Antioxidant Activities of Phenothiazines and Related Compounds: Correlation between the Antioxidant Activities and Dissociation Energies of O–H or N–H Bonds

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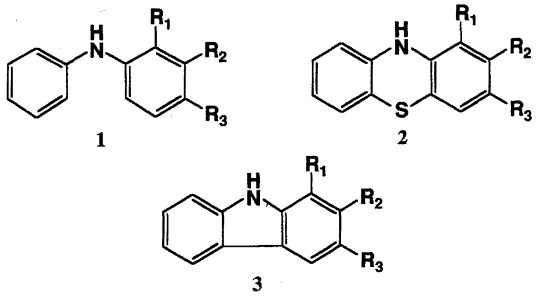
The antioxidant activities of phenothiazines, carbazoles, and related diphenylamines were evaluated in the oxidation of tetralin at 60 °C and linoleic acid micelles in aqueous dispersion at 37 °C induced by an azo initiator. Phenothiazines were highly antioxidant in both systems. Although diphenylamine and carbazole were not good antioxidants, those having a hydroxy group as a substituent at the *ortho* or *para* position to the amino group were potently antioxidant. The antioxidant activity of *o*-hydroxydiphenylamine was much greater than that of other compounds in both systems due to a stabilization of the phenoxyl radical by delocalization of the unpaired electron to the p-type lone pair of the amino group. A semiempirical MNDO-AM1 calculation was applied to study hydrogen abstractions of antioxidants in the chain process of autoxidation. These results indicated that the rates of oxidation during the induction period correlated with the dissociation energies of the O–H or N–H bonds.

The inhibition of radical polymerization is very important in the chemical industry for preventing premature polymerization during the processing, storage, and transportation of unsaturated monomers, such as those of vinyl. At the same time, however, oxidation is the main cause of deterioration among rubber products, plastics, lubricating oils, foods, and cosmetics.[1—3] The autoxidation process involves a radical chain reaction initiated by heat, light, or metal ions. Therefore, autoxidation inhibition may be briefly classified as that which prevents or retards the formation of initiating radicals, or that which intercepts primary chain reactions.

Various kinds of phenols[4—6] and aromatic amines[4,7] have been extensively explored as synthetic antioxidants. We have reported that benzylphenols, alkylidenebisphenols, thiobisphenols, and iminobisphenols are good chain-breaking antioxidants.[8—11] Furthermore, xanthenediols and thianthrenetetrols, which have a fused heterocyclic ring, exhibit excellent antioxidant activities.[12,13] The hetero atom at the *para* position to the hydroxy group may play an important role in the stability of phenoxyl radicals.

In this study, we compared the antioxidant activities of phenothiazines and carbazoles in the autoxidation of tetralin and linoleic acid micelles in aqueous dispersion with those of related diphenylamines. Furthermore, their antioxidant activities are discussed in connection with their D(O–H) and D(N–H), calculated using a semiempirical molecular-orbital method.



1a, 2a, 3a: $R^1 = R^2 = R^3 = H$
1b, 2b, 3b: $R^1 = OH$, $R^2 = R^3 = H$
1c, 2c, 3c: $R^2 = OH$, $R^1 = R^3 = H$
1d, 2d, 3d: $R^3 = OH$, $R^1 = R^2 = H$
1e, 2e, 3e: $R^1 = OMe$, $R^2 = R^3 = H$
1f, 2f, 3f: $R^2 = OMe$, $R^1 = R^3 = H$
1g, 2g, 3g: $R^3 = OMe$, $R^1 = R^2 = H$

Scheme 1.

Results

The antioxidants examined in this study were divided into the three classes shown in Scheme 1: diphenylamines **1**, phenothiazines **2**, and carbazoles **3**. Figure 1 shows examples of the oxygen-uptake curves for the oxidation of tetralin initiated by α,α'-azobisisobutyronitrile (AIBN) at 60 °C. After a very brief initiation period, the rate of oxygen uptake was constant in the control solution in the absence of an antioxidant. When antioxidants **1**—**3** were added to tetralin, oxidation was suppressed, and there was a measurable induction period (except for diphenylamine **1a**), which proportionally increased with the concentration (Fig. 2). The data regarding

