

Kinetic Study of the Phthalimide *N*-Oxyl Radical in Acetic Acid. Hydrogen Abstraction from Substituted Toluenes, Benzaldehydes, and Benzyl Alcohols

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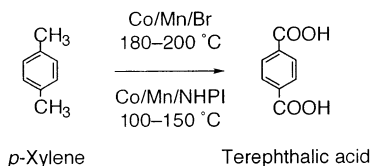
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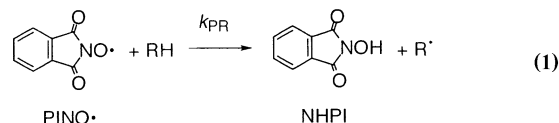
The phthalimide *N*-oxyl (PINO) radical was generated by the oxidation of *N*-hydroxyphthalimide (NHPI) with Pb(OAc)₄ in acetic acid. The molar absorptivity of PINO• is 1.36×10^3 L mol⁻¹ cm⁻¹ at λ_{max} 382 nm. The PINO radical decomposes slowly with a second-order rate constant of 0.6 ± 0.1 L mol⁻¹ s⁻¹ at 25 °C. The reactions of PINO• with substituted toluenes, benzaldehydes, and benzyl alcohols were investigated under an argon atmosphere. The second-order rate constants were correlated by means of a Hammett analysis. The reactions with toluenes and benzyl alcohols have better correlations with σ^+ ($\rho = -1.3$ and -0.41), and the reaction with benzaldehydes correlates better with σ ($\rho = -0.91$). The kinetic isotope effect was also studied and significantly large values of k_H/k_D were obtained: 25.0 (*p*-xylene), 27.1 (toluene), 27.5 (benzaldehyde), and 16.9 (benzyl alcohol) at 25 °C. From the Arrhenius plot for the reactions with *p*-xylene and *p*-xylene-*d*₁₀, the difference of the activation energies, $E_a^D - E_a^H$, was 12.6 ± 0.8 kJ mol⁻¹ and the ratio of preexponential factors, A^H/A^D , was 0.17 ± 0.05 . These findings indicate that quantum mechanical tunneling plays an important role in these reactions.

The autoxidation of hydrocarbons is a commercial reaction that can be made to run economically.¹ For example, the aerobic oxidation of *p*-xylene produces terephthalic acid which is in turn used to prepare polyethylene terephthalate (PET). The industrial oxidation processes mostly use a Co/Mn/Br combined catalyst that is called the Amoco-MC catalyst.² A major drawback is the use of bromide ions that corrode expensive titanium reactors and form a side product, CH₃Br, that can photocatalyze ozone loss. Ishii et al. have developed a new catalyst for the oxidation of hydrocarbons using *N*-hydroxyphthalimide (NHPI) and Co(OAc)₂.³ The autoxidation of *p*-xylene catalyzed by 10 mol % of NHPI with Co(OAc)₂ and Mn(OAc)₂ gave 82% terephthalic acid in HOAc at 100 °C.⁴



In the proposed scheme, Co(III) reacts with NHPI to form the PINO radical, an oxidized form of NHPI. The

PINO radical in turn abstracts a hydrogen atom from the hydrocarbon (RH) to produce a carbon-centered radical (R•).⁵



The hydrogen abstraction mechanism is supported by the kinetic isotope effect (KIE = 3.8) for the catalytic reaction of ethylbenzene, in which eq 1 is one component step.⁶ The resulting carbon-centered radical (R•) reacts with O₂ to form a peroxy radical ROO•, which is further converted to an alcohol, aldehyde (or ketone), or carboxylic acid. Despite its unique character, only one kinetic study of PINO• has been reported by Masui et al., who studied the kinetics in acetonitrile.^{7,8} The PINO radical was generated electrolytically, and then its self-decomposition and the reactivity of PINO• toward benzhydrol and other substrates were investigated. A remarkably large KIE (10.6) for the reaction of PINO• with benzhydrol was found, which is larger than the theoretical maximum of 7.8 based on the bond-stretching mode.⁹ Moreover, the

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difference of the activation energies for $\text{Ph}_2\text{CH}(\text{OH})$ and $\text{Ph}_2\text{CD}(\text{OH})$ was 7.9 kJ mol^{-1} , which is beyond the difference in zero-point energies of C–H and C–D (4.6 kJ mol^{-1}).

On the other hand, Ingold et al. obtained a large KIE (15) for the reaction of $(\text{CF}_3)_2\text{NO}^\bullet$ with toluene,¹⁰ which implies quantum mechanical tunneling might play a role there. The $(\text{CF}_3)_2\text{NO}$ radical is one of the most reactive nitroxyl radicals, which is reflected by a fairly large O–H bond dissociation energy (BDE) of $(\text{CF}_3)_2\text{NO-H}$, 346 kJ mol^{-1} . Recently, Minisci et al. proposed that the O–H BDE of NHPI might be $>360 \text{ kJ mol}^{-1}$ from a study of an equilibrium with phenoxy radical.^{11,12} On that basis, one can imagine that the reactivity of PINO^\bullet must be higher than that of $(\text{CF}_3)_2\text{NO}^\bullet$. Thus the remarkable behavior of PINO^\bullet has attracted our interest in the fields of catalytic and free radical chemistry.

