 μL, 1.0 mmol) in benzene (10 mL) was placed in an ampule, which was degassed and sealed under vacuum. The ampule was immersed into a water bath at 50 °C. After DBPO was allowed to decompose completely, the amount of carbon dioxide evolved was volumetrically measured with a Toepler pump. Further, the *tert*-butyl alcohol formed was quantified, and no acetone formation was confirmed by gas chromatography.

The trapping of BOO• by **1** is visualized in Figure 2. A mixture of DBPO (21 mg, 90 μmol), BOOH (100 μL, 1.0 mmol), and **1** (13 mg, 30 μmol) in benzene (10 mL) was placed in an ampule, which was connected to a Toyoda PMS-5M pressure transducer (Toyoda Machine Works, Kariya, Japan). The ampule was immersed into a water bath at 37 °C. The rate of gas evolution during the DBPO-induced chain decomposition of BOOH was followed by the measurement of the pressure change.[7] For the quantification of carbon dioxide and molecular oxygen, the gas phase was analyzed by gas chromatography.

Quantitative Analysis of Reaction Products. The yields of reaction products and recoveries of starting materials were estimated on the basis of the results of quantitative analysis by HPLC and/or ^{1}H NMR spectroscopy. (A) HPLC. A Micropak Si-10 column (Varian Associates; 4 mm × 30 cm) was used for the separation of **1**, **2**, and **3**. The chromatographic conditions were as follows: mobile phase, *n*-hexane–2-propanol (99.25:0.75, v/v); flow rate, 1.5 mL/min; detection, optical density at 245 nm for **2** and **3**, and at 290 nm for **1**. A Micropak MCH-10 column (Varian Associates; 4 mm × 30 cm) was used for the separation of **4**, **5**, **6**, **7a**, **8a**, and **9a**. The conditions were as follows: mobile phase, acetonitrile–water (55:45 to 100:0, v/v); gradient, 55–100% acetonitrile in 22.5 min; flow rate 1.0 mL/min; detection, optical density at 245 nm for **5** and **6**, at 290 nm for **4**, **7a**, **8a**, and **9a**. The intensities of the peaks were quantified with a Chromatopac C-R1B data processor (Shimazu Seisakusho) and calibrated by an internal standard method using 1-naphthol. (B) ^{1}H NMR spectroscopy. A reaction mixture was concentrated into dryness under reduced pressure. To the residue obtained was added a mixture of chloroform-*d* (0.60 mL) and methanol (1.0 μL, 25 μmol). The ^{1}H NMR spectrum of the chloroform solution was taken. The yield of a reaction product was estimated on the basis of the intensity of a signal due to a methyl group attached to a sp^2 carbon atom in the product, the intensity which was calibrated in comparison to that of a signal due to a methyl group in methanol added as internal standard.

Products from the Vitamin E Model Compound in the *tert*-Butylperoxyl Radical-Generating System. (A) 4a,5-Epoxy-4a,5-dihydro-8a-hydroperoxy-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one (5). A mixture of **4** (11 mg, 50 μmol), DBPO (5.4 mg, 23 μmol), and BOOH (100 μL, 1.0 mmol) in benzene (1.0 mL) was heated at 50 °C for 5 h (unless otherwise noted). Its volatile components were evaporated under reduced pressure. The oily residue obtained was fractionated on a silica gel column. A small amount of **6** was removed from the column with a 20:1 mixture of *n*-hexane and ethyl ether, and then **5** was eluted with the 5:1 mixture. Compound **5** was obtained in a 46% yield (6.2 mg) as a white solid. Recrystallization from a mixture of *n*-hexane and ethyl ether gave colorless needles of **5**. **5**: mp 84–85 °C; IR (KBr) ν 962, 1082, 1134, 1237, 1260, 1373, 1385, 1442, 1452, 1671, 3345 cm^{-1}; UV (CH_3CN) λ_{max} 246 nm (ϵ 6300); ^{1}H NMR ($CDCl_3$) δ 1.36 (s, 3 H), 1.47 (s, 6 H), 1.54–1.64 (m, 1 H), 1.82 (s, 3 H), 1.92 (s, 3 H), 1.96–2.04 (m, 1 H), 2.50–2.65 (m, 2 H), 7.71 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.2 (q), 12.4 (q), 13.9 (q), 20.7 (t), 28.5 (q), 30.9 (q), 34.0 (t), 61.6 (s), 63.2 (s), 75.9 (s), 101.8 (s), 129.7 (s), 145.7 (s), 196.2 (s). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67%; H, 7.51%. Found: C, 63.02%; H, 7.51%.

