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Molecular Orbital Approach to Antioxidant Mechanisms of Phenols by an Ab Initio Study

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An ab initio molecular orbital theory has been applied to a study of the hydrogen abstractions of phenolic antioxidants in the chain process of autoxidation. The optimum structures of phenols, of peroxides, and of those compounds in the transition states were obtained with a Hartree-Fock/STO-3G basis set. From the values of enthalpy (ΔH) and activation energy (E_a) obtained, it was found that the rates of the reaction of peroxyl radical with phenolic antioxidant were faster than those with organic substrate in the propagation, and that the effect of the aromatic ring of the antioxidants not only stabilized a product state but also decreased an energy level in the transition state. The para-substituent effect that an electron-releasing substituent increased the antioxidant activity, whereas an electron-withdrawing one decreased it, was recognized. The relationship between ΔH and E_a values followed the Evans–Polanyi rule. The transition states in the hydrogen abstractions with lower E_a values prefer reactant-like structures, whereas those with higher E_a values prefer product-like ones.

Antioxidants have commonly been used to prevent deterioration due to the autoxidation of organic substrates. Autoxidations at various temperatures have been well characterized as radical chain reactions. Such antioxidants as phenol and aromatic amine derivatives react as chain-breaking inhibitors of the peroxyl radical:¹⁾

$$\mathrm{ROO\cdot + ArOH \rightarrow ROOH + ArO\cdot}, \qquad \text{(a)}$$

where ROO· denotes the peroxyl radical and ArOH represents antioxidant phenols. Another possible reaction is the direct attack on the alkyl radical:

$$\mathrm{R\cdot + ArOH \rightarrow RH + ArO\cdot} \qquad \text{(b)}$$

In the absence of the antioxidant, the following propagation reactions proceed:

$$\mathrm{R\cdot + {}^3O_2 \rightarrow ROO\cdot} \qquad \text{(c)}$$
$$\mathrm{ROO\cdot + RH \rightarrow ROOH + R\cdot}, \qquad \text{(d)}$$

where RH is the organic substrate. It is assumed that reaction (c) proceeds with zero activation energy.¹⁾ The main reactions can be represented by reactions (a) and (d) and thus, reaction (a) occurs easily in comparison with reaction (d). The radical ArO· from the antioxidant is less reactive and consequently it is difficult for a new chain reaction to become initiated (e), as was first reported by Bolland and Ten Have.²⁾

$$\mathrm{ArO\cdot + RH \rightarrow ArOH + R\cdot} \qquad \text{(e)}$$

The ArO· radical would be expected to act as the ideal radical to capture other ROO· radicals. Namely, the reactivity of ArO· is attributed to its resonance structure to fulfill the ideal conditions.

In 1988, Scott described in his review³⁾ that electron-releasing groups in the aromatic ring increase antioxidant activity, whereas electron-attracting groups decrease it, and substituents delocalizing the electron in the aryloxyl or arylaminyl radicals increase the antioxidant activity. These facts can be rationalized on the basis of the transition state involved in hydrogen abstraction by alkylperoxyl radical. There is both partial separation of charge between the alkylperoxyl and the aromatic ring and partial delocalization of the electron in the π-bond system. Consequently, substituents which release electrons or delocalize the unpaired electron decrease the transition state energy.

In this paper, further examinations of the reactivities of elementary reactions in autoxidations in the absence or presence of the antioxidants are described on the following model reactions:

Reaction between R· and triplet oxygen

$$\mathrm{C_6H_5\cdot + {}^3O_2 \rightarrow C_6H_5OO\cdot} \qquad (1)$$

Reaction between R· and an antioxidant

$$\mathrm{C_6H_5\cdot + ArOH \rightarrow C_6H_6 + ArO\cdot} \qquad (2)$$

Propagation reaction

$$\mathrm{CH_4 + \cdot OOH \rightarrow CH_3\cdot + HOOH} \qquad (3)$$
$$\mathrm{C_6H_6 + \cdot OOH \rightarrow C_6H_5\cdot + HOOH} \qquad (4)$$

Chain-breaking reaction

$$\mathrm{HOH + \cdot OOH \rightarrow HO\cdot + HOOH} \qquad (5)$$
$$\mathrm{ArOH + \cdot OOH \rightarrow ArO\cdot + HOOH} \qquad (6)$$

Reaction between methoxyl or phenoxyl radical and a substrate

$$\mathrm{CH_3O\cdot + CH_4 \rightarrow CH_3OH + CH_3\cdot} \qquad (7)$$
$$\mathrm{ArO\cdot + CH_4 \rightarrow ArOH + CH_3\cdot} \qquad (8)$$

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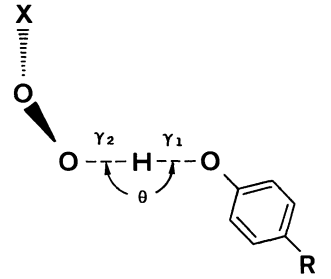
Subsequently, the para-substituent effects of phenol antioxidants in the hydrogen abstraction by ROO· radicals are investigated in detail.