In the present work, we generated PINO^\bullet in acetic acid by oxidation of NHPI with $\text{Pb}(\text{OAc})_4$.^{13,14} The PINO radical is reasonably persistent in HOAc, which enables the direct study of its kinetics with other substrates. We investigated the reactions of PINO^\bullet with substituted toluenes, benzaldehydes, and benzyl alcohols under an argon atmosphere. We will discuss its reactivity in terms of polar effects (Hammett analysis) and kinetic isotope effects.

Experimental Section

Materials. NHPI and lead tetraacetate were purchased from Aldrich and used as received. Glacial acetic acid and anhydrous acetonitrile were used as solvents. All the substituted toluenes, benzaldehydes (except 4-carboxybenzaldehyde), and benzyl alcohols were obtained commercially and used without further purification. 4-Carboxybenzaldehyde was provided from BP Chemicals. For the study of kinetic isotope effects, *p*-xylene-*d*₁₀ (99+% D), toluene-*d*₈ (99+% D), benzaldehyde-*d* (98% D), and benzyl alcohol-*d*₇ (98% D) were purchased from Aldrich and used as received.

General Procedure. PINO^\bullet was prepared in glacial acetic acid by the oxidation of NHPI with lead tetraacetate. An acetic acid solution that contained 0.15 mmol L^{-1} of $\text{Pb}(\text{IV})$ and 1.5 mmol L^{-1} of NHPI was prepared, and the solution was bubbled with Ar for 15 min. The absorbance of the resulting solution was ca. 0.3 at 382 nm, which indicated that about 0.2 mmol L^{-1} of PINO^\bullet had been generated in the solution ($\epsilon_{382} = 1.36 \times 10^3 \text{ L mol}^{-1} \text{ cm}^{-1}$; see below).¹⁵ An oxygen-free acetic acid solution that contained the substituted toluene, benzaldehyde, or benzyl alcohol was injected into the PINO^\bullet solution, and then the absorbance change was monitored at 382 nm. The organic substrates were always in large excess in this study, and each kinetic trace conformed excellently to first-order kinetics. Most of the rate constants were measured at $25.0 \pm 0.1 \text{ }^\circ\text{C}$ spectrophotometrically. To study the temperature dependence of the rate constants, oxygen-free solutions of NHPI, $\text{Pb}(\text{IV})$, and *p*-xylene or toluene were prepared. The solution of NHPI in a cell was placed in the spectrophotometer

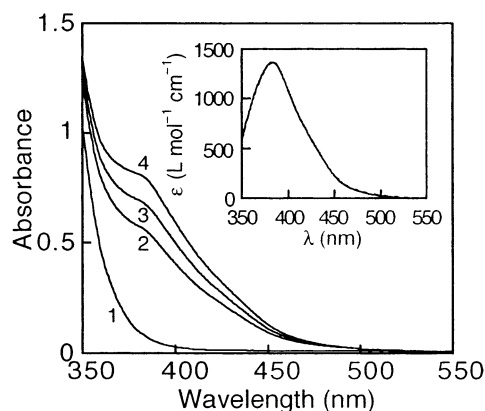


FIGURE 1. UV-vis spectra of 20 mmol L^{-1} of $\text{Pb}(\text{IV})$ with different concentrations of NHPI in acetic acid: 0 (**1**), 0.36 (**2**), 0.44 (**3**), and 0.53 (**4**) mmol L^{-1} of NHPI. Inset: plot of molar absorptivity of the PINO radical against wavelength.

with a temperature-controlled cell holder. After 15–20 min, the $\text{Pb}(\text{IV})$ solution was injected into the cell. The absorbance at 382 nm increased until all $\text{Pb}(\text{IV})$ had reacted with NHPI. Finally, *p*-xylene or toluene solution was injected into the cell. The kinetic traces could be fitted by the first-order equation even under the lowest concentration at each temperature, which means that the decomposition of PINO^\bullet is negligible under the experimental condition. For reactions in acetonitrile, a solution of NHPI (1.5 mmol L^{-1}) was prepared in acetonitrile, and then a small amount of a $\text{Pb}(\text{OAc})_4$ solution in acetic acid was added to the acetonitrile solution (finally, the mixture contained ca. 1 vol % HOAc). After the addition, the solution was bubbled by Ar for 15 min, and then an oxygen-free acetonitrile solution of *p*-xylene or *p*-xylene-*d*₁₀ was injected.

