Kinetics of Self-Decomposition and Hydrogen Atom Transfer Reactions of Substituted Phthalimide *N*-Oxyl Radicals in Acetic Acid

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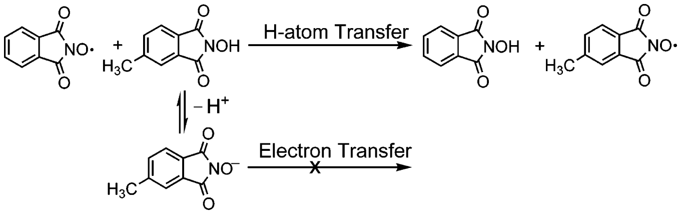
Received September 8, 2004

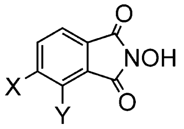


Kinetic data have been obtained for three distinct types of reactions of phthalimide *N*-oxyl radicals (PINO$^•$) and *N*-hydroxyphthalimide (NHPI) derivatives. The first is the self-decomposition of PINO$^•$ which was found to follow second-order kinetics. In the self-decomposition of 4-methyl-*N*-hydroxyphthalimide (4-Me-NHPI), H-atom abstraction competes with self-decomposition in the presence of excess 4-Me-NHPI. The second set of reactions studied is hydrogen atom transfer from NHPI to PINO$^•$, e.g., PINO$^•$ + 4-Me-NHPI $\rightleftarrows$ NHPI + 4-Me-PINO$^•$. The substantial KIE, $k_H/k_D = 11$ for both forward and reverse reactions, supports the assignment of H-atom transfer rather than stepwise electron−proton transfer. These data were correlated with the Marcus cross relation for hydrogen-atom transfer, and good agreement between the experimental and the calculated rate constants was obtained. The third reaction studied is hydrogen abstraction by PINO$^•$ from *p*-xylene and toluene. The reaction becomes regularly slower as the ring substituent on PINO$^•$ is more electron donating. Analysis by the Hammett equation gave $\rho = 1.1$ and 1.8 for the reactions of PINO$^•$ with *p*-xylene and toluene, respectively.

Introduction

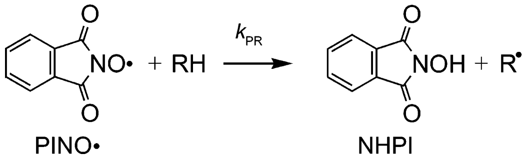
N-Hydroxyphthalimide (NHPI, X = Y = H in Chart 1) has gained considerable attention in organic and catalytic chemistry.[1−4] Since fascinating catalysis of NHPI with Co(II) has been found by Ishii,[1] a number of studies of its reactivity and applications have been reported.[2−4] It is proposed that NHPI is oxidized to phthalimide *N*-oxyl radical (PINO$^•$), which is a key species in the catalytic cycles.[2] We have previously studied the kinetics for hydrogen abstraction reactions by PINO$^•$ from methyl arenes and other organic substrates.[5,6]

CHART 1



	X	Y
4-Me-NHPI	Me	H
4-Cl-NHPI	Cl	H
4-F-NHPI	F	H
3-F-NHPI	H	F

These reactions are characterized by large kinetic isotope effects, and we proposed that quantum tunneling plays an important role there. This is not without further qualification, however, as will be taken up at the end of the Discussion.



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In this study, we present new kinetic data using ring-substituted NHPI derivatives (Chart 1) and discuss self-

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[1] Ishii, Y.; Iwahama, T.; Sakaguchi, S.; Nakayama, K.; Nishiyama, Y. *J. Org. Chem.* **1996**, *61*, 4520−4526.
[2] Ishii, Y.; Sakaguchi, S.; Iwahama, T. *Adv. Synth. Catal.* **2001**, *343*, 393−427.
[3] Amorati, R.; Lucarini, M.; Mugnaini, V.; Pedulli, G. F.; Minisci, F.; Recupero, F.; Fontana, F.; Astolfi, P.; Greci, L. *J. Org. Chem.* **2003**, *68*, 1747−1754.
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[5] Koshino, N.; Saha, B.; Espenson, J. H. *J. Org. Chem.* **2003**, *68*, 9364−9370.
[6] Koshino, N.; Cai, Y.; Espenson, J. H. *J. Phys. Chem. A.* **2003**, *107*, 4262−4267.