(B) 8a-(*tert*-Butyldioxy)-4a,5-epoxy-4a,5-dihydro-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one (6). The reaction was carried out under the conditions described above, but the mixture was heated for 48 h instead of 5 h. The reaction product was purified by silica gel column chromatography. A fraction eluted with a 20:1 mixture of *n*-hexane and ethyl ether gave **6** in a 47% yield (7.2 mg) as a colorless oil. **6**: IR ν 957, 1090, 1137, 1198, 1262, 1366, 1452, 1671 cm^{-1}; UV (CH_3CN) λ_{max} 246 nm (ϵ 5300); ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 9 **H**), 1.33 (s, 3 H), 1.46 (s, 6 H), 1.51–1.64 (m, 1 H), 1.78 (s, 3 H), 1.85 (s, 3 H), 1.90–2.07 (m, 1 H), 2.50–2.66 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 10.2 (q), 12.2 (q), 13.4 (q), 20.7 (t), 26.1 (3 q), 28.6 (q), 31.2 (q), 34.2 (t), 62.4 (s), 63.5 (s), 75.5 (s), 78.9 (s), 100.2 (s), 129.3 (s), 144.7 (s), 195.7 (s). Anal. Calcd for $C_{18}H_{28}O_5$: C, 66.64%, H, 8.70%. Found: C, 66.92%, H, 8.76%.

Conversion of 5 into 6. When a mixture of **5** (4.0 mg, 15 μmol) and BOOH (50 μL, 0.50 mmol) in benzene (0.50 mL) was heated at 50 °C for 20 h, **5** was almost quantitatively converted into **6**. The reaction was followed by ^{1}H NMR spectroscopy (see above), HPLC (on a MCH-10 column under the conditions described above), and thin-layer chromatography [on silica gel G (E. Merck AG, Darmstadt, Federal Republic of Germany) with a 1:1 mixture of *n*-hexane and ethyl ether (R_f 0.3 for **5** and 0.5 for **6**)].

Products from α-Tocopherol in the *tert*-Butylperoxyl Radical-Generating System. A mixture of **1** (83 mg, 193 μmol), DBPO (20 mg, 85 μmol), and BOOH (400 μL, 4.0 mmol) in benzene (4.0 mL) was heated at 50 °C for 5 h. The reaction mixture was concentrated into dryness under reduced pressure. The oily residue obtained was chromatographed on a silica gel column using mixtures of *n*-hexane and ethyl ether as eluate. Firstly, **3** was eluted with the 19:1 mixture; secondly, unreacted **1** with the 9:1 mixture; and lastly, **2** with the 4:1 mixture.