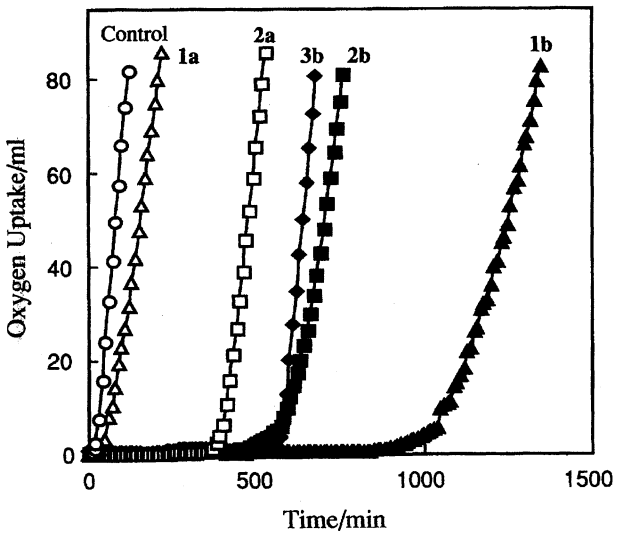


Fig. 1. Rate of oxygen uptake in the oxidation of tetralin (neat) initiated by 10 mmol dm^{-3} AIBN in the absence and presence of 1 mmol dm^{-3} antioxidant at 60 °C under oxygen.

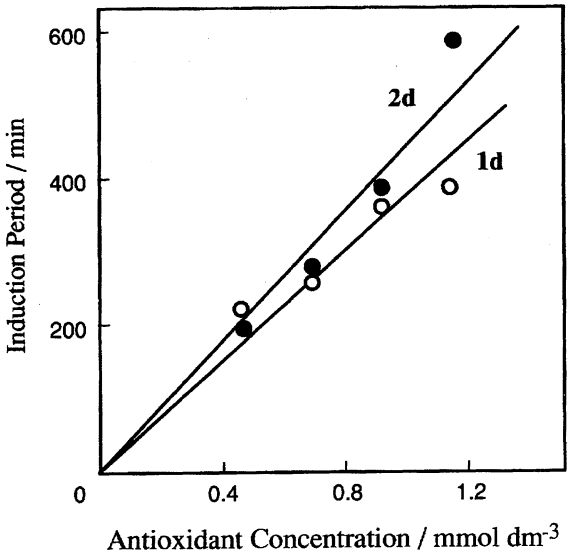


Fig. 2. Induction period produced by **1d** (○) and **2d** (●) in the oxidation of tetralin initiated by 10 mmol dm^{-3} AIBN at 60 °C under oxygen.

the antioxidant activities of **1**—**3**, denoted by the induction period (t_{inh}), the stoichiometric number (n) of peroxyl radicals trapped by each antioxidant, and the rate of oxygen absorption (R_{inh}) during the induction period, are listed in Table 1. The stoichiometric factors (n) were determined using the induction-period method relative to 2,6-di-*t*-butyl-4-methylphenol (BHT), for which $n=2$ was assumed.[14—16] Diphenylamine **1a**, which lacks the fused six-membered heterocyclic ring, was not a good antioxidant, as measured by t_{inh} and R_{inh}; however, those having a hydroxy group at the *ortho* or *para* position to the bridged amino group, **1b** or **1d**, were good antioxidants. Although the t_{inh} value of *o*-hy-

Table 1. Antioxidant Activities [a] and Dissociation Energy of Diphenylamines, Phenothiazines, and Carbazoles

Compd No.	t_{inh} / min	n [b]	R_{inh} [c] / $\times 10^8$ mol dm^{-3} s^{-1}	D(O–H) / kJ mol^{-1}	D(N–H) / kJ mol^{-1}
1a	47	0.2	107.0		379
1b	1058	5.1	0.9	333	358
1c	88	0.4	50.1	380	382
1d	391	1.9	0.7	350	370
1e	19	0.1	215.0		379
1f	36	0.2	59.4		381
1g	253	1.2	41.4		370
2a	381	1.8	3.8		328
2b	591	2.9	2.2	337	322
2c	301	1.5	0.5	344	331
2d	360	1.7	0.8	350	327
2e	193	0.9	11.3		339
2f	156	0.8	10.8		331
2g	415	2.0	9.1		326
3a	—	0.0	—		398
3b	555	2.7	7.7	347	380
3c	519	2.5	8.8	375	400
3d	476	2.3	6.9	359	388
3e	—	0.0	—		394
3f	66	0.3	107.3		400
3g	—	0.0	—		389
BHT	414	(2.0)	2.0	349	
Control	0	—	—		

a) Oxidation of tetralin (neat) initiated by 10 mmol dm^{-3} AIBN in the absence and presence of 1 mmol dm^{-3} antioxidant at 60 °C under oxygen. b) Stoichiometric factor determined relative to BHT as a standard. c) Rate of oxygen uptake for inhibited oxidation during the induction period.