10.1021/jo048418t CCC: $30.25

TABLE 1. Maximum Absorption Wavelengths and Molar Absorptivities of Substituted PINO Radicals in Acetic Acid[a]

X-PINO•	λ_{max}/nm	ϵ_{max}/10^3 L mol^{-1} cm^{-1}
4-Cl	394	1.38
4-F	382	1.21
4-H	382[b]	1.36[b]
4-Me	397[c]	1.39[d]
3-F	367[c]	1.32[d]

[a] In HOAc at 25 °C. [b] Reference 5. [c] Reference 10. [d] Redetermined more accurately.

decomposition reactions, hydrogen atom self-exchange reactions, and hydrogen abstraction reactions from *p*-xylene and toluene

Experimental Section

Materials. *N*-hydroxyphthalimide (NHPI) was purchased from Aldrich and used as received. 3-Fluoro- and 4-methyl-substituted NHPI derivatives were synthesized as previously reported.[7] 4-Fluoro-NHPI, whose synthesis had not been reported, was prepared from 4-fluorophthalic anhydride and hydroxylamine hydrochloride by the same method[7] and obtained in 25% yield. It was characterized by ^{1}H NMR spectroscopy in DMSO-d_6: δ 7.62−7.67 (m, 1H), 7.74−7.76 (m, 1H), 7.89−7.92 (m, 1H), 10.89 (s, 1H). Glacial acetic acid (Fischer) and acetic acid-d_4 (99.5% D, CIL) were used as received. Each PINO radical was generated by the oxidation of its NHPI precursor with Co(III) acetate or lead tetraacetate. Cobalt(III) solutions were prepared by passing ozone through a solution of $Co(OAc)_2$ in acetic acid.[8] The Co(III) solutions were then bubbled with a vigorous stream of argon to remove excess ozone. Lead tetraacetate (Aldrich) was also used to produce the PINO radicals for hydrogen abstraction reactions with *p*-xylene and toluene.[9] To study kinetic isotope effects for hydrogen abstraction reactions, *p*-xylene-d_{10} (99+% D, Aldrich) and toluene-d_8 (99+% D, Aldrich) were used as received. Other chemical reagents were obtained commercially and used without purification.

General Methods. The UV/vis spectra of the PINO radicals were recorded on a Shimadzu UV-3101 spectrophotometer. The kinetics of self-decomposition of the PINO radicals was monitored by using a UV/Vis spectrophotometer equipped with a temperature-controlled cell holder. The rate constants for reactions between X-PINO• and Y−NHPI were measured in glacial acetic acid and acetic acid-d_4 by a stopped-flow spectrophotometer (OLIS RSM 1000) with a temperature-controlled water circulation bath. The rate constants for reactions of the PINO radicals with *p*-xylene and toluene were measured spectrophotometrically in HOAc at 25.0 ± 0.1 °C under an argon atmosphere.

Results and Discussion

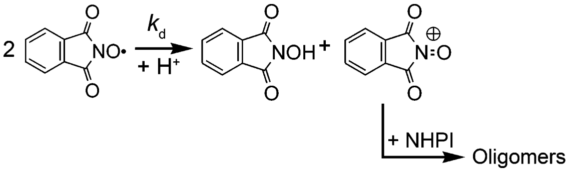
Molar Absorptivities of the Substituted PINO Radicals. The substituted PINO radicals were generated by the oxidation of the parent NHPI compounds with Co(III) in HOAc. Although the PINO radicals decompose slowly, they persist long enough for accurate UV/vis spectra to be recorded (Figure S1, Supporting Information). Table 1 shows the wavelengths of the absorption maxima and the molar absorptivities of the PINO radicals, which differ relatively little from one another. It seems that there is no obvious correlation between substitutents on NHPI and maximum absorption wavelengths or molar absorptivities.

TABLE 2. Rate Constants for Self-Decomposition of Substituted PINO Radicals in HOAc at 25 °C

X-PINO•	k_d/L mol^{-1} s^{-1}
4-Cl	0.4
4-F	0.7
4-H	0.6[a]
4-Me	1.7[b]
3-F	0.8[c]

[a] Reference 5. [b] Net self-decomposition (see text). [c] At 15 °C, ref 13.

