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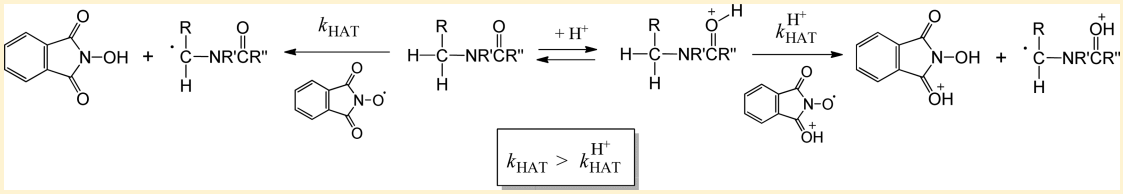
Kinetic Study of the Reaction of the Phthalimide-*N*-oxyl Radical with Amides: Structural and Medium Effects on the Hydrogen Atom Transfer Reactivity and Selectivity

Massimo Bietti,[‡] Veronica Forcina,[†] Osvaldo Lanzalunga,*[,†] Andrea Lapi,[†] Teo Martin,[†] Marco Mazzonna,[†] and Michela Salamone[‡]

[†]Dipartimento di Chimica, Sapienza Università di Roma and Istituto CNR di Metodologie Chimiche (IMC−CNR), Sezione Meccanismi di Reazione, c/o Dipartimento di Chimica, Sapienza Università di Roma, Piazzale Aldo Moro 5, I-00185 Rome, Italy

[‡]Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica 1, I-00133 Rome, Italy

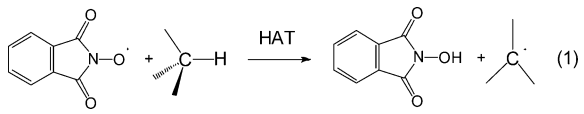
Supporting Information



ABSTRACT: A kinetic study of the hydrogen atom transfer (HAT) reactions from a series of secondary *N*-(4-X-benzyl)acetamides and tertiary amides to the phthalimide-*N*-oxyl radical (PINO) has been carried out. The results indicate that HAT is strongly influenced by structural and medium effects; in particular, the addition of Brønsted and Lewis acids determines a significant deactivation of C−H bonds α to the amide nitrogen of these substrates. Thus, by changing the reaction medium, it is possible to carefully control the regioselectivity of the aerobic oxidation of amides catalyzed by *N*-hydroxyphthalimide, widening the synthetic versatility of this process.

INTRODUCTION

The use of *N*-hydroxyphtalimide (NHPI) as a valuable catalyst in the aerobic oxidation of organic compounds has stimulated the interest of several research groups in recent years. NHPI has found application in synthetically useful oxidations of aliphatic and alkylaromatic hydrocarbons under moderate temperatures and O_2 pressures, as reported by Ishii and his group at the end of the last century.[1,2] Catalytic systems based on NHPI have also been developed for the oxidation of several classes of organic compounds, including alcohols, olefins, amides, amines, ethers, and aldehydes.[1,3] In all these processes, a key step is represented by a hydrogen atom transfer (HAT) reaction from the most reactive C−H bonds of the substrates to the phthalimide-*N*-oxyl radical (PINO) (eq 1).



(1)

The reactivity of PINO with a series of hydrogen atom donor substrates has been investigated in detail by kinetic studies that highlighted the importance of polar and enthalpic effects.[4−18] Among the reactions promoted by PINO, HAT from amides deserves special attention since it may represent a good model for the reactions of oxygen-centered radicals with peptides and proteins, processes of great importance in biological systems.[19] In addition, a large number of new synthetic procedures for C−H bond functionalization of amides are based on HAT to oxygen-centered radicals such as alkoxyl radicals.[20]

Product analysis of the aerobic oxidation of *N*-alkylamides catalyzed by *N*-hydroxyphtalimide has been previously reported by the group of Minisci.[8] A mixture of carbonyl derivatives (aldehydes, ketones, carboxylic acids, and imides) was formed with a product distribution that was found to depend on the structure of the amide and the reaction conditions. Imide products were accompanied by selective formation of benzaldehydes in the oxidation of secondary *N*-benzylamides and of carboxylic acids in the oxidation of nonbenzylic amides. This observation was a clear indication that significant polar effects are operative in the HAT process. As shown in Scheme 1, the amide nitrogen activates the C−H bonds in the α-position by stabilizing the partial positive charge that develops in the transition state (TS) for HAT.[21]