droxydiphenylamine **1b** was 23-fold higher than that for **1a**, *o*-methoxydiphenylamine **1e** was a poor antioxidant. Phenothiazine **2a** without an OH group was a potent antioxidant. By comparing the structures between **1a** and **2a**, the thioether group *ortho* to the NH group decreased R_{inh} and increased t_{inh}. This indicated that the sulfur atom exerts the predominant effect attributed to the electronic nature and stabilization of the amynyl radical in the rate-determining step of the antioxidant action. Biddles et al.[17] have reported that the sulfur atom effectively stabilizes a neighboring radical center. The t_{inh} values for hydroxyphenothiazines **2c** and **2d** were the same as that for the phenothiazine **2a**, indicating that the OH group has no effect on the antioxidant activity. 1-Hydroxyphenothiazine **2b** produced a longer t_{inh} than did the other phenothiazines. 1-Methoxyphenothiazine **2e** showed moderate antioxidant activity. On the other hand, 3-methoxyphenothiazine **2g**, having an electron-donating group at the *para* position to the NH group, was more active than the *ortho* and *meta* derivatives. Although carbazole **3a** and methoxycarbazols, **3e-g**, did not act as antioxidants, carbazoles with an OH group on the benzene ring, **3b—3d**, were good antioxidants.

Typical oxygen uptake curves for the autoxidation of linoleic acid micelles in aqueous dispersions induced by the water-soluble initiator, 2,2′-azobis(2-amidinopropane) dihydrochloride (AAPH), and the lipid-soluble initiator, 2,2′-azobis(2,4-dimethylvaleronitrile) (AMVN), at 37 °C are shown in Figs. 3 and 4, respectively. Under both conditions, the rate of oxygen consumption was constant without any noticeable induction period in the control solution. The antioxidant incorporated into linoleic acid micelles markedly suppressed the oxidation and produced a clear induction period. The antioxidant activities for the autoxidation of a linoleic acid micelle in aqueous dispersions are shown in Table 2. That is, diphenylamine **1a** and carbazole **3a** were poor antioxidants, but become active when they had an OH group at the *ortho* or *para* position to the NH group in both micelle dispersions. On the other hand, phenothiazine **2a** with no OH group and the hydroxyphenothiazines, **2b** and **2c**, but not **2d**, were potent antioxidants. There was a similarity in the order of effectiveness of the antioxidants, as measured by t_{inh} and R_{inh}, in both linoleic acid micelle dispersions. However, our data show that the antioxidant activities from a micellar system do not parallel data obtained in tetralin perfectly. Differences in the antioxidant activities are assumed to arise due to the nature of the inhibitor changing from a homogeneous solution to micelles, as well as the nature of the initiator and the surfactant.

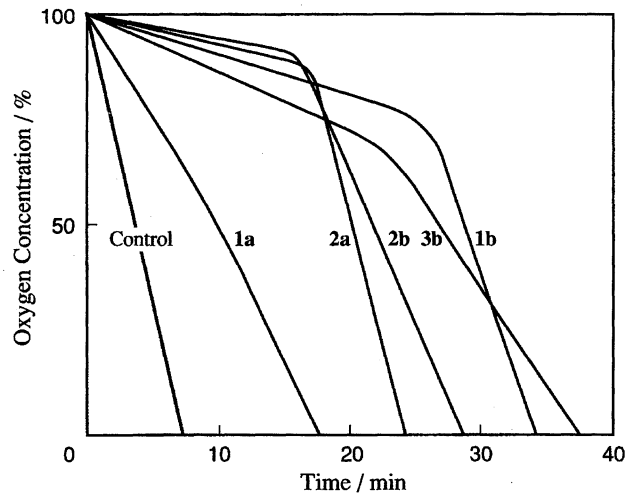


Fig. 3. Rate of oxygen uptake in the oxidation of 50 mmol dm^{-3} linoleic acid in Tween 20 aqueous micelle dispersions initiated by 20 mmol dm^{-3} AAPH in the absence and presence of 0.008 mmol dm^{-3} antioxidant at 37 °C under oxygen.