Self-Decomposition of the Substituted PINO Radicals. We previously studied self-decomposition reaction of the unsubstituted PINO radical and found that the reaction obeys second-order kinetics in glacial acetic acid.[5] The products of this reaction have been identified as some oligomers (primarily a trimer) formed by subsequent reactions of the initial disproportionation.[11]



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The second-order rate constant, k_d, was obtained from eq 3, where Y represents absorbance, [X-PINO•]$_0$ the initial concentration of the X-PINO radical, given by $(Y_0 - Y_\infty)/\epsilon$.[5,12] The value of ϵ for PINO• in C_6H_6/MeCN have been reported to be 1.46×10^3 L mol^{-1} cm^{-1};[11] we have used the value in HOAc from Table 1 for the calculation of the rate constant for sake of solvent consistency. In any event, the values of the rate constant would be very similar no matter which value of ϵ were used. The decomposition rate constants (k_d) are summarized in Table 2.

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

We have previously reported that the reactivity of substituted NHPI compounds in the autoxidation of *p*-xylene follows the order of 4-Me-NHPI < 3-F-NHPI < NHPI[10] and proposed that the reactivity order could be explained by the persistence of the corresponding radical species. As shown in Table 2, the unsubstituted PINO• (4-H-PINO•) is much more persistent than 4-Me-PINO•. The comparison of the stability of 3-F-PINO• with those of 4-substituted PINO radicals cannot be straightforward because of the temperature differences. However, the self-decomposition of 4-Me-PINO• would be faster than 1.7

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[7] Wentzel, B. B.; Donners, M. P. J.; Alsters, P. L.; Feiters, M. C.; Nolte, R. J. M. *Tetrahedron* **2000**, *56*, 7797−7803.

[8] Lande, S. S.; Falk, C. D.; Kochi, J. K. *J. Inorg. Nucl. Chem.* **1971**, *33*, 4101−4109.

[9] When Co(III) was used to generate PINO•, we obtained slightly different rate constants of hydrogen abstraction reactions even under an argon atmosphere. Probably, Co(II) takes part in the subsequent reactions.

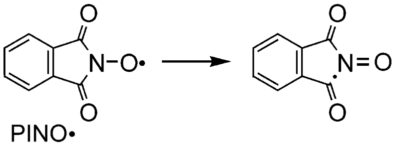
[10] Saha, B.; Koshino, N.; Espenson, J. H. *J. Phys. Chem. A* **2004**, *108*, 425−431.

[11] Ueda, C.; Noyama, M.; Ohmori, H.; Masui, M. *Chem. Pharm. Bull.* **1987**, *35*, 1372−1377.

[12] Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill: New York, 1995.

s^{-1} in practical conditions because hydrogen abstraction from methyl group also takes place (see below). Therefore, the stability of the three PINO radicals would be in the order of 4-Me-PINO$^\bullet$ < 3-F-PINO$^\bullet$ < PINO$^\bullet$, consistent with the reactivity of the NHPIs in the catalytic cycle.

The self-decomposition reactions of nitroxyl radicals are usually observed to follow second-order kinetics.[14] However, Amorati et al. reported that the self-decomposition of PINO$^\bullet$ obeys first-order kinetics in benzene containing 10% CH_3CN,[3] which is inconsistent with our data in HOAc and those of Masui in CH_3CN.[11] According to their experimental data, the decomposition of the PINO radical in benzene obeys the first-order kinetics, and they proposed a fragmentation at one of the carbonyl carbon−nitrogen bonds.[3,15]


PINO•

(4)

We generated the PINO radical in benzene containing 10% CH_3CN by the oxidation of NHPI with AgO (Aldrich) and monitored the self-decomposition. The result is shown in Figure S2a,b (Supporting Information). It seems that the decomposition of the PINO radical is more likely to follow second-order kinetics. We have not obtained the accurate molar absorptivity of PINO$^\bullet$ in benzene; however, if we suppose ϵ_{382} in benzene/CH_3CN is equal to ϵ_{382} in HOAc, k_d in benzene/CH_3CN is calculated as 31 L mol^{-1} s^{-1}, which is not too far from its value in CH_3CN, 24.1 L mol^{-1} s^{-1}.[11] Even if we hypothesize that the reaction follows first-order kinetics, the pseudo-first-order rate constant is given as 1.2×10^{-3} s^{-1}. This rate constant is much smaller than that reported (0.1 s^{-1}).[3] The discrepancy may arise from the procedures to generate the PINO radical.[3,5] Amorati et al. used dicumyl peroxide to generate the PINO radical.