In this context, it is rather surprising that a detailed kinetic analysis of HAT from amide substrates to PINO, of fundamental importance in order to optimize the reaction conditions for potential synthetic applications of this process, was never performed.[4a] Along this line, to provide a comprehensive analysis of the structural and medium effects on the reactivity of PINO with *N*-alkylamides, we report herein a kinetic study on the reactions of PINO with a series of *N*-(4-X-benzyl)acetamides

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Scheme 1

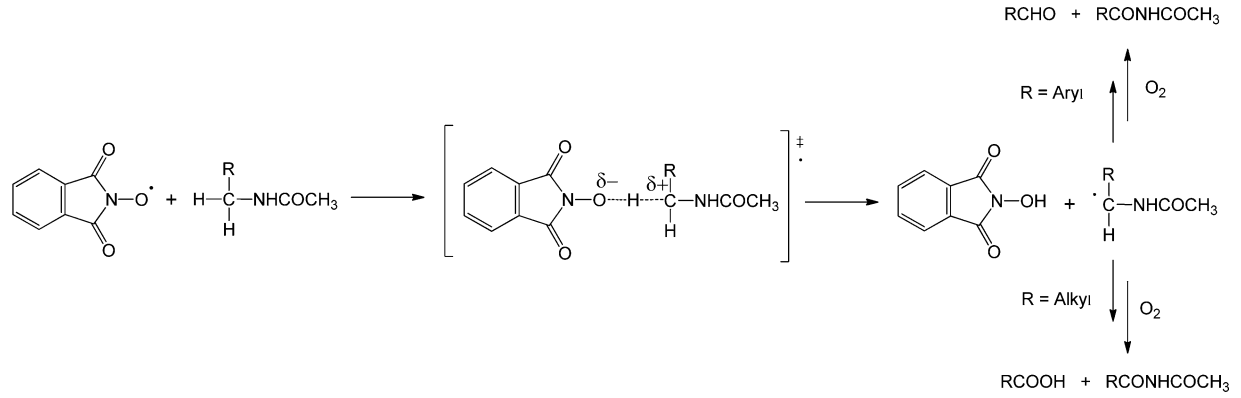
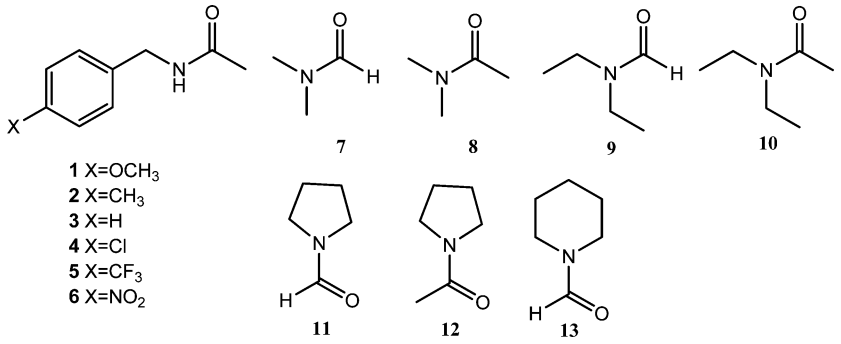


Chart 1



and of tertiary amides, the structures of which are displayed in Chart 1.

HAT from these substrates was also investigated in the presence of two Brønsted acids of different strength ($HClO_4$ and CF_3CO_2H) and of the Lewis acid $Mg(ClO_4)_2$. All additives were employed at 0.1 M concentration. The results obtained will enable us to compare the reactivity toward amide C–H bonds of short-lived aminoxyl radicals like PINO with that observed previously for the corresponding reactions of another important class of oxygen radicals, i.e., alkoxyl radicals.[22]

RESULTS

Kinetic studies were carried out by UV–vis spectrophotometry generating PINO by oxidation of NHPI with cerium(IV) ammonium nitrate in CH_3CN[23] in the absence or in the presence of acid additives at T = 25 °C. The decay of PINO, recorded at the absorption maximum (380 nm),[4a] occurred by a second-order process[1d] and was accelerated by the addition of the amide substrates. Using an excess of amide (at least 10-fold) to attain pseudo-first-order conditions, clean first-order decays were observed and excellent linear fits were obtained by plotting the pseudo-first-order rate constants (k_{obs}) as a function of the concentration of added amide. From the slope of these plots, the second-order rate constants for HAT (k_H) were determined, as shown in Figure 1 for the reactions of PINO with *N*-(4-X-benzyl)acetamides.