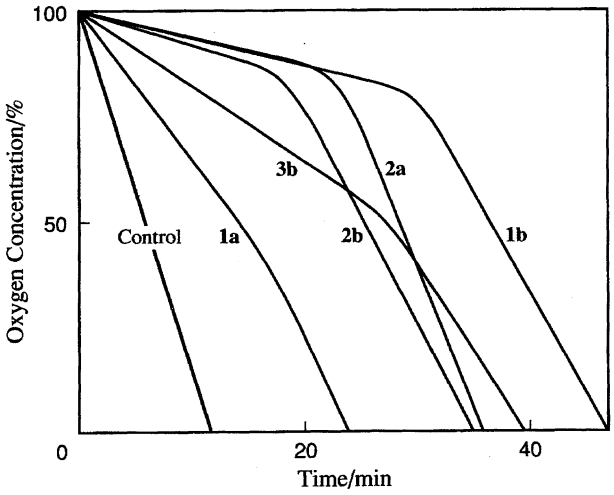


Fig. 4. Rate of oxygen uptake in the oxidation of 50 mmol dm^{-3} linoleic acid in Tween 20 aqueous micelle dispersions initiated by 20 mmol dm^{-3} AMVN in the absence and presence of 0.008 mmol dm^{-3} antioxidant at 37 °C under oxygen.

Discussion

We have reported on the hydrogen abstraction of phenolic antioxidants in the chain process of autoxidation by means of ab initio molecular orbital calculations.[18,19] From the obtained enthalpy (ΔH), activation (E_a), and OH bond dissociation (D(O–H)) energies, it was found that these three parameters indicate a good relationship with each other; particularly, between the ΔH and E_a values follows the Evans–Polanyi rule.[20] In this study, however, E_a of compounds **1–3** was impossible to obtain by ab initio molecular-orbital calculations, because this procedure requires a high-capacity computer memory. On the other hand, the enthalpy was easily calculated with high precision using a semiempirical molecular-orbital method.

We attempted to understand the factors affecting hydrogen abstraction in the chain-breaking reaction of **1—3**, from the standpoint of the dissociation energies of the N–H (D(N–H)) and O–H (D(O–H)) bonds, calculated using semiempirical MNDO-AM1. The values of D(N–H) and D(O–H) were obtained from the difference between the enthalpy for **1—3** and the relative phenylaminyl or phenoxyl radical species

Table 2. Antioxidant Activities of Diphenylamines, Phenothiazines, and Carbazoles in the Oxidation of Linoleic Acid in Aqueous Micelle Dispersions

Compd No.	AAPH[a]			AMVN[b]		
	t_{inh} / min	n	R_{inh} / $\times 10^7$ mol dm^{-3} s^{-1}	t_{inh} / min	n	R_{inh} / $\times 10^7$ mol dm^{-3} s^{-1}
1a	9.6	0.9	6.6	17.1	1.4	4.8
1b	25.9	2.4	1.3	30.2	2.4	0.9
1c	10.0	0.9	6.3	18.0	1.5	4.4
1d	17.8	1.7	1.5	29.0	2.3	2.1
1e	9.4	0.9	8.0	14.6	1.2	5.9
1f	10.3	1.0	6.5	15.6	1.3	4.7
1g	20.8	2.0	1.9	28.6	2.3	1.8
2a	17.1	1.6	1.0	23.1	1.9	0.9
2b	15.9	1.5	0.8	18.7	1.5	1.1
2c	18.5	1.8	0.3	24.1	1.9	1.3
2d	9.7	0.9	0.7	9.9	0.8	1.8
2e	12.2	1.2	0.9	16.3	1.3	1.2
2f	19.1	1.8	0.6	24.0	1.9	0.9
2g	13.0	1.2	0.7	21.9	1.8	1.1
3a	—	0.0	—	—	0.0	—
3b	22.8	2.2	1.9	27.5	2.2	2.4
3c	4.3	0.4	6.9	12.4	1.0	5.1
3d	26.5	2.5	1.2	33.0	2.7	1.9
3e	—	0.0	—	5.9	0.5	8.4
3f	—	0.0	—	7.0	0.6	6.3
3g	5.9	0.6	4.3	6.9	0.6	8.1
BHT	21.2	(2.0)	2.6	24.9	(2.0)	2.6
Control	—		—	—		—

a) Oxidation of 50 mmol dm^{-3} linoleic acid in Tween 20 aqueous micelle dispersions initiated by 5 mmol dm^{-3} AAPH in the absence and presence of 0.008 mmol dm^{-3} antioxidant at 37 °C under oxygen. b) Oxidation of 50 mmol dm^{-3} linoleic acid in Tween 20 aqueous micelle dispersions initiated by 5 mmol dm^{-3} AMVN in the absence and presence of 0.008 mmol dm^{-3} antioxidant at 37 °C under oxygen.