Product in the Reaction of PINO Radical with *p*-Xylene. An acetic acid solution of $\text{Pb}(\text{OAc})_4$ (0.2 mmol) was added slowly to an acetic acid solution that contained NHPI (0.4 mmol) and *p*-xylene (2 mmol) under Ar. After the completion of the reaction, all the solvent was removed under reduced pressure and the residue was dissolved in CDCl_3 . The ^1H NMR spectrum indicated that the major product is $\text{PINO-CH}_2\text{C}_6\text{H}_4\text{-CH}_3$, along with minor amounts of other compounds. The mixture was purified by column chromatography; a silica gel column was prepared in CHCl_3 , which was also used as the eluting solution. The ^1H NMR spectrum in CDCl_3 obtained by a Varian VXR-300 NMR spectrometer is shown in Figure S1.¹⁶

Results and Discussion

Molar Absorptivity and Stability of the PINO Radical in Acetic Acid. Before we studied the kinetics of PINO^\bullet , the molar absorptivity of PINO^\bullet was determined in HOAc. At first, 20 mmol L^{-1} of $\text{Pb}(\text{IV})$ solution was prepared, and then three aliquots of NHPI were injected into a stoichiometric excess of $\text{Pb}(\text{IV})$. It was observed that the absorbance around 380 nm increased strongly. The spectra of the generated transients are shown in Figure 1. Because these spectra contained contributions from the PINO radical and the excess $\text{Pb}(\text{IV})$,¹⁷ the absorbance from the excess of $\text{Pb}(\text{IV})$ was subtracted from each spectrum. The spectra so obtained were then divided by the concentration of NHPI to obtain the molar absorptivity of PINO^\bullet . These spectra then

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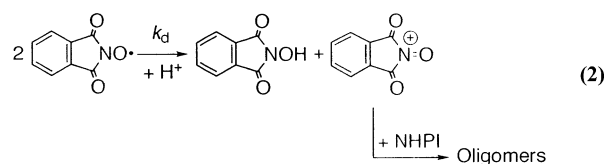
(15) The stoichiometry of the reaction is $[\text{Pb}(\text{IV})]:[\text{NHPI}] = 1:2$.

(16) ^1H NMR (300 MHz, CDCl_3 , δ): 2.36 (s, 3H), 5.18 (s, 2H), 7.19 (d, 2H), 7.43 (d, 2H), 7.74 (m, 2H), 7.80 (m, 2H).

(17) The changes in the spectra of NHPI and $\text{Pb}(\text{IV})$ can be neglected, because they are excess components and the reduced $\text{Pb}(\text{II})$ is colorless.

coincided with each other, as shown in the inset in Figure 1. The PINO radical has a maximum absorption at 382 nm with a molar absorptivity of $1.36 \times 10^3 \text{ L mol}^{-1} \text{ cm}^{-1}$. The reported value in acetonitrile is $1.46 \times 10^3 \text{ L mol}^{-1} \text{ cm}^{-1}$ at 380 nm,⁷ a small difference probably due to solvent polarity.

It was found that the formation of PINO• was followed by a slower decomposition, which we investigated in HOAc. Masui et al. reported that the self-decomposition of PINO• in acetonitrile obeys second-order kinetics.⁷



The second-order rate constant can be obtained by using eq 3, where Y = absorbance, as presented in the Supporting Information.

$$Y_t = Y_\infty + \frac{Y_0 - Y_\infty}{1 + [\text{PINO}^\bullet]_0 k_d t} \quad (3)$$

$[\text{PINO}^\bullet]_0$ is the initial concentration of PINO•, and eq 3 can be represented by using its molar absorptivity: $[\text{PINO}^\bullet]_0 = (Y_0 - Y_\infty)/\epsilon_{382}$,

$$Y_t = Y_\infty + \frac{Y_0 - Y_\infty}{1 + (Y_0 - Y_\infty) k_d t / \epsilon_{382}} \quad (4)$$

The absorbance change at 382 nm was monitored, and eq 4 was used for fitting (Figure S2). From several experimental runs with different concentrations of NHPI and Pb(IV), the second-order rate constant for the self-decomposition of PINO•, k_d , was obtained as $0.6 \pm 0.1 \text{ L mol}^{-1} \text{ s}^{-1}$ at 25 °C in HOAc. One can calculate the half-life ($t_{1/2}$) of PINO• by eq 5.

$$t_{1/2} = \frac{1}{[\text{PINO}^\bullet]_0 k_d} \quad (5)$$

For example, when $[\text{PINO}^\bullet]_0 = 0.2 \text{ mmol L}^{-1}$, the half-life is 2.2 h, which is long enough to study the reactions of PINO• with *p*-xylene and other hydrocarbons. Therefore, 0.2 mmol L^{-1} of PINO• was used for the subsequent kinetic studies. Because self-decomposition of PINO• is unimportant with respect to its reactions with RH and the experiments used, $[\text{RH}]_0 \geq 10[\text{PINO}^\bullet]_0$, the kinetic data can be analyzed by pseudo-first-order kinetics: $Y_t = Y_\infty + (Y_0 - Y_\infty) \exp(-k_{\text{obs}} t)$, where k_{obs} represents the pseudo-first-order rate constant referred to subsequently.