Additional plots for HAT from *N*-(4-X-benzyl)acetamides and tertiary amides to PINO are displayed in Figures S1–S29 of the Supporting Information (SI). The k_H values are collected in Table 1 for the reactions of PINO with *N*-(4-X-benzyl)-acetamides and in Table 2 for the reactions of PINO with tertiary amides.

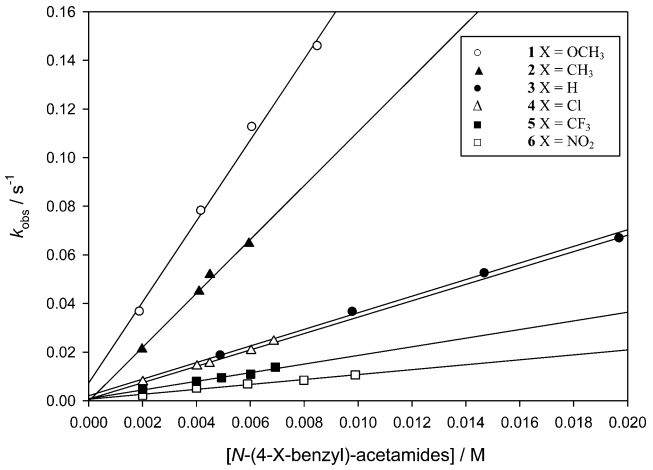


Figure 1. Dependence of the observed rate constants (k_{obs}) against [substrate] for the reactions of PINO with *N*-(4-X-benzyl)acetamides (**1**–**6**) measured in CH_3CN solution at T = 25 °C by following the decay of PINO at 380 nm.

DISCUSSION

Reactions of *N*-(4-X-benzyl)acetamides. In the reactions of *N*-(4-X-benzyl)acetamides (X = OCH_3, CH_3, H, Cl, CF_3, NO_2) with PINO, HAT might involve either the benzylic or the acetyl C–H bonds or eventually the C–H bonds in the para substituent group. HAT from the benzylic position (Scheme 2) is favored by both enthalpic (lower C–H bond dissociation energy value) and polar effects (greater stabilization of the partial positive charge that develops in the HAT TS).

Selective HAT from the benzylic position of these substrates is confirmed by the much higher rate constant measured for the

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Table 1. Second-Order Rate Constants (k_H) for Hydrogen Atom Transfer from *N*-(4-X-Benzyl)acetamides (1−6) to PINO Measured in CH_3CN at T = 25 °C, in the Absence and in the Presence of Acid Additives

	k_H ($M^{-1}s^{-1}$) [a]	
	CH_3CN	CH_3CN + acid (0.1 M)
1 X = OCH_3	18	1.9[c]
2 X = CH_3	11	0.69[c]
3 X = H	3.4	0.11[c]
	0.42 [b]	1.0 [d]
		1.3 [e]
4 X = Cl	3.4	0.11[c]
5 X = CF_3	1.8	0.055[c]
6 X = NO_2	1.0	0.06[c]

[a]Average of at least three independent determinations. Error ±5%. [b]Deuterated substrate $C_6H_5CD_2NHCOCH_3$. [c]$HClO_4$. [d]CF_3CO_2H. [e]In the presence of 0.1 M $Mg(ClO_4)_2$.