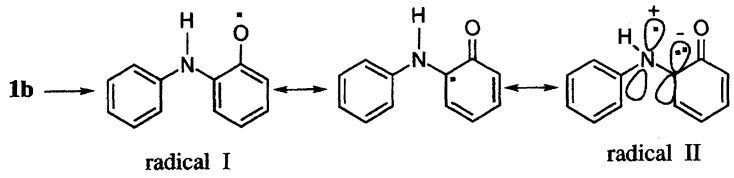
and hydrogen radical, and are also listed in Table 1. The D(N–H) and D(O–H) values given in Table 1 show that the hydroxydiphenylamines **1b—d** and the hydroxycarbazoles **3b—d** have lower D(O–H) values than do D(N–H), whereas the D(N–H) values of hydroxyphenothiazines **2b—d** showed lower values than that of D(O–H). The results of the antioxidant activity and the dissociation energies suggest that the hydroxy group for hydroxydiphenylamines **1b—d** and hydroxycarbazoles **3b—d** is more effective than the amino group. On the other hand, the N–H hydrogen atom for hydroxyphenothiazines **2b—d** is more effective than the O–H hydrogen atom in determining the antioxidant activity.

As described in a previous section, *ortho*- and *para*-hydroxydiphenylamines were more effective than the *meta* derivative. The potent antioxidant activity of **1b** and **1d** may be ascribed to stabilization of the phenoxyl radical formed when hydroxydiphenylamine scavenges the peroxyl radical (Scheme 2). For example, the phenoxyl radical I can be stabilize by a p-type lone pair on the *ortho* amino group, i. e., radical I ↔ radical II. On the other hand, the R_{inh} values of hydroxycarbazoles **3b–d** were almost the same, indicating that the phenoxyl radical would not provide this enhanced phenoxyl stabilization; for steric reasons, the p-type lone pair on the amino group adopts an orientation that is less perpendicular to the plane of the aromatic ring. As to the structure-activity relationships involved in antioxidant activity, Burton et al.[21] and Scott[3] have reported that substituents which delocalize electrons in the phenylaminyl or phenoxyl radicals increase the antioxidant activity.

Hydroxyphenothiazines **2b—d** have lower values of D(N–H) than D(O–H), and the t_{inh} and R_{inh} values for phenothiazine **2a**, having no OH group, were almost the same as those for the hydroxyphenothiazines **2b—d**. Furthermore, **2a** exhibited a lower D(N–H) value compared with those of **1a** and **3a**. These results suggest that the antioxidant activities of **1–3**, correlate with the ease of abstraction of a hydrogen atom. Therefore, we examined the relationships between the antioxidant activity and dissociation energy. In Fig. 5 the calculated D(O–H) values for compounds **1c**, **1d**, **3c**, and **3d** are plotted against the rate of oxidation (R_{inh}) for the oxidation of tetralin initiated by AIBN at 60 °C. Figure 6 also shows a linear relation between the D(N–H) and R_{inh} values for compounds **1a**, **1e—g**, **2a**, **2c—g**, **3a**, and **3e—g**. As shown in Figs. 5 and 6, the R_{inh} values are linearly correlated with D(O–H) or D(N–H). However, the activities of **2c** and **2d** were markedly higher than that considering only the D(N–H) energy. From these results, the antioxidant activity is dependent not only on the importance of resonance effect[4] but also on the dissociation energy of the O–H or N–H bonds.

Conclusion

The antioxidant activities of diphenylamines **1**, which lack



Scheme 2.