Masui reported $k_d = 24.1 \text{ L mol}^{-1} \text{ s}^{-1}$ at 25 °C for the decomposition of PINO• in acetonitrile solution containing 0.1 mol L^{-1} of NaClO_4 (as supporting electrolyte) and 5 mmol L^{-1} of pyridine (for electrochemical reversibility).⁷ We also monitored the decay of PINO in acetonitrile containing 1% of acetic acid, and the decay was almost the same as that in acetic acid, even with 0.1 mol L^{-1} of NaClO_4 . On the other hand, addition of pyridine accelerated the decay of PINO• in acetonitrile (Figure S3). The effect of pyridine on the decomposition of PINO• lies outside the scope of this subject, however.

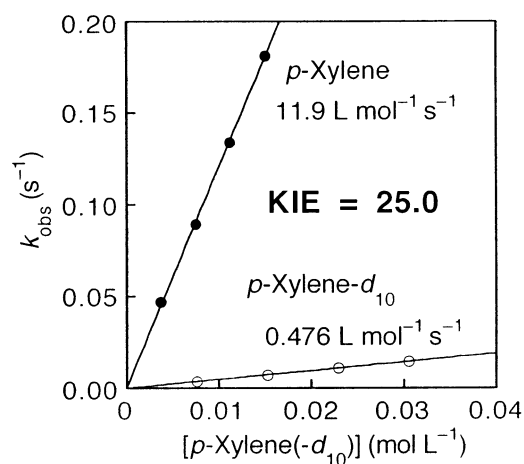
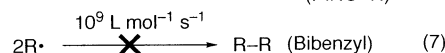
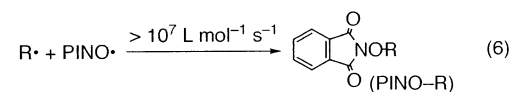
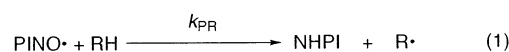


FIGURE 2. Dependence of k_{obs} on the concentrations of *p*-xylene or *p*-xylene- d_{10} in HOAc at 25 °C.

SCHEME 1. Reaction Scheme for PINO Radical with Hydrocarbon



Reaction of PINO Radical with *p*-Xylene. The reaction of PINO• with *p*-xylene was investigated under the pseudo-first-order conditions, $[\text{PINO}^\bullet]_0 \ll [\text{p-xylene}]_0$. Figure 2 shows the dependence of k_{obs} on $[\text{p-xylene}]$.

The second-order rate constant for *p*-xylene is $11.9 \text{ L mol}^{-1} \text{ s}^{-1}$ at 25 °C. The initial step of the reaction represents hydrogen atom transfer from a methyl group of *p*-xylene to PINO•, which produces NHPI and a benzylic radical (R^\bullet), as shown in Scheme 1. The following step is a radical recombination between the benzylic radical and another PINO• to form an adduct PINO-R.

There are several reports for radical recombination reactions of TEMPO• with carbon-centered radicals (mostly benzylic radical), and the rate constants of such reactions are normally ca. $10^7 \text{ L mol}^{-1} \text{ s}^{-1}$.^{18–20} Moreover, a radical recombination of TEMPO• with benzoyl radical takes place very rapidly ($1 \times 10^9 \text{ L mol}^{-1} \text{ s}^{-1}$).²¹ As we know, TEMPO• is a fairly stable radical, and its O–H BDE is 293 kJ mol^{-1} , which is much lower than that of NHPI.^{11,22} These data indicate that radical recombination reactions of PINO• with a carbon-centered radical must be faster than those of TEMPO•. Therefore, it can be concluded that the reactions of PINO• with hydrocarbons take place through Scheme 1. We also considered the self-reaction between two benzylic radicals. Although this reaction has a nearly diffusion-controlled rate constant (ca. 10^9 L mol^{-1}

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s⁻¹),¹⁹ the concentration of benzyl radical at the steady state is quite low in comparison with that of PINO•. In that case, the reaction scheme can safely ignore radical dimerization (eq 7). A kinetic simulation was performed with the KinSim program to confirm this reaction pattern.²³ The kinetic simulation result is shown in Figure S4.

According to Scheme 1, the observed rate constant, k_{obs} , corresponds to $2k_{\text{PR}}[\text{RH}]$. Therefore, the net second-order rate constant, k_{PR} , for the reaction of PINO• with *p*-xylene can be obtained as 5.95 L mol⁻¹ s⁻¹ at 25.0 °C in HOAc.