Structure I depicts the hydrogen abstraction in the transition state and the various substituents, R and X, are shown below.



Structure I

Eq.[a]	R	X	Eq.	R	X
6	H	H	14	H	CH_3
9	CH_3	H	15	CH_3	CH_3
10	OCH_3	H	16	OCH_3	CH_3
11	NH_2	H	17	NH_2	CH_3
12	F	H	18	Cl	CH_3
13	Cl	H			

a) $R\text{-}C_6H_4OH + \cdot OOX \rightarrow R\text{-}C_6H_4O\cdot + HOOX$.

Experimental

Determination of Antioxidant Activity. Measurements of oxygen-absorption rates were performed with an isobaric gas-absorption apparatus under a closed-flow system (2.0±0.1 L oxygen h^{-1}) provided with an electrolyser using 50 cm^3 of tetralin containing an antioxidant (0.001 mol dm^{-3}) and azobis(isobutyronitrile) as the initiator (0.01 mol dm^{-3}). The oxidation temperature was kept at 60±0.1 °C and oxygen absorption was periodically measured in a constant-pressure closed system. The induction period (IP) was determined in the usual way.[4)]

Computation

Ab initio molecular orbital calculations were carried out for the reactions, Eqs. 1—18, corresponding to the elementary reactions, (a)—(e), with the GAUSSIAN 80 programs.[5)] Geometries for all the structures were optimized at the HF level with the STO-3G basis set[6)] by using the energy gradient method.[7)] The energies and structures of the transition states were also calculated in the same way mentioned above, but the aromatic ring involved in reactions 4, 6, and 8—18, was only fixed with that of optimized phenol geometry. Concerning reactions 3, 5, and 7, these values were calculated with the HF/3-21G basis set.[8,9)] Thus, the electronic correlation energies in these three reactions were computed by means of Møller–Plesset (MP) pertubation up to the third order.[10)] The ΔH and E_a values were obtained from the total energies for the optimum structures of both systems and the energy of the transition state (E_{ts}), as follows:

$$\Delta H(\text{kJ mol}^{-1}) = -2625.460[E_{\text{total}}(\text{reactants}) - E_{\text{total}}(\text{products})]$$

$$E_a(\text{kJ mol}^{-1}) = -2625.460[E_{\text{total}}(\text{reactants}) - E_{ts}]$$

$$1 \text{ A.U.} = 2625.460 \text{ kJ mol}^{-1}$$

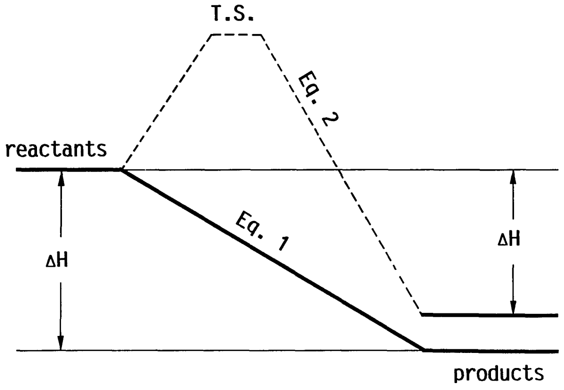
The activation parameters obtained are shown in Tables 1—4.

Results and Discussion

The Initial Channel of the Chain-Breaking Inhibition. Table 1 shows the calculated ΔH values of Eqs. 1 and 2, along with the energy profiles of both exothermic reactions. The difference between the ΔH values in Eqs. 1 and 2 is 33.48 kJ mol^{-1}. Therefore, the $C_6H_5OO\cdot$ radical is stable in comparison with the product of Eq. 2. In Eq. 1, the direct interaction between the radical and triplet oxygen having the feature of a biradical proceeds with no barriers, whereas the reaction of Eq. 2 reaches the product state through the transition state.

In the autoxidation of organic substrates, an alkyl radical is formed by addition of an initiator such as azobis(isobutyronitrile) and is further transformed into the ROO· radical after interaction with triplet oxygen (Eq. c). Bolland and ten Have[2)] determined the initial rates of the autoxidations under several conditions: The variations of antioxidants or substrates, concentration, and oxygen pressure. Thus, they concluded that antioxidants react with ROO· radicals and not with R· radicals. This conclusion agrees with the results of our calculations supporting the idea that the initial channel of the chain-breaking inhibition by antioxidants is the

Table 1. Activation Parameters for Eqs. 1 and 2



Eq.	ΔH/kJ mol^{-1}	
	HF/STO-3G	HF/3-21G
1	−161.34	—
2	−127.86	−54.06

reaction with the ROO· radical.