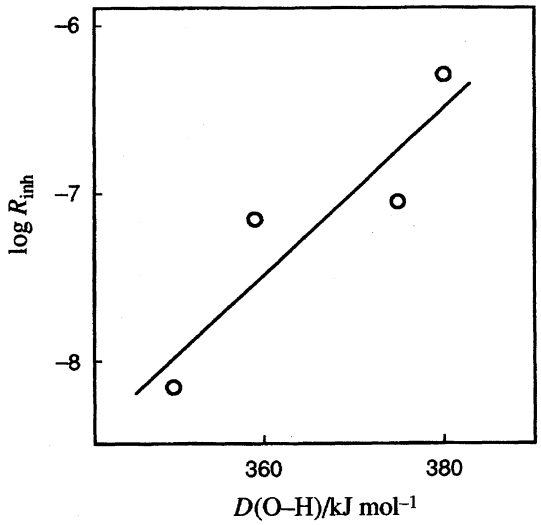


Fig. 5. Plot of O–H bond dissociation energy of hydroxydiphenylamines and hydroxycarbazoles against the log R_{inh} in the oxidation of tetralin initiated by AIBN ($r = 0.912$).

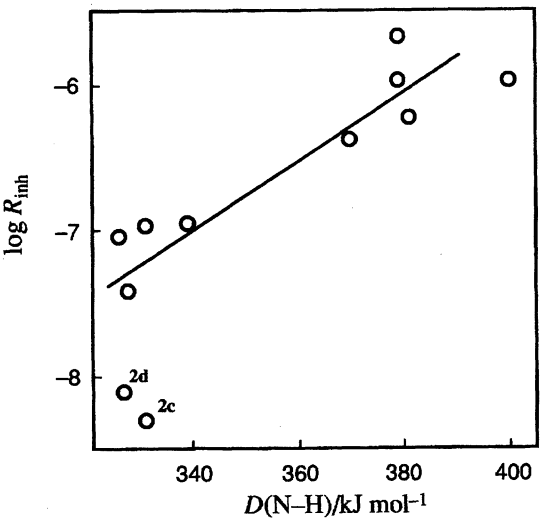


Fig. 6. Plot of N–H bond dissociation energy of diphenylamines, phenothiazines, and carbazoles against the log R_{inh} in the oxidation of tetralin initiated by AIBN ($r = 0.943$).

a fused sixmembered heterocyclic ring (except for **1b** and **1d**), were smaller than that of their corresponding phenothiazines **2** and hydroxycarbazoles **3b—d**. On the other hand, the *ortho* and *para* hydroxydiphenylamines, **1b** and **1d**, had higher antioxidant activities, as measured by the t_{inh} and R_{inh} values. In particular, **1b** exhibited a much higher activity, due to the stabilization of the phenoxyl radical by delocalization of the unpaired electron to the p-type lone pair of the amino group. The R_{inh} values during the induction period correlated with D(O–H) or D(N–H). These results indicated that the R_{inh} values decrease along with a decrease in the dissociation energy of the O–H or N–H bonds.

Experimental

General. All of the temperatures are uncorrected. The melting points were measured with a Yanaco MP-J3 micro-melting apparatus. The nuclear magnetic resonance spectra were recorded using a JEOL GSX-400 spectrometer operating at 400 MHz for ^{1}H and 100.6 MHz for ^{13}C in $CDCl_3$; the chemical shifts are referenced to the peak of $(CH_3)_4Si$. Mass spectra were recorded using a Perkin–Elmer Model 910 gaschromatographic mass spectrometer at 70 eV.

Assay of the Antioxidant Activity. The rate of oxidation was determined either by following the oxygen concentration in solution or by measuring the volume of oxygen consumption during oxidation. The oxygen concentration in solution was monitored with a Biological Oxygen Monitor, Model YSI 5300 (Yellow Springs Instrument Co., Inc., Yellow Springs, OH) at 37 °C. The volume of oxygen consumption was measured as a function of time under 760 Torr (1 Torr = 133.322 Pa) of O_2 with 50.0 ml of tetralin containing an antioxidant (5×10^{-5} mol) and AIBN (5×10^{-4} mol) as the initiator. The oxidation temperature was maintained at 60±0.1 °C. The t_{inh} was determined graphically from the length of time between initiator injection and the point of intersection of tangents to the oxidation curve, corresponding to the initial inhibited and final uninhibited rates of oxidation.

The micelle solution was prepared as follows: Linoleic acid (5 mmol) and antioxidant (0.002 mmol) were dissolved in Tween 20 (3.6 g) and then dispersed in 100 ml distilled water. The micelle solutions were oxidized immediately after preparation.