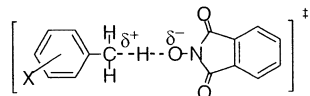
$$k_{\text{obs}} = 2k_{\text{PR}}[\text{RH}] \quad (8)$$

Following Scheme 1, an adduct of PINO• with a carbon-centered radical is produced. This kind of adduct was reported by Ishii; however, its NMR spectrum was not reported.³ We confirmed the product in the reaction of PINO• with *p*-xylene by ¹H NMR spectroscopy. The major product was identified as PINO–CH₂C₆H₄CH₃. The ¹H NMR spectrum obtained is shown in Figure S1, which is similar to that of *N*-benzyloxyphthalimide (PINO–CH₂C₆H₅).²⁴

Figure 2 also shows a large KIE of 25.0 for the reaction of PINO• with *p*-xylene, which supports the rate-determining step being hydrogen abstraction. However, the KIE is much larger than the maximum value for a normal hydrogen abstraction on the basis of bond-stretching modes and zero-point energies. The large KIE implies quantum mechanical tunneling participates in this reaction. We will discuss the tunnel effect later.

Reactions of PINO Radical with Substituted Toluenes, Benzaldehydes, and Benzyl Alcohols. The rate constants for the reactions of PINO• with substituted toluenes, benzaldehydes, and benzyl alcohols were measured in HOAc at 25 °C. The second-order rate constants are listed in Table 1, and the rate constants for the reactions with para- and meta-substituted substrates were plotted against Hammett substituent parameters (σ or σ^+) as shown in Figure 3.^{25,26}

These plots show that each reaction is accelerated by electron-donating substituents, which suggests that the reaction center is more positive at the transition state. This result corresponds with the proposed transition state for PINO• reactions.^{3,27}



The ρ value of the reaction with substituted toluenes is larger than those of the reactions with benzaldehydes and benzyl alcohols.²⁸ For the reaction with toluenes, the correlation with σ^+ values is more suitable than that with σ values, which indicates a significant contribution of a

TABLE 1. Second-Order Rate Constants (L mol⁻¹ s⁻¹) for the Reaction of the PINO Radical with Substituted Toluenes, Benzaldehydes, and Benzyl Alcohols in HOAc at 25 °C

	no. of H	k_{PR}	k_{PR} (per H)
X–C ₆ H ₄ CH ₃			
<i>p</i> -MeO	3	10.3	3.43
<i>p</i> -Me	6	5.95	0.992
(<i>p</i> -xylene- <i>d</i> ₁₀)	6	0.240	0.0400
<i>m</i> -Me	6	3.06	0.509
<i>o</i> -Me	6	2.99	0.498
<i>p</i> -H	3	0.620	0.207
(toluene- <i>d</i> ₈)	3	0.0229	0.00763
<i>p</i> -Br	3	0.595	0.198
<i>p</i> -COOH	3	0.272	0.0907
<i>m</i> -COOH	3	0.200	0.0667
<i>o</i> -COOH	3	0.113	0.0375
<i>p</i> -NO ₂	3	0.119	0.0395
<i>p</i> -X–C ₆ H ₄ CHO			
MeO	1	13.9	13.9
Me	1	12.4	12.4
H	1	10.6	10.6
(benzaldehyde- <i>d</i>)	1	0.386	0.386
COOH	1	3.16	3.16
NO ₂	1	1.73	1.73
<i>p</i> -X–C ₆ H ₄ CH ₂ OH			
MeO	2	44.9	22.4
Me	2	27.4	13.7
H	2	11.3	5.65
(benzyl alcohol- <i>d</i> ₇)	2	0.670	0.335
Br	2	16.1	8.03
Cl	2	13.5	6.75
CF ₃	2	9.85	4.93
NO ₂	2	11.1	5.53

resonance effect by the electron-donating group (correlation coefficient, $r = 0.976$ for σ^+ vs 0.927 for σ). The obtained ρ value for σ^+ is -1.3 , which is fairly close to previously reported values for hydrogen abstraction from substituted toluenes.^{29–31} One might speculate that electron-donating groups weaken the C–H bond of the methyl group and thus cause the rate to increase.^{32–34} However, Ingold et al. calculated the bond dissociation energies of substituted toluenes and concluded that any substituents, even electron-withdrawing groups, in the para position of toluenes make the C–H bonds weaker.³⁵ Therefore, it can be concluded that the reactions of PINO• with substituted toluenes have a contribution from the polar effect, which supports the previously proposed transition state.

On the other hand, for the reaction of benzaldehydes, the correlation with σ is better than that with σ^+ ($r = 0.992$ for σ vs 0.932 for σ^+). There are a few studies of

(28) In the reactions of *p*-tolualdehyde and *p*-methylbenzyl alcohol, there are two reactive groups, –CH₃ and –CHO or –CH₂OH. The obtained rate constants are fairly large for hydrogen abstraction from the CH₃ group. Therefore, the obtained rate constants must be for hydrogen abstraction from the –CHO and –CH₂OH groups.