$$\{PhCMe_2O\}_2 \xrightarrow{h\nu} 2PhCMe_2O^\bullet \qquad (5)$$

The PINO radical is then generated in the following step:

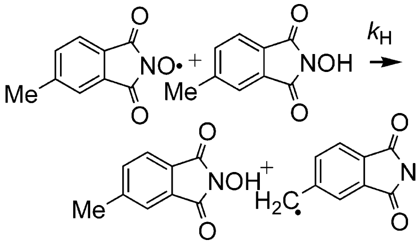
$$PhCMe_2O^\bullet + NHPI \rightarrow PhCMe_2OH + PINO^\bullet \qquad (6)$$

However, the cumyloxyl radical might produce other species such as acetophenone by β-scission:[16]

$$PhCMe_2O^\bullet \rightarrow PhCOMe + Me^\bullet \qquad (7)$$

It is well-known that acetophenone is also photoactive.[17] Therefore, we postulate that during the irradiationin their experiments, the resulting acetophenone could produce some byproducts with which PINO$^\bullet$ may react.

Self-Decomposition of 4-Me-PINO Radical. An exception to the general pattern of second-order kinetics was found for 4-Me-PINO$^\bullet$, which follows second-order kinetics only at lower concentrations of 4-Me-NHPI (<0.83 mmol L^{-1}). Deviations from second-order kinetics were noted at higher concentrations of 4-Me-NHPI. As the concentration of 4-Me-NHPI increased, the absorbance−time data approached first-order kinetics, but both first- and second-order terms were needed for precise fitting. Considering the fairly high H-atom abstraction ability of PINO radicals, we concluded that the 4-Me-PINO radical decomposes in two parallel reactions: one is the self-decomposition as expressed by eq 2, and the other is hydrogen abstraction of 4-Me-PINO$^\bullet$ from the methyl group on 4-Me-NHPI, eq 8.



(8)

In that case, the differential rate law and its integrated form are[12]

$$-\frac{d[\text{4-Me-PINO}]}{dt} = k_d[\text{4-Me-PINO}^\bullet]^2 + k_H[\text{4-Me-NHPI}][\text{4-MePINO}^\bullet] \qquad (9)$$

$$Y_t = Y_\infty + \frac{k_{H(obs)}(Y_0 - Y_\infty)_0[\text{4-Me-PINO}^\bullet]e^{-k_{H(obs)}t}}{k_{H(obs)} + k_d[\text{4-Me-PINO}^\bullet]_0(1 - e^{-k_{H(obs)}t})} \qquad (10)$$

where k_H is the rate constant for reaction 8 and $k_{H(obs)}$ is the related pseudo-first-order rate constant in the presence of excess 4-Me-NHPI ($k_{H(obs)} = k_H$[4-Me-NHPI]). The value of [4-Me-PINO]$_0$ is calculated from the absorbance at 397 nm and its molar absorptivity. We determined the rate constant for the self-decomposition (eq 2) of 4-Me-PINO$^\bullet$ using experimental data at the lowest 4-Me-NHPI concentrations. Figure S3a (Supporting Information) shows the resulting fitting, which gave $k_d = 1.7$ L mol^{-1} s^{-1}. On the other hand, at higher concentrations of 4-Me-NHPI (>2 mmol L^{-1}), eq 10 was used to obtain $k_{H(obs)}$ by fixing k_d (1.7 L mol^{-1} s^{-1}). The values of $k_{H(obs)}$ so obtained were plotted against [4-Me-NHPI]$_0$ as illustrated in Figure 1. This procedure gave $k_H = 0.080$ L mol^{-1} s^{-1} at 25.0 °C as the rate constant of H-atom abstraction from 4-methyl group (reaction 8). We previously reported the rate constants of H-atom abstraction by PINO$^\bullet$ from toluic acids as $k_{PR} = 0.20$ (*m*-toluic acid) and 0.28 (*p*-toluic acid) L mol^{-1} s^{-1} under an argon atmosphere.[5] The difference of the rate constants between k_H and k_{PR} of the two toluic

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[13] The rate constant was measured at 15 °C, because the formation and decomposition steps of 3-F-PINO$^\bullet$ were comparable at 25 °C, and thus, the kinetic trace could not be separated into its components.