Molecular Orbital Calculations. The semiempirical MNDO-AM1 calculation was applied to the **1**—**3** antioxidants. The geometries were optimized to give the heat of formation at the singlet ground state using the restricted Hartree–Fock method for antioxidants, and at the doublet using the unrestricted Hartree–Fock method for radicals. The D(O–H) and D(N–H) values were obtained from the enthalpy of the optimum structures of antioxidants and relative radicals, as follows:

$$D\text{(O–H)},\ D\text{(N–H)}\ (\text{kJ mol}^{-1}) = E_r + E_H - E_o$$

E_r : Enthalpy of radical, E_H : Enthalpy of hydrogen radical, E_o : Enthalpy of antioxidant

Materials. Tetralin was washed with concentrated sulfuric acid, aqueous sodium hydrogencarbonate, and water, then dried over anhydrous sodium sulfate and distilled under nitrogen before use. AIBN was recrystallized from methanol. Linoleic acid, AAPH, and AMVN were purchased from commercial sources.

Commercial diphenylamine **1a**, 3-hydroxydiphenylamine **1c**, 4-hydroxydiphenylamine **1d**, 3-methoxydiphenylamine **1f**, phenothi-

azine **2a**, 2-methoxyphenothiazine **2f**, carbazole **3a**, and 2-hydroxycarbazole **3c** were further purified by recrystallization from a mixture of benzene and hexane.

Synthesis of 2-Hydroxydiphenylamine. A solution of **1e** (2.0 g, 0.01 mol) and 25 ml HBr in acetic acid (40/60 vol%) was refluxed for 170 h under nitrogen. The resultant precipitate was dissolved with water and extracted with ethyl acetate after neutralization with 15% $NaHCO_3$. The solvent was removed under reduced pressure. The residue was recrystallized from hexane to give white crystals of **1b** (1.02 g, 55%). Mp 66.9—67.1 °C. ^{13}C NMR δ=116.0, 117.3, 119.7, 120.3, 120.7, 122.7, 129.8, 131.9, 145.5, 149.0. Found: C, 77.55; H, 6.04; N, 7.42%. Calcd for $C_{12}H_{11}ON$: C, 77.81; H, 5.99, N, 7.56%.

Synthesis of Hydroxyphenothiazines. Phenothiazines were prepared by sulfuration of the relative diphenylamines according to Chandra et al.[22] A mixture of the 2-hydroxydiphenylamine (9.25g, 0.05 mol), sulfur (1.8 g, 0.05 mol), and iodine (0.14 g, 1.1 mmol) was stirred for 2.5 h at 120—130 °C under nitrogen. Purification of the crude products by silica-gel column chromatography and recrystallization from benzene–petroleum ether gave 1-hydroxyphenothiazine **2b** (4.8 g, 46%) as a silver-white solid. Mp 133.4—134.6 °C. ^{13}C NMR δ=114.1, 115.9, 118.2, 118.4, 118.6, 122.5, 122.8, 127.1, 128.2, 131.2, 143.2, 144.2. Found: C, 67.00; H, 4.23; N, 6.46%. Calcd for $C_{12}H_9ONS$: C, 66.95; H, 4.22; N, 6.51%.

2-Hydroxyphenothiazine (2c): Yield 32%, mp 168.2—169.3 °C. ^{13}C NMR δ=103.6, 110.2, 115.5, 122.9, 122.9, 127.3, 128.0, 128.2, 134.4, 141.1, 144.9, 158.5. Found: C, 66.92; H, 4.24; N, 6.43%.

3-Hydroxyphenothiazine (2d): Yield 31%, mp 170 °C (decomp). ^{13}C NMR δ=113.9, 114.9, 115.1, 116.0, 117.9, 119.3, 122.2, 127.1, 128.2, 135.8, 144.3, 153.7. Found: C, 66.85; H, 4.29, N, 6.48%.

Synthesis of Hydroxycarbazole. A solution of **3e** (1.96 g, 0.01 mol) and 25 ml HBr in phosphinic acid (100/1 vol%) was stirred at 75—80 °C for 3 d. The reaction mixture was extracted with ethyl acetate after neutralization with NaOH. Purification by recrystallization from hexane gave 1-hydroxycarbazole **3b** (0.58 g, 32%) as a white solid. ^{13}C NMR δ=112.4, 119.4, 119.5, 120.2, 120.8, 124.4, 125.6, 126.1, 130.5, 140.7, 140.8, 143.9. Found: C, 78.57; H, 5.03; N, 7.51%. Calcd for $C_{12}H_9NO$: C, 78.66, H, 4.96; N, 7.65%.