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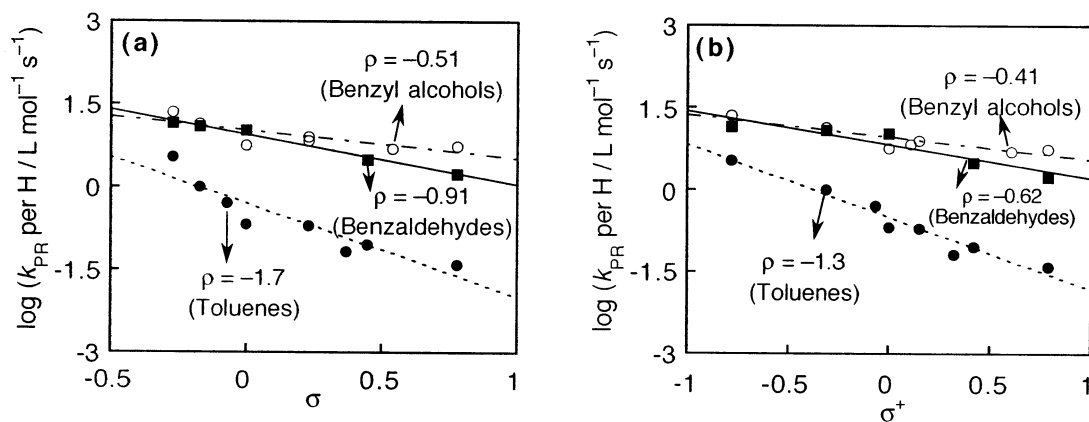
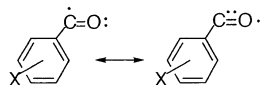


FIGURE 3. Plots of the rate constants for the reactions of the PINO radical with substituted toluenes, benzaldehydes, and benzyl alcohols against (a) σ constants and (b) σ^+ constants in HOAc at 25 °C

hydrogen abstraction from benzaldehydes.^{36,37} We propose that σ values should be applied to the hydrogen abstraction from benzaldehydes. This is because benzoyl radicals are stabilized by a conjugation between an unpaired electron on a carbon atom and a lone pair on an oxygen atom, however, there is no contribution by resonance with benzene ring.³⁸



For the reaction with substituted benzyl alcohols, it is hard to say which of the σ or the σ^+ should be used because of large experimental errors. However, it seems that the correlation with σ^+ is slightly better than that with σ ($r = 0.897$ for σ^+ vs 0.790 for σ). If we select the correlation with σ^+ for the reaction, the ρ value is -0.41 . The kinetic studies of hydrogen abstraction from substituted benzyl alcohols are quite limited; however, there are several studies of catalyzed oxidations of substituted benzyl alcohols.^{39–41} The reported ρ values against σ or σ^+ lie between -0.32 and -0.58 , even though the reaction mechanisms are different. Moreover, in the reaction of PINO \cdot with substituted benzyl alcohols, probably the obtained ρ has contributions not only from polar effect but also from the differences in the C–H BDEs of benzyl alcohols.^{35,42} One can notice from Figure 3 that the reaction of PINO \cdot with substituted benzyl alcohols is less sensitive to its substituents than that of PINO \cdot with substituted benzaldehydes. Generally speaking, therefore, electron-withdrawing groups on benzyl alcohol lead to higher selectivity in its oxidation to benzaldehyde. Indeed, high selectivities were reported in the Co/NHPI-

catalyzed oxidation of benzyl alcohols in acetonitrile.¹¹ Even the oxidation of unsubstituted benzyl alcohol has a remarkable selectivity. However, the rate constants for benzyl alcohol and benzaldehyde in Table 1 show no difference between the two reactions in HOAc. We presume that the selectivity in oxidation of benzyl alcohol can be attributed to a solvent effect and thus the measured rate constants for hydrogen abstraction by PINO \cdot in acetonitrile (Table S1). The rate constants for *p*-xylene and benzaldehyde in HOAc are larger than those in acetonitrile probably due to thermodynamic favorability in HOAc; the O–H BDE of NHPI in HOAc could be higher than that in CH₃CN because hydrogen bonding between NHPI and HOAc increases the O–H BDE.^{12,43} On the other hand, the reaction of PINO \cdot with benzyl alcohol in HOAc is slower than that in acetonitrile. In this case, the O–H group in benzyl alcohol forms a hydrogen bond with HOAc, which increases the C–H BDE in benzyl alcohol. Presumably, selectivities for the oxidation of benzyl alcohol by NHPI catalysis would vary in different solvents.