[14] (a) Blackley, W. D.; Reinhard, R. R. *J. Am. Chem. Soc.* **1965**, *87*, 802−805. (b) Bowman, D. F.; Gillan, T.; Ingold, K. U. *J. Am. Chem. Soc.* **1971**, *93*, 6555−6561.

[15] Minisci, F.; Recupero, F.; Cecchetto, A.; Gambarotti, C.; Punta, C.; Paganelli, R. *Org. Process Res. Dev.* **2004**, *8*, 163−168.

[16] Baciocchi, E.; Bietti, M.; Salamone, M.; Steenken, S. *J. Org. Chem.* **2002**, *67*, 2266−2270.

[17] (a) Wagner, P. J.; Truman, R. J.; Puchalski, A. E.; Wake, R. *J. Am. Chem. Soc.* **1986**, *108*, 7727−7738. (b) Wagner, P. J.; Zhang, Y.; Puchalski, A. E. *J. Phys. Chem.* **1993**, *97*, 13368−13374.

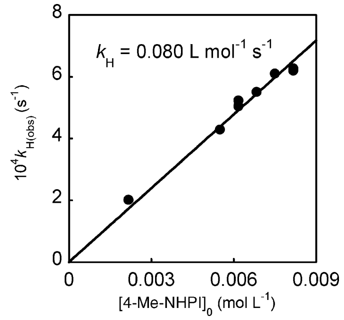

FIGURE 1. Plot of $k_{H(obs)}$ against $[4\text{-Me-NHPI}]_0$. $k_{H(obs)}$ was obtained from eq 10 with k_d fixed (1.7 L mol^{-1} s^{-1}) in HOAc at 25.0 °C.

acids can be attributed to two factors. First, 4-Me-NHPI has two carbonyl groups on the benzene ring which withdraw more electron density, making hydrogen abstraction from the methyl group more difficult. Second, the BDE of the O−H group of 4-Me-NHPI is smaller than that of unsubstituted NHPI, which is reflected in the equilibrium constant of reaction 11 (see below). Therefore, it is reasonable that the rate constant of H-atom abstraction from 4-methyl group on 4-Me-NHPI by 4-Me-PINO$^•$ (k_H) is smaller than those from methyl group on *m*- or *p*-toluic acids by the unsubstituted PINO$^•$.

Hydrogen Atom Transfer Reaction. The combination of NHPI with $Co(OAc)_2$ catalyzes the autoxidation of hydrocarbons.[2] This feature is interpreted by the high H-atom abstraction ability of the PINO radical, and we found that quantum mechanical tunneling plays a role in the hydrogen abstraction.[5] We also proposed that the kinetic isotope effect would be maximum when the reaction is thermoneutral.[6] On the basis of this interpretation, we were interested in a pseudo self-exchange reaction between PINO$^•$ and substituted NHPI as shown in eq 11.

$$\text{PINO}^\bullet + \text{4-Me-NHPI} \underset{k_r}{\overset{k_f}{\rightleftarrows}} \text{NHPI} + \text{4-Me-PINO}^\bullet \quad (11)$$

Reaction 11 is nearly thermoneutral considering the difference in bond dissociation energies.[18] Although reaction 11 represents hydrogen atom transfer in a stoichiometric sense, there are two possible mechanisms for it: one is hydrogen atom transfer itself (or proton coupled electron transfer), and the other is stepwise transfer of an electron and a proton.[19] We measured rate constants for the reaction 11 with excess 4-Me-NHPI and NHPI in HOAc at 25 °C. Reaction 11 takes place quite rapidly, therefore hydrogen abstraction from the 4-Me group observed in self-decomposition of 4-Me-PINO$^•$ is negligible. The reaction was safely monitored by the growth of the absorbance at 397 nm, which is λ_{max} for 4-Me-PINO$^•$. The rate constant for the reaction 11 is given by eq 12 in the presence of excess 4-Me-NHPI and NHPI.