Table 2. Second-Order Rate Constants (k_H) for Hydrogen Atom Transfer from Tertiary Amides (7−13) to PINO Measured in CH_3CN at T = 25 °C, in the Absence and in the Presence of Acid Additives (0.1 M)

Amide	k_H ($M^{-1}s^{-1}$) [a]		
	No acid	CF_3CO_2H	$HClO_4$
7	0.14	$< 3\times10^{-3}$	$< 3\times10^{-3}$
	DMF-d_1 0.12		
	DMF-d_6 0.02		
	DMF-d_7 0.0034		
8	0.51	0.15	$< 3\times10^{-3}$
9	0.19	0.052	$< 3\times10^{-3}$
10	0.43	0.06	$< 3\times10^{-3}$
11	1.9	0.15	0.018
	0.048[b]		
12	5.9	0.18	0.047
13	0.44	0.084	$< 3\times10^{-3}$

[a]Average of at least three independent determinations. Error ±5%. [b]In the presence of 0.1 M $Mg(ClO_4)_2$.

reaction of PINO with *N*-benzylacetamide (**3**) (3.4 M^{-1} s^{-1}) as compared to that determined in the corresponding reaction with acetanilide (0.028 M^{-1} s^{-1}), where HAT necessarily involves the C−H bonds of the methyl group (Scheme 3).

Moreover, the significant kinetic isotope effect determined from the ratio of the rate constants for $C_6H_5CH_2NHCOCH_3$ (**3**) and $C_6H_5CD_2NHCOCH_3$ (k_H/k_D = 8.1) is also consistent with a HAT process that selectively occurs from the benzylic

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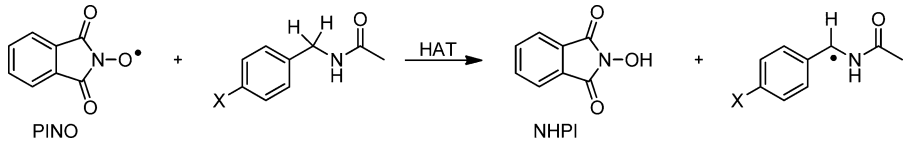
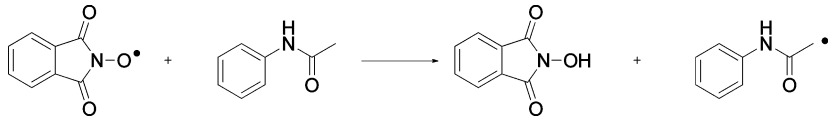
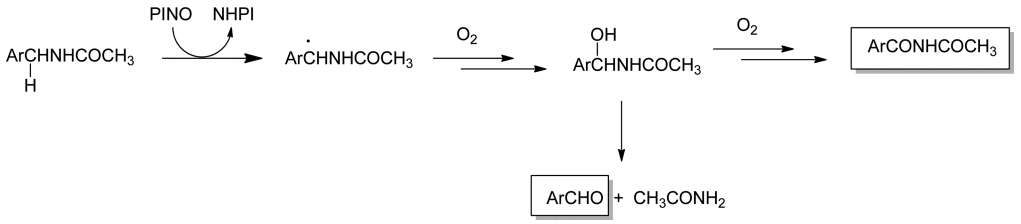
Scheme 2



Scheme 3



Scheme 4



C−H bonds. It has to be noted that k_H/k_D values >7 have been previously observed in HAT from several hydrogen atom donors promoted by PINO[9,10,12,13] and other short-lived aminoxyl radicals like benzotriazole-*N*-oxyl radical (BTNO)[23b,c] and rationalized on the basis of the contribution from quantum mechanical tunneling.

Finally, selective HAT from the benzylic position is in accordance with product analysis results in the aerobic oxidation of *N*-(4-X-benzyl)acetamides with the NHPI/Co(II)/O_2 system previously reported by Minisci.[8] The main reaction products, imides and benzaldehydes, were both proposed to derive from the initially formed α-amido benzylic radical according to the reaction sequence described in Scheme 4.

Comparison between the k_H value measured for reaction of PINO with *N*-(4-CH_3-benzyl)acetamide (**2**) (k_H = 11 M^{-1} s^{-1}) and that measured under identical experimental conditions for the corresponding reaction with *p*-xylene (k_H = 3.4 M^{-1} s^{-1}; see the SI) clearly indicates that HAT from **2** also involves the *p*-CH_3 group. By taking into account the statistic factor, we can reasonably estimate that with this substrate HAT from this position accounts for ≤15% of the overall reactivity.