Kinetic Isotope and Tunnel Effects. As shown in Figure 2, a large kinetic isotope effect (KIE = 25.0) was observed in the reaction of PINO \cdot with *p*-xylene in acetic acid at 25 °C. This KIE value is much larger than that reported (3.8) for ethylbenzene in the overall catalytic system.⁶ We also studied the NHPI/Co(OAc)₂-catalyzed oxidation of *p*-xylene by monitoring O₂ consumption to determine the initial rate and found KIE = 3.4 in HOAc at 70 °C.⁴⁴ Because of the multistep reaction for the catalytic system, the observed KIE must be a mixed value of several reaction steps.^{5,45} Therefore, we emphasize that the KIE for the specific reaction of PINO \cdot with *p*-xylene is 25.0, which is far from the usual ones. Even if a secondary isotope effect is considered, the KIE value is still beyond the theoretical maximum. Moreover, the KIE for the reaction of benzaldehyde, which does not have a secondary isotope effect, is 27.5 (see below). Therefore, the large KIE implies tunneling takes part in this hydrogen abstraction reaction. We also investigated the

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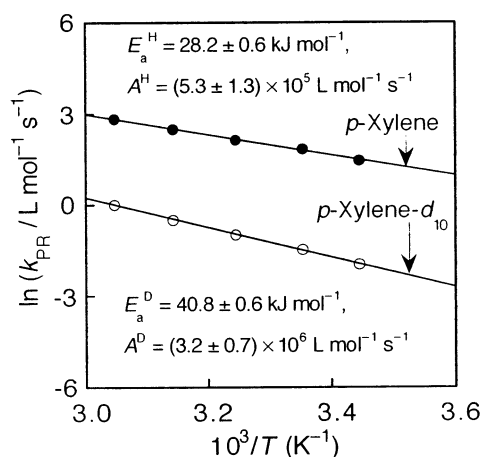


FIGURE 4. Arrhenius plot for the reaction of the PINO radical with *p*-xylene and *p*-xylene- d_{10} in HOAc. $T = 17$ – 65 °C.

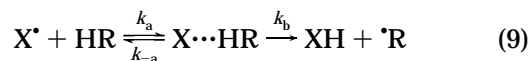
same reaction in acetonitrile containing 1 vol % acetic acid to evaluate the solvent effect on the KIE. The KIE in acetonitrile is 28.4, as shown in Figure S5. Therefore, it is noteworthy that the large KIE value of the PINO \cdot reaction does not originate from a solvent effect such as hydrogen bonding. Sometimes, a large KIE value is explained by a loss of one or more C–H bending modes at the transition state.⁴⁶ However, according to Bell's calculation, the maximum semiclassical isotope effect after allowance for bending modes is 10 at 25 °C.^{47,48} Therefore, the large KIE value for the PINO \cdot reactions cannot be explained without allowance for the tunnel effect. We also investigated the reaction of PINO \cdot with *p*-xylene and *p*-xylene- d_{10} at various temperatures. Figure 4 shows the Arrhenius plot for *p*-xylene and *p*-xylene- d_{10} . The difference of activation energies, $E_a^D - E_a^H$, was 12.6 ± 0.8 kJ mol $^{-1}$, which is almost twice as large as the difference in zero-point energies of C–H and C–D bonds.⁴⁷ Moreover, the ratio of preexponential factors, A^H/A^D , was 0.17 ± 0.05 which is remarkably larger than those of normal hydrogen abstraction reactions. Without a tunnel effect, A^H/A^D is usually close to unity.^{47,49} The kinetic isotope effects for the reactions of PINO \cdot with other substrates were also investigated, and the values of KIE were 27.1 (toluene), 27.5 (benzaldehyde), and 16.9 (benzyl alcohol) in HOAc at 25 °C (Figures S7–S9). These results further indicate that tunneling plays an important role in the PINO \cdot reactions.⁵⁰

The preexponential factors for the reactions of PINO \cdot with *p*-xylene and *p*-xylene- d_{10} are quite low ($\log A \approx 6$) compared with those for other hydrogen abstraction reactions.⁴⁷ The temperature dependence for the reactions of PINO \cdot with toluene and toluene- d_8 was also investigated, and low preexponential factors were obtained: $A^H = (8.8 \pm 0.9) \times 10^5$ L mol $^{-1}$ s $^{-1}$, $A^D = (2.2 \pm 0.9) \times 10^6$ L mol $^{-1}$ s $^{-1}$ (Figure S8). We must ask why the preexponential factors are so low in the PINO \cdot reactions.

Such low preexponential factors were also obtained for the reaction with benzhydrol and benzhydrol- d in acetonitrile by Masui (Figure S10).⁷ The low preexponential factors might be attributed to the large tunnel effect, since if tunneling participates in the reaction, the Arrhenius plot becomes curved, and a limited temperature range often leads low preexponential factors.^{47,48}

Ingold et al. studied the reaction of (CF $_3$) $_2$ NO \cdot with toluene and other hydrocarbons.^{10,51} They found a large KIE in the reaction with toluene ($k_H/k_D = 15$ at 25 °C), and $E_a^D - E_a^H$ was 6.7 kJ mol $^{-1}$. These results indicate that the tunnel effect takes part in the reactions of (CF $_3$) $_2$ NO \cdot . They also obtained low preexponential factors in the reaction ($\log A = 3.6$ – 6.5).⁵¹ However, they claimed that the low preexponential factors cannot be attributed to the tunnel effect, and they mentioned an intermediate formation of a hydrogen-bonded complex or the triplet repulsion in the transition state.⁵¹ The existence of such a hydrogen-bonded complex is supported by several studies of (*tert*-Bu) $_2$ NO \cdot or TEMPO \cdot by spectroscopic data and theoretical calculations.^{52–54}