$$k_{obs} = k_f[\text{4-Me-NHPI}] + k_r[\text{NHPI}] \quad (12)$$

This equation can be rearranged to the following form:

$$\frac{k_{obs}}{[\text{NHPI}]} = \frac{k_f[\text{4-Me-PINO}^\bullet]}{[\text{NHPI}]} + k_r \quad (13)$$

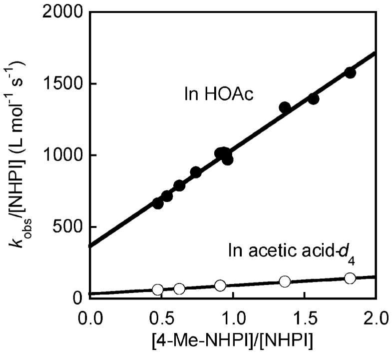

FIGURE 2. Plot of the kinetic data according to eq 13 to evaluate k_f and k_r of reaction 11.

From a series of experiments with varying concentrations (Figure 2), each rate constant was obtained at 25.0 °C: $k_f = 677 \pm 24$ L mol^{-1} s^{-1} and $k_r = 354 \pm 23$ L mol^{-1} s^{-1}, which means that the equilibrium constant, K_{eq} ($= k_f/k_r$), for reaction 11 is 1.91 ± 0.10 at 25 °C. Therefore, from eq 14, the O−H bond dissociation energy of 4-Me-NHPI is found to be1.6 kJ mol^{-1} lower than that of NHPI.[18]

$$\text{BDE (X-NHPI)} = \text{BDE(NHPI)} - RT \ln K_{eq} \quad (14)$$

We also measured rate constants for the following pseudo-self-exchange reaction:

$$\text{4-F-PINO}^\bullet + \text{NHPI} \underset{k_r}{\overset{k_f}{\rightleftarrows}} \text{4-F-NHPI} + \text{PINO}^\bullet \quad (15)$$

The rate constants k_f and k_r for reaction 15 are 651 and 241 L mol^{-1} s^{-1} in HOAc at 25.0 °C, which means the equilibrium constant of the reaction 16 is 2.70. Therefore, the O−H bond dissociation energy of 4-F-PINO$^•$ is calculated to be 2.46 kJ mol^{-1} higher than that of NHPI. Thus, it is confirmed that electron-withdrawing groups on NHPI strengthen the O−H bond and electron-donating groups weaken it.

For reaction 11, rate constants were also measured in acetic acid-d_4 to evaluate the KIE, noting the rapid exchange of protons (deuterons) between R_2NOH and acetic acid-d_4. The rate constants of the reaction 11 in acetic acid-d_4 are $k_f = 61.3 \pm 2.1$ L mol^{-1} s^{-1} and $k_r = 31.8 \pm 2.0$ L mol^{-1} s^{-1}. Therefore, the values of KIE for k_f and k_r are 11.0 and 11.1, respectively. This indicates that reaction 11 takes place through H-atom transfer, not electron transfer (Scheme 1). This conclusion is also supported by the finding that the rate constants for reaction 11 are not affected by addition of CF_3COOH (Table S1, Supporting Information).[20]

As described above, reaction 11 takes place through direct H-atom transfer, and the KIEs (11.0 and 11.1) of the rate constants in both directions are larger than the theoretical maximum value from ground-state energy differences (7.8).[12] In previous reports, quantum mechan-

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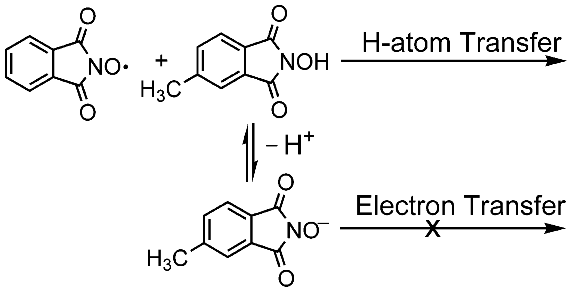
(18) Annunziatini, C.; Gerini, M. F.; Lanzalunga, O.; Lucarini, M. *J. Org. Chem.* **2004**, *69*, 3431−3438.

(19) Roth, J. P.; Lovell, S.; Mayer, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 5486-5498.

(20) We assumed that if the reaction 11 takes place through electron transfer via preequilibrium of proton dissociation, the rate constants would be affected by addition of strong acid; pK_a = 0.52 (CF_3COOH) and 4.76 (CH_3COOH).