When the fraction of **2** was rechromatographed repeatedly with the 5:1 mixture, isomers **2a** and **2b** were eluted in that order. **2a**: MS *m/e* 478.3639 (calcd for $C_{29}H_{50}O_5$, 478.3661); IR (neat) ν 952, 1090, 1142, 1228, 1262, 1380, 1462, 1668 (sh), 1682, 3380 cm^{-1}; UV (*n*-hexane) λ_{max} 244 nm (ϵ 5600); CD (*n*-hexane) λ 215 ($\Delta\epsilon$ −3.6), 231 (0), 247 (+3.5), 333 nm (+2.6); ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3 H), 1.50 (s, 3 H), 1.85 (s, 3 H), 1.91 (s, 3 H), 7.42 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.4 (q), 12.4

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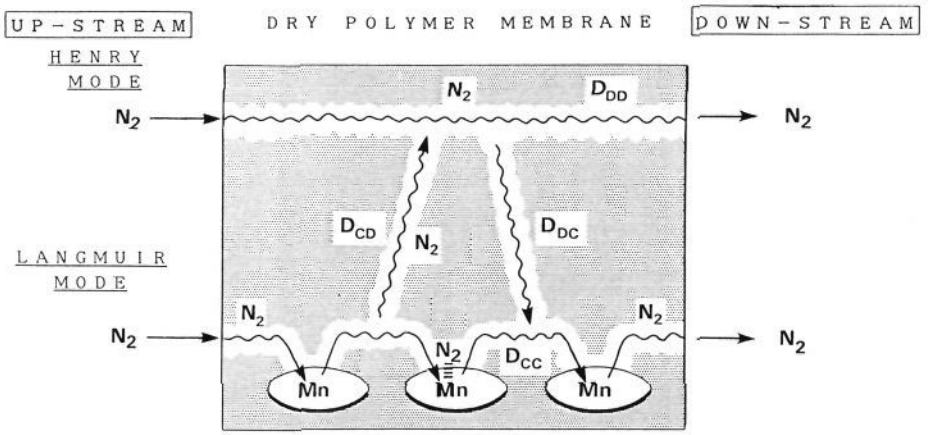
Scheme II



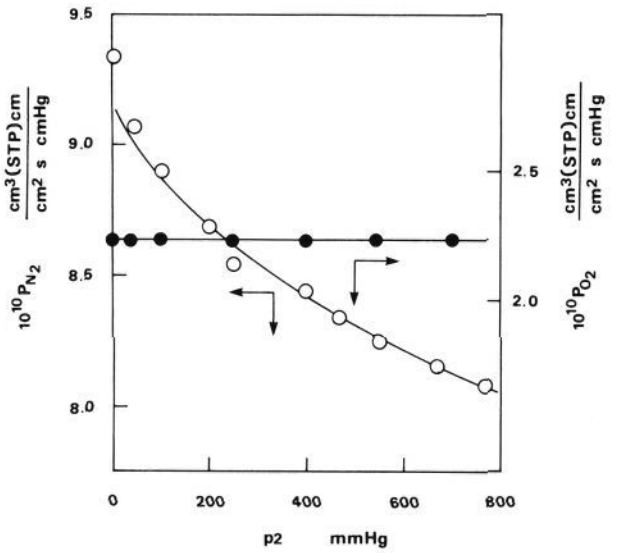


Figure 3. Effect of upstream gas pressure (p^2) on nitrogen (○) and oxygen (●) permeability coefficients for the $CpMn(CO)_2$–OMA membrane at 45 °C. $C_C' = 0.08$ cm³ (STP)/cm³. The solid line represents P_{N_2} calculated by eq 2.

of a penetrant in a polymer membrane has been observed for carbon dioxide permeation in glassy polymers.[12] But in those investigations, application of the dual-mode transport model was not rigorously justified since the nature of a microvoid existing in a glassy polymer was not elucidated and the glassy polymer matrix underwent plasticization during the penetrant sorption and transport. On the other hand, the CpMn polymer membranes were in a rubber state at the temperature for the permeation measurement (glass transition temperature were 10 and 21 °C for the membranes containing 18.5 and 32.0 mol % CpMn, respectively). We hereafter verified this facilitated transport or the dual-mode transport using a much simpler system.