Reactivity of the HOO· Radical. Concerning Eq. 3 in Table 2, the values of ΔH and E_a at the MP3/3-21G level are 119.62 and 130.88 kJ mol^{-1}, and in Eq. 5 these values are 69.50 and 97.86 kJ mol^{-1}, respectively. The differences in the ΔH and E_a values between Eqs. 3 and 5 are 50.12 and 33.02 kJ mol^{-1}, respectively. The rate of hydrogen abstraction from the O–H bond was much faster than that from the C–H bond. In other words, the methyl radical is unstable compared with the hydroxyl radical and Eq. 3 has the feature of reversible reaction.

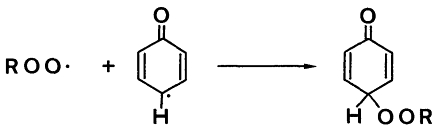
Subsequently, the influence of an aromatic ring was considered at the STO-3G level (see Table 2). The differences in the ΔH and E_a values between Eqs. 3 and 4 are 97.36 and 67.66 kJ mol^{-1}, respectively, while those between Eqs. 5 and 6 are 79.88 and 43.68 kJ mol^{-1}, respectively. Consequently, by introducing an aromatic ring to the reaction system, their reactivities are increased. The E_a value of Eq. 4, which is the model of the propagation reaction (d), was exceedingly large in comparison with that of Eq. 6 which is the model of the chain-breaking reaction (a).

From these results, it was confirmed that the rate of the chain-breaking reaction was much faster than the propagation reaction and that the aromatic ring in the antioxidant molecules tends to decrease the activation energy of the chain-breaking reaction and to stabilize the energy of the phenoxyl radical produced after the hydrogen abstraction.

Table 2. Activation Parameters for Reaction Models, Eqs. 3—8

Eq.	Basis set//geometry	ΔH/kJ mol^{-1}	E_a/kJ mol^{-1}
3	HF/STO-3G//STO-3G	231.25	237.99
	HF/3-21G//3-21G	136.15	166.31
	MP2/3-21G//3-21G	115.02	123.72
	MP3/3-21G//3-21G	119.62	130.88
4	HF/STO-3G//STO-3G	133.89	170.33
5	HF/STO-3G//STO-3G	85.90	139.70
	HF/3-21G//3-21G	61.30	129.96
	MP2/3-21G//3-21G	83.64	92.93
	MP3/3-21G//3-21G	69.50	97.86
6	HF/STO-3G//STO-3G	6.02	96.02
7	HF/STO-3G//STO-3G	187.28	199.03
	HF/3-21G//3-21G	105.73	143.01
	MP2/3-21G//3-21G	72.09	79.96
	MP3/3-21G//3-21G	83.14	93.68
8	HF/STO-3G//STO-3G	225.22	211.04

Reactivity of the Phenoxyl Radical. It is known that one molecule of simple phenol captures two molecules of ROO· radicals; one is captured by the hydrogen abstraction of the phenolic OH group, and the other by the coupling reaction with the 4-oxo-2,5-cyclohexadienyl radical produced from the phenoxyl radical by the rearrangement of the π-electron (see reactions a and f).[1)]



(f)

The data from Eqs. 7 and 8 in Table 2 indicate the closeness of both energy levels of the transition and product states, and the E_a values of Eq. 8 is larger than that of Eq. 7 at the STO-3G level. Both Eqs. 7 and 8 are the model system of the reaction (e). It was noted that the system returns readily from the transition state to the reaction state. From these results, it can be concluded that the reaction between the phenoxyl radical and a substrate cannot proceed readily, whereas the 4-oxo-2,5-cyclohexadienyl radical reacts with the peroxyl radical smoothly to terminate chain reactions.

Substituent Effect of Phenolic Antioxidant. The calculated ΔH and E_a values in the cases of Eq. 6 and Eqs. 9—18, of the reactions of p-substituted phenols with two kinds of peroxyl radicals (see Structure I, X=H and CH_3), are shown in Table 3. By using the values in Eqs. 6 (R=H) and 14(R=H), the $\Delta(\Delta H)$ and ΔE_a were evaluated. An approximately linear relationship between both values is shown in Fig. 1. The slope value (α), $\Delta E_a/\Delta(\Delta H)$, is 0.395 except for the value in Eq. 17. This fact indicates that the hydrogen abstraction in the chain-breaking reaction follows the Polanyi–Evans rule.[11)]