SCHEME 1. Reaction Scheme for Pseudo-Self-Exchange Reaction of PINO• and 4-Me-NHPl



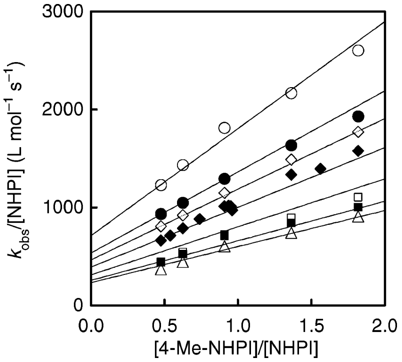


FIGURE 3. Comparison of experimental data with the calculated values (solid lines) according to eq 16 for H-atom transfer of the reaction 11 in HOAc at various temperatures: 308.45 K (○); 303.45 K (●); 301.05 K (◇); 298.15 K (◆); 294.45 K (□); 291.25 K (■); 289.75 K (△).

ical tunneling has been proposed to play an important role in PINO radical reactions,[5] such as those with *p*-xylene and toluene, for which remarkably small preexponential factors were found, log $A \approx 5-6$. This also implies that tunneling participates in the reactions. Therefore, we predicted that the reaction 11 also has a small preexponential factor (in other words, a large negative activation entropy). The rate constants for reaction 11 were measured at various temperatures, and were in turn analyzed by using the following equation with Scientist 2.0.[21]

$$k_{\text{obs}} = \frac{k_{\text{B}}T}{h}\exp\left(\frac{\Delta S_{\text{f,r}}^{\ddagger}}{R}\right)\exp\left(-\frac{\Delta H_{\text{f}}^{\ddagger}}{RT}\right)[\text{4-Me-NHPI}] + \frac{k_{\text{B}}T}{h}\exp\left(\frac{\Delta S_{\text{f,r}}^{\ddagger}}{R}\right)\exp\left(-\frac{\Delta H_{\text{r}}^{\ddagger}}{RT}\right)[\text{NHPI}] \quad (16)$$

In this treatment, we set the activation entropies for k_{f} and k_{r} equal to one another because each direction should have almost the same activation entropy considering its structural symmetry. As a result, the activation parameters obtained are $\Delta H_{\text{f}}^{\ddagger} = 40.8 \pm 1.0$ kJ mol^{-1}, $\Delta H_{\text{r}}^{\ddagger} = 41.9 \pm 1.0$ kJ mol^{-1}, $\Delta S_{\text{f,r}}^{\ddagger} = -55 \pm 3$ J K^{-1} mol^{-1}; an Arrhenius plot of the same data gave log $A = 9.5$. This value of log A along with the KIE indicates that tunneling occurs but not to the extent it does in certain other reactions of PINO•.[5,6] Using the obtained activation enthalpies and activation entropy, we compared the experimental data with the calculated values. The result is illustrated in Figure 3, in which the points are experimental data and each line comes from the calculated values.

TABLE 3. Rate Constants and Kinetic Isotope Effect for the Reaction of PINO Radicals with *p*-Xylene in HOAc at 25 °C

	p-xylene		
4-X-PINO•, X =	k_{H}/s^{-1}	k_{D}/s^{-1}	$k_{\text{H}}/k_{\text{D}}$
Cl	10.6 ± 0.07	0.426 ± 0.002	24.9
F	8.40 ± 0.18	0.338 ± 0.002	24.9
H[a]	5.95 ± 0.07	0.240 ± 0.001	24.8
CH_3	3.90 ± 0.04	0.166 ± 0.002	23.5

[a] Reference 5.

Hydrogen Atom Transfer between PINO• and NHPI. This study has shown that reaction 11 takes place through H-atom transfer with rate constants, $k_{\text{f}} = 677$ and $k_{\text{r}} = 354$ L mol^{-1} s^{-1}. Therefore, one estimate the rate constant of electron-exchange reaction between PINO• and NHPI as being near the average of these values, or ca. 500 L mol^{-1} s^{-1}.

$$\text{PINO}^{\bullet} + {}^{*}\text{NHPI} \xrightarrow{k_{\text{ex}}\,(=k_{\text{AA}})} \text{NHPI} + {}^{*}\text{PINO}^{\bullet} \quad (17)$$

A second approach to estimating k_{AA} is based on applying the Marcus cross relation to H-atom transfer reactions, as has been establlished.[19,22] There is enough uncertainty in BDE(NHPI) (364–375 kJ mol^{-1}),[3,6] however, as to make this approach unreliable.