The mathematics of the dual-mode transport has been theoretically proposed.[13,14] The facilitated transport behavior in this paper is adequate for an approximate analysis in terms of the following dual-mode transport model (schematically represented in Scheme II):

$$P = k_D D_{DD} + \frac{C_C' K D_{CC}}{1 + Kp^2} + \frac{C_C' K D_{CD} - k_D D_{DC}}{1 + Kp^2} + \frac{2k_D D_{DC}}{Kp^2} \ln (1 + Kp^2) \quad (2)$$

That is, P is equal to the sum of the first term representing the Henry mode attributed to a physical permeation through a polymer matrix, the second term representing the Langmuir mode attributed to a specific sorption (coordination) and diffusion of nitrogen to and through the CpMn complex, and the third term representing the additive Langmuir mode attributed to an exchanging term between the first and second term. Here, D_{DD}, D_{DC}, D_{CD}, and D_{CC} are the diffusion coefficients for the Henry-type physical permeation, for the polymer matrix to the fixed CpMn complex, for the fixed complex to the polymer matrix, and for the jumping between the fixed complexes. The K, C_C', and k_D values determined spectroscopically and gravimetrically are substituted in eq 2; by using these parameters, we could calculate the transport parameters and gave them in Table II. The the P_{N_2} versus $p^2(N_2)$ curve is calculated and drawn as the solid line in Figure 3. The experimental plots agree with the solid line, which supports the facilitated and dual-mode transport of nitrogen in the membrane and a pathway of nitrogen permeation via the fixed complex (carrier).

Table II suggests the following aspects of the facilitated transport. (i) A rapid penetrant exchange between two transport modes is established, as has been expected by the kinetic constants determined spectroscopically for nitrogen binding and dissociation to and from the CpMn fixed in the membrane. (ii) $(D_{CC} + D_{CD})/D_{DD}$ shows that the Langmuir-sorbed or -coordinated nitrogen has one-quarter of the mobility of that due to the Henry mode. (iii) D_{CC}/D_{DD} increases with the fixed CpMn concentration, which suggests a penetrant jumping accompanied by the decrease in the distance between the fixed complexes (carriers).

Experimental Section

Materials. 1,2- and 1,3-isomers (molar ratio ca.2/8) of tricarbonyl(methylvinylcyclopentadienyl)manganese were synthesized as in the literature.[5] ^{13}C NMR (CCl_4): δ 13.6, 14.4 (CH_3), 101.4, 102.7 (CCH_3), 115.0, 115.6 (=CH_2), 127.9, 129.4 (CH=vinyl), and 226 (br, 3C:CO), the first of the two peaks always having lower intensity. The polymer was prepared by radical copolymerization with octyl methacrylate in benzene solution using azobis(isobutyronitrile) (1 mol % of the total monomers) as an initiator at 60 °C for 3 h after three alternate freeze–thaw–degassing cycles. The mole fraction of the (vinylcyclopentadienyl)manganese in the feed monomers (1 M) was 7, 20, and 33 mol % for copolymers 1, 2, and 3, respectively. The copolymer was precipitated from methanol, purified by being reprecipitated twice, and dried in vacuo. Yield 45%, 38%, and 34%. The (vinylcyclopentadienyl)manganese residue and weight-average molecular weight of the copolymers were 6.4, 18.5, and 32.0 mol % and 3.5×10^5, 2.0×10^5, and 1.8×10^5 for copolymers 1, 2, and 3, respectively, determined by elemental analysis and gel permeation chromatography (with tetrahydrofuran as the solvent and polystyrene as the standard).

A benzene solution of the copolymer was carefully cast on a Teflon plate under an argon atmosphere, followed by drying in vacuo, to yield a transparent and pale brownish membrane (λ_{max} 327 nm). The transparent membrane was irradiated with UV light (a 32-W low-pressure mercury lamp) for 30–90 min under an absolute argon atmosphere at room temperature. The tricarbonyl CpMn complex was converted to the corresponding CpMn complex (λ_{max} 320 nm; IR ν_{CO} 1870 cm^{-1}).

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