As expected for a HAT process promoted by an electrophilic radical and in accordance with the enthalpic and polar effects discussed above, the k_H values increase with the electron-donating strength of the *p*-X substituent. When the $\log(k_H^X/k_H^H)$ values for the reactions of PINO with *N*-(4-X-benzyl)-acetamides were plotted against the Okamoto−Brown substituent constants σ^+, a good Hammett-type correlation was obtained (Figure 2, r^2 = 0.97).[24] The negative ρ value obtained (−0.8) and the observation that a better linearity was found with the σ^+ rather than the σ constants are in support of a reaction that is accompanied by the development of a partial positive charge on the benzylic position, in direct conjugation with the para-substituent, in the HAT transition state (Figure 3a). In addition, the ρ value compares well with those determined in HAT processes from benzylic substrates to PINO[9,12−14,18] and in closely related studies of HAT from *N*-benzylacetamides to the aminoxyl radical BTNO (ρ = −0.65)[23] and to alkylperoxy-λ^3-iodane (ρ = −0.56).[25]

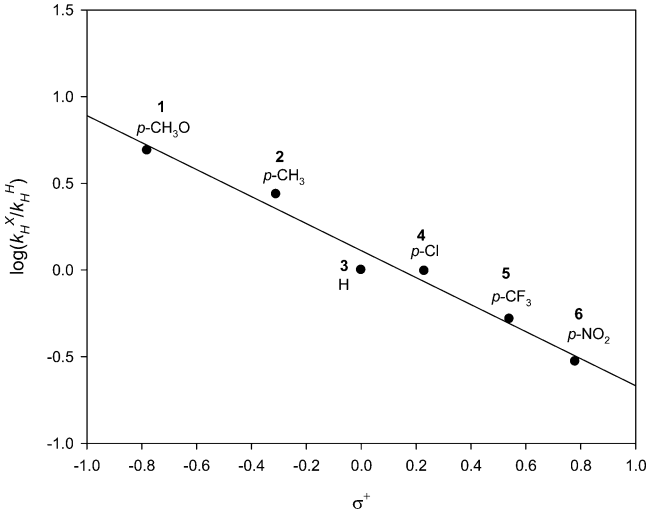


Figure 2. Hammett plot for the reaction of *N*-(4-X-benzyl)acetamides **1**−**6** with PINO in CH_3CN at 25 °C.[23]

In order to investigate the effect of acid additives on HAT from *N*-(4-X-benzyl)acetamides to PINO, kinetic studies have been carried out in the presence of 0.1 M $HClO_4$. The strength of this acid (pK_a = 2.0 in CH_3CN)[26] is sufficient to ensure the quantitative protonation of the amide substrate (e.g., for acetamide, pK_a = 6.0 in CH_3CN).[26]

Oxygen protonation in the amides should lead to a deactivation of the C−H bonds by both enthalpic and polar effects, as already observed for the effect of alkali and alkaline earth metal ions on the HAT processes promoted by alkoxyl radicals.[22d] This interaction increases the extent of positive charge at nitrogen, decreasing the electron density in proximity to the incipient carbon radical, leading to a destabilization of the transition state (Figure 3b).

For the same reason, protonation of PINO will lead to the radical cation $PINOH^{+\bullet}$ characterized by an increased electrophilicity with an activating effect on HAT as a consequence of the destabilization of the charge-separated resonance structure

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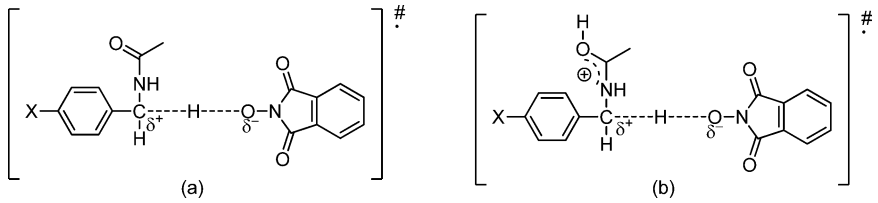


Figure 3. Transition state for HAT from amides to PINO (a) in the absence and (b) in the presence of protic acid.