Hydrogen Abstraction by PINO Radicals from *p*-Xylene. As described previously, the O–H bonds of substituted NHPI derivatives are strengthened by electron-withdrawing groups. Therefore, the H-atom abstraction ability of PINO• substituted by electron-withdrawing groups would be higher than those of PINO• substituted by electron-donating groups. To confirm this issue, we measured rate constants for H-atom abstraction by substituted PINO radicals from *p*-xylene and toluene. The obtained rate constants are shown in Table 3 and Table S2 (Supporting Information).

In both reactions, the reactivity of substituted PINO• follows the order 4-Me < 4-H < 4-F < 4-Cl, which corresponds to the order of the O–H bond dissociation energies. The first three BDEs are known, and the ordering of 4-Cl is inferred from the Hammett-based inductive effect of this substituent.

Alternatively, the acceleration of the rate constants by electron withdrawing groups might be explained by a polar effect at the transition state.

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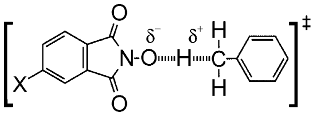
[21] Micro-Math Scientific Software, Inc., Salt Lake City, UT.



A correlation between redox potentials of the 4-substituted NHPI derivatives and σ_p Hammett constants has been reported.[23] We constructed plots against σ_p, and obtained the reaction constants, $\rho = 1.1$ for *p*-xylene and 1.8 for toluene, Figure S4a,b (Supporting Information).

We also evaluated the KIE for the reactions with *p*-xylene and toluene. It is noted that the values of KIE for the reaction in the series of the PINO radicals lie in the narrow range of 23.5−25.7. This finding further supports that quantum mechanical tunneling plays a role in the hydrogen abstraction of the PINO radicals. We have reported that H-atom abstraction reaction by PINO$^{\bullet}$ has a maximum with toluene (27.1) or benzaldehyde (27.5).[6] It is expected that a maximum value for H-atom abstraction reaction can be obtained when the reaction is symmetric.[24] Therefore, we expected that the maximum of KIE would shift in the reaction of 4-substituted NHPI derivatives which have different O−H BDEs. However, the difference of BDE of NHPI derivatives is not large enough to see the shift. Recently, Annunziatini et al. investigated that aerobic oxidation of benzyl alcohol by substituted NHPIs, and found that 3,6-$(CH_3O)_2$-NHPI has the largest KIE (19.5).[18] The O−H BDE of 3,6-$(CH_3O)_2$-NHPI is 4 kJ mol^{-1} smaller than that of NHPI because of the two electron donating methoxy groups. And it is well-known that the C−H BDE of benzyl alcohol is fairly low (340 kJ mol^{-1}). Therefore, it is understandable that the largest KIE was obtained with 3,6-$(CH_3O)_2$-NHPI which has the lowest O−H BDE in the series of Annunziatini's experiments, where the reaction with 3,6-$(CH_3O)_2$-NHPI is more symmetric than others with substituted NHPIs.

Further comments on tunneling are in order. In an earlier publication, the large KIE values were attributed to tunneling as the major or exclusive factor.[5,6] Actually, there is now cause to reassess that view. After allowance for a secondary KIE of 1.15 per D atom in going from sp^3 to sp^2 hybridization,[25] the primary KIE is reduced to 19.2 at 25 °C and only 5.23 at 55 °C, the latter being a normal isotope effect. On that basis, the tunneling effect is ca. 27% at 17 °C and 7.2% at 55 °C.

Acknowledgment. This research was supported by a grant from the National Science Foundation under Grant No. CHE-020409. Some experiments were conducted with the use of the facilities of the Ames Laboratory of the U.S. Department of Energy, which is operated by Iowa State University of Science and Technology under Contract No. W-7405-Eng-82.

Supporting Information Available: UV/vis spectra of the substituted PINO radical in HOAc and plots of kinetic data to illustrate agreement to selected mathematical forms and to evaluate numerical parameters. This material is available free of charge via the Internet at http://pubs.acs.org.

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