Table 3. p-Substituent Effects of Phenols with Activities as Antioxidants

Eq.	X	R	ΔH/kJ mol^{-1}	E_a/kJ mol^{-1}	$n^{a)}$	IP/min$^{b)}$	IP/min$^{c)}$	IP/min$^{d)}$
6	H	H	6.02	96.02	2.1			
9	H	CH_3	5.48	95.44	2.5			
10	H	OCH_3	19.46	100.71	2.0			
11	H	NH_2	11.05	96.69				
12	H	F	10.29	96.44				
13	H	Cl	10.75	97.03	1.7			
14	CH_3	H	3.60	93.35		75	60	23
15	CH_3	CH_3	3.05	92.80		210	165	121
16	CH_3	OCH_3	17.03	97.99				
17	CH_3	NH_2	8.58	92.01		2340	1470	551
18	CH_3	Cl	8.33	94.18		45		

a) The n value was obtained by the induction period method in Ref. 12 (cumene was used as the substrate). b) The data in Ref. 13 (cracked gasoline). c) The data in Ref. 14 (Pennsylvania gasoline). d) This work (tetralin).

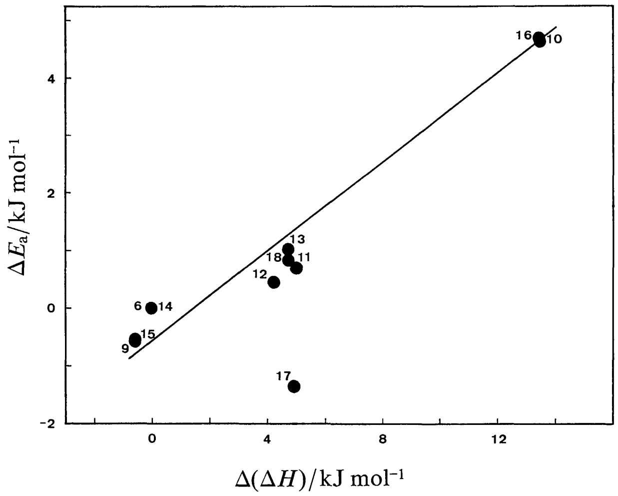


Fig. 1. Plot of ΔE_a vs. $\Delta(\Delta H)$ values.

Ingold et al.[12] reported on the stoichiometric coefficient, n, for substituted phenols using cumene as a substrate at 65 °C by the induction period method. The n values in Table 3, change inversely with the ΔH and E_a values except for those in Eq. 10. This indicates that the electron-releasing substituent in phenol decreases the ΔH and E_a values and increases the antioxidant activity, whereas the electron-attracting substituent increases both values and decreases the activity. The relationship between the E_a and induction period (IP) values indicates an antioxidant activity, by the uses of two kinds of gasolines[13,14] and tetralin as substrates, and confirms the result mentioned above, as can be seen in Table 3.

Geometry of the Transition State. The geometry of the molecular model of the hydrogen abstraction in the transition state was defined by both distance and angle parameters, as shown in Table 4. These values indicate linear binding between the hydrogen atom of the OH substituent of the phenol and the oxygen atom of the peroxyl radical. Figure 2 shows the relation between the E_a and r_1 values, except for Eqs. 10, 11, 16, and 17, in the cases of the substituents OCH_3 and NH_2. The E_a values increase with increasing r_1 values. It was, therefore, thought that the structures of the transition states in the reactions which have lower E_a values are reactant-like, whereas those which have higher values are product-like. This result agrees with the postulation by Hammond.[15]

Table 4. Structural Parameters of the Transition States[a)]

Eq.	r_1/Å	r_2/Å	θ/deg.
6	1.220	1.156	180.5
9	1.219	1.157	180.7
10	1.221	1.156	180.6
11	1.215	1.160	180.1
12	1.222	1.155	180.2
13	1.227	1.151	180.2
14	1.220	1.156	180.3
15	1.219	1.157	180.4
16	1.221	1.158	180.4
17	1.200	1.178	180.1
18	1.227	1.151	180.3

a) See Structure I.

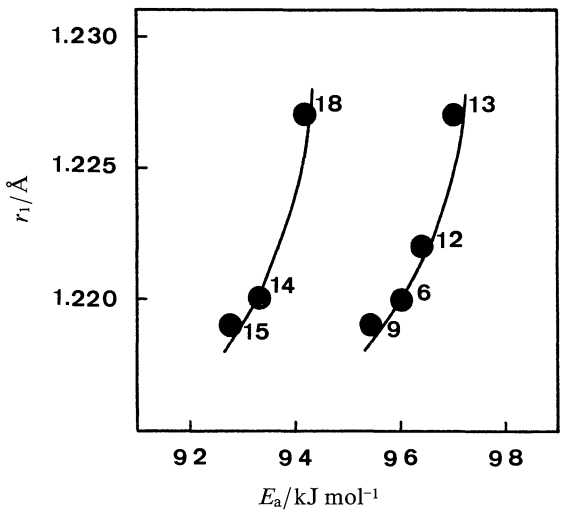


Fig. 2. Plot of r_1 vs. E_a values.

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