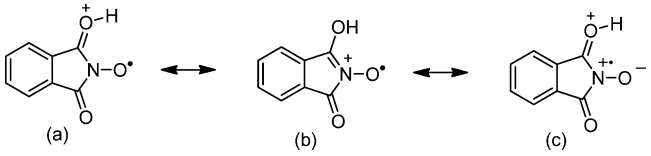


Figure 4. Resonance structures of the radical cation $PINOH^{+\bullet}$.

shown in Figure 4c. An activating effect was indeed observed in the presence of electron-withdrawing aryl substituents;[3d,13,27] moreover, we observed a slight increase of the rate constant for HAT from ethylbenzene to PINO (from 1.9 to 3.5 M^{-1} s^{-1}) and from *p*-xylene to PINO (from 3.4 to 4.1 M^{-1} s^{-1}) by addition of 0.1 M $HClO_4$ in CH_3CN (see Figures S30−S33 in the SI).[28]

From the k_H values reported in Table 1, it can be immediately noted that the deactivating effect due to the protonation of the amide substrate prevails over the activating effect on the aminoxyl radical. The k_H values measured for HAT from *N*-(4-X-benzyl)acetamides to PINO in the presence of 0.1 M $HClO_4$ are at least 1 order of magnitude lower than those observed in the absence of added acid. HAT from *N*-benzylacetamide (**3**) to PINO has also been investigated in the presence of CF_3CO_2H, a much weaker Brønsted acid than $HClO_4$ (pK_a = 12.6 in CH_3CN),[26] and of the Lewis acid $Mg(ClO_4)_2$, both at 0.1 M concentration. As compared to $HClO_4$ (for which k_H = 0.11 M^{-1} s^{-1}), a smaller extent of deactivation was observed in the presence of CF_3CO_2H, with a k_H value that decreased from 3.4 M^{-1} s^{-1} in CH_3CN to 1.0 M^{-1} s^{-1} after addition of 0.1 M CF_3CO_2H. This behavior reflects the partial protonation of the amide by this weaker acid. Concerning the addition of $Mg(ClO_4)_2$, recent studies reported the deactivating effect of Lewis acids on HAT from the C−H bonds of ethers, amines, and amides to alkoxyl radicals.[22,31] With amide substrates it was proposed that the interaction of the metal ion with the oxygen atom increases the extent of positive charge at nitrogen and the electron deficiency of the C−H bonds of these substrates, leading to their deactivation toward HAT. In the presence of 0.1 M $MgClO_4$, a k_H value of 1.3 M^{-1} s^{-1} was measured for HAT from *N*-benzylacetamide (**3**) to PINO, with an effect that is comparable to that observed in the presence of the relatively weak acid CF_3CO_2H.[32]

It is interesting to note that the kinetic effect determined by $HClO_4$ is more pronounced for the substrates containing electron-withdrawing (EW) substituents (**4**, X = Cl; **5**, X = CF_3; **6**, X = NO_2) as compared to those containing electron-donating (ED) substituents (**1**, X = OCH_3; **2**, X = CH_3). This difference can be easily visualized in the $\log(k_H^X/k_H^H)$ vs σ^+ Hammett plot, for the reactions of PINO with *N*-(4-X-benzyl)acetamides carried out in the presence of 0.1 M $HClO_4$ (Figure 5).

For the amides bearing EW substituents, a good linearity is observed with a ρ value (−0.43) less negative than that determined in the absence of $HClO_4$. A lower HAT selectivity

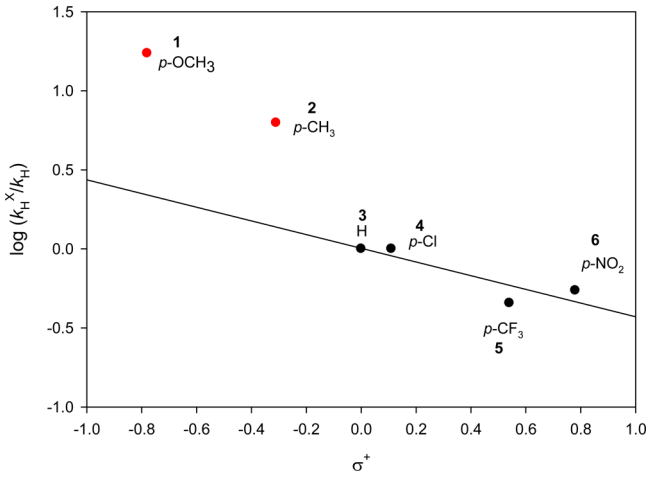
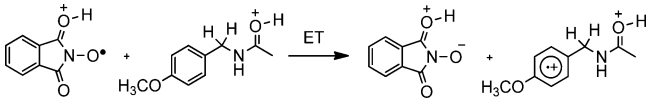