It is often proposed that unusually low preexponential factors might be attributed to the formation of a hydrogen-bonded intermediate in hydrogen abstraction from phenols.^{55–57}



$$\text{rate} = \frac{k_a k_b}{k_{-a} + k_b} [X^{\bullet}] [RH] \quad (10)$$

When $k_{-a} \ll k_b$, the rate-determining step is k_a and the Arrhenius preexponential factor will be high ($\approx 10^{11}$ L mol $^{-1}$ s $^{-1}$), which is a normal value for a diffusion-controlled reaction in normal viscosity solvents. On the other hand, if $k_{-a} \gg k_b$, the rate equation is obtained as eq 11.

$$\text{rate} = K_a k_b [X^{\bullet}] [RH] \quad (11)$$

In such a case, the preexponential factor is expressed by eq 12.

$$\ln(A_{\text{obs}}/\text{L mol}^{-1} \text{ s}^{-1}) = \ln(A_b/\text{s}^{-1}) + \Delta S_a^{\circ}/R \quad (12)$$

Thus, if the PINO \cdot reaction involves the formation of a hydrogen-bonded intermediate, the observed preexponential factor will be smaller by the entropy loss, $\Delta S_a^{\circ}/R$. If hydrogen and deuterium have different equilibrium constants for the formation of a hydrogen-bonded intermediate, one cannot say whether this reaction is really

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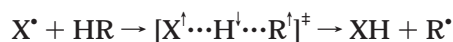
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tunneling or not. There is a report of a study of the hydrogen-bonding interaction of C_6H_5OH and C_6H_5OD with acetone and quinuclidine, where no detectable difference is to be expected in the enthalpy of adduct formation.⁵⁸ If the hydrogen abstraction by PINO• really involves such a hydrogen-bonded intermediate, the reaction should be classified as a case of *proton-coupled electron transfer*.⁵⁹ Recently, quite large KIEs were reported in proton-coupled electron transfers from nitrogen, sulfur, and phosphorus (KIE = 31–178).^{60–62}

On the other hand, the triplet repulsion is also a large factor in hydrogen abstraction.^{51,63–65}



In hydrogen abstraction, the transition state has parallel spins, which leads to triplet repulsion. It is reported that reaction of a nitroxyl radical with a hydrocarbon has a large triplet repulsion energy ($E_T = 28 \text{ kJ mol}^{-1}$) but also a large negative electron affinity energy ($E_{EA} = -23 \text{ kJ mol}^{-1}$).⁶⁵ It is not clear how much the triplet repulsion energy or the electron affinity energy affect the pre-exponential factor. However, it might be necessary to take account of such energies because the electron affinity of PINO• must be larger than those of usual nitroxyl radicals such as TEMPO•.

In this article, we have discussed some possible reasons why the preexponential factor of the PINO• reaction is so small compared with other hydrogen abstraction reactions. As Ingold proposed, the transition state in the reaction of $(CF_3)_2NO^{\bullet}$ as well as PINO• might have a highly restrictive geometry that demands a very specific orientation.⁵¹ More kinetic studies of PINO• with several substrates such as phenols and hydroperoxides could be helpful to understand the origin of the low preexponential factor.

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Conclusions

Kinetic studies on the reactions of the PINO radical with substituted toluenes, benzaldehydes, and benzyl alcohols were performed under an argon atmosphere. The reactions take place through hydrogen atom abstraction from C–H bonds by the PINO radical. This step is rate controlling and is followed by radical recombination of the carbon-center radical so generated with another PINO radical. From the analysis of the Hammett plot, it was found that the reaction with substituted toluenes has a large polar effect compared with the other reactions.

The detailed investigations of kinetic isotope effect indicate quantum mechanical tunneling participates in the PINO radical reactions. We expect that our findings will lead to further understanding of the tunnel effect in hydrogen atom transfer reaction.⁶⁶ However, the reason the preexponential factors in Arrhenius plots are so small is less clear. Hydrogen abstraction by the PINO radical might be an instance in which not only quantum mechanical tunneling but also the formation of a hydrogen-bonded intermediate contribute.

Further kinetic studies in the presence of air or O_2 are necessary to understand the NHPI-catalyzed aerobic catalytic system. To do so, precise information such as the bond dissociation energy of NHPI will be helpful to interpret the catalytic mechanism. From this work, it can be said that the PINO radical is more reactive than other nitroxyl radicals. The reactivities of nitroxyl radicals must be related to bond dissociation energies of the corresponding hydroxylamines. Direct evaluation of the O–H bond dissociation energy of NHPI will help to define the reactivity of PINO radical.⁴³

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Supporting Information Available: The NMR spectrum of PINO– $CH_2C_6H_4CH_3$, additional plots of kinetic data in acetic acid and acetonitrile. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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