3-Hydroxycarbazole (3d). Yield 35%. ^{13}C NMR δ=106.0, 111.7, 112.1, 115.9, 119.0, 120.8, 124.0, 124.8, 126.2, 133.2, 135.4, 151.7. Found: C, 78.52; H, 4.94; N, 7.57%.

Synthesis of Methoxydiphenylamine. A mixture of acetanilide (20.25 g, 0.15 mol), 2-iodoanisol (35.1 g, 0.15 mol), potassium carbonate (15.2 g, 0.11 mol), copper (0.6 g), and 30 ml nitrobenzene was stirred at 200—210 °C for 10 h using a Dean–Stark trap. After the reaction was completed, the catalyst was filterd off, and the solvent was removed under reduced pressure. The reaction mixture was refluxed with 200 ml HCl in ethanol (3/2 vol%) for 20 h. After the solution was neutralized with 20% NaOH, the reaction mixture was extracted with ethyl acetate. Purification by column chromatography yielded 2-methoxydiphenylamine **1e** (36.2 g, 70%) as an orange liquid. ^{13}C NMR δ=56.1, 112.0, 116.4, 118.8, 121.1, 121.3, 121.5, 129.9, 133.9, 144.5, 150.1. Found: C, 78.14; H, 6.68; N, 7.11%. Calcd for $C_{13}H_{13}ON$: C, 78.36; H, 6.59; N, 7.03%.

4-Methoxydiphenylamine (1g): Yield 84%. ^{13}C NMR δ= 53.0, 115.3, 116.0, 119.5, 122.0, 129.9, 137.2, 146.5, 155.7. Found: C, 78.09; H, 6.62; N, 6.98%.

Synthesis of Methoxyphenothiazines. To a solution of **2b** (20.0 g, 0.093 mol) in 10% NaOH (50 ml) was added dropwise dimethyl sulfate (1.17 g, 0.0093 mol) at room temperature. The mixture was poured into water and extracted with ethyl acetate. The ethyl acetate extract was washed with water and dried over Na_2SO_4. Evaporation of the solvent and recrystalized from hexane afforded 1-methoxyphenothiazine **2e** (13.8 g, 65%). Mp 87.4—88.5 °C. ^{13}C NMR δ=56.2, 110.2, 116.0, 118.1, 119.3, 122.6, 123.0, 127.1, 127.1, 128.2, 132.1, 143.0, 147.1. Found: C, 61.00; H, 5.76; N, 4.72%. Calcd for $C_{13}H_{11}ONS$: C, 68.10; H, 4.84; N, 6.11%.

3-Methoxyphenothiazine (2g): Yield 56%, mp 163.9—164.8 °C. ^{13}C NMR δ=55.8, 112.7, 113.8, 115.2, 115.9, 117.8, 119.5, 122.4, 127.1, 128.3, 136.8, 144.0, 156.4, Found: C, 68.04; H, 4.97; N, 6.02%. Calcd for $C_{13}H_{11}ONS$: C, 68.10; H, 4.84; N, 6.11%.

Synthesis of Methoxycarbazole. 1-Methoxycarbazole was synthesized from methoxydiphenylamine using a modification of the method of Akermark et al.[23] A solution of methoxydiphenylamine **1e** (6.0 g, 0.03 mol) and palladium acetate (6.7 g, 0.03 mol) in acetic acid was refluxed for 1.5 h. After evaporating the solvent, the crude products were isolated by silica-gel column chromatography to give **3e** (1.96 g, 33%) as a clear liquid. ^{13}C NMR δ=55.8, 113.5, 119.6, 119.7, 120.2, 120.2, 124.3, 125.1, 126.2, 126.3, 131.0, 140.8, 146.9. Found: C, 78.92; H, 5.62; N, 7.07%. Calcd for $C_{13}H_{11}ON$: C, 79.16; H, 5.63; N, 7.10%.

2-Methoxycarbazole (3f): Yield 67%. ^{13}C NMR δ=108.7, 108.8, 120.0, 120.0, 124.2, 125.0, 130.0, 132.8, 135.1, 141.0, 142.4, 160.1. Found: C, 78.90; H, 5.51; N, 7.10%.

3-Methoxycarbazole (3g): Yield 72%, mp 150.0—151.2 °C (lit,[17] 149—151 °C). ^{13}C NMR δ=56.0, 112.3, 115.7, 119.1, 120.8, 120.9, 124.0, 124.3, 126.2, 126.3, 135.8, 141.7, 154.6. Found C, 78.97; H, 5.73; N, 7.06%.

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