Figure 5. Hammett plot for the reaction of *N*-(4-X-benzyl)acetamides with PINO in CH_3CN in the presence of 0.1 M $HClO_4$ at 25 °C.

is not so surprising in view of the minor contribution of polar effects when the amide substrate is protonated (see Figure 3b). The positive deviation from the correlation line of *N*-(4-CH_3-benzyl)acetamide (**2**) might be explained on the basis of a change in regioselectivity of the HAT process from the benzylic C−H bonds α to the amide group to the *p*-methyl group.[33] On the other hand, as a possible explanation for the high reactivity observed for *N*-(4-CH_3O-benzyl)acetamide (**1**) in the reaction with PINO, we propose a mechanistic changeover from HAT to an electron transfer (ET) process, as shown in Scheme 5.

Scheme 5



Electron transfer reactions promoted by PINO have been previously reported with easily oxidizable substrates.[34] In the presence of $HClO_4$, a significant increase in the reduction potential of PINO (0.69 V vs SCE in CH_3CN)[34a] can be expected, making the transfer of an electron from the anisole ring of the substrate energetically feasible. The ET process from electron-rich alkyl aromatics to the highly electrophilic $PINOH^{+\bullet}$ is also strongly supported by the significant increase of the rate constant, from 4.2 to 2.0 × 10^2 M^{-1} s^{-1}, for HAT from *p*-methoxytoluene to PINO observed in the presence of $HClO_4$ (0.1 M) (see the SI).

Reactions of Tertiary Amides. In order to analyze the role of structural effects on HAT, we have investigated the reaction of PINO with a series of tertiary amides, the structures of which are displayed in Chart 1 and Table 2. In the absence of acid additives, HAT from *N*,*N*-dimethylacetamide (**8**) involves the C−H bonds of the *N*-methyl groups (Scheme 6), which,

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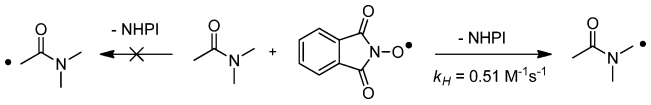
Scheme 6



as discussed previously, are activated by both enthalpic and polar effects. HAT from the acetyl methyl group is disfavored by the ca. 5 kcal mol^{-1} higher bond dissociation energy (BDE) of these bonds as compared to those of the *N*-methyl groups.[22a] This selectivity is confirmed by the very low reactivity observed for acetamide, for which HAT should necessarily involve the acetyl C−H bonds.[35] Because of the faster self-decay of PINO, the k_H value was too low to be measured and only an upper limit could be given ($k_H < 3 \times 10^{-3}$ M^{-1} s^{-1}).

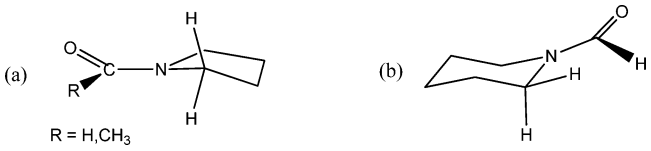
HAT from *N*,*N*-dimethylformamide (**7**) might involve either the C−H bonds α to the nitrogen or the formyl C−H bond. In a related study on HAT reactions promoted by alkoxyl radicals, it was reported that HAT can occur from both positions, with a regioselectivity that is strongly influenced by the reaction medium.[22c] In CH_3CN, kinetic isotope effect studies and theoretical calculations indicated that HAT from the formyl C−H bonds prevails over that from the C−H bonds that are α to nitrogen.[22a] The analysis of kinetic isotope effects in HAT from DMF, DMF-d_1, DMF-d_6, and DMF-d_7 promoted by PINO revealed that the k_H values for HAT from the C−H bonds α to nitrogen and the formyl C−H bond are the same within the error limit (0.02 M^{-1} s^{-1}; see details of calculations in the SI). This result is in perfect agreement with the similar C−H BDEs calculated using the composite CBS-QB3 approach (95.0, 94.7, and 94.8 kcal mol^{-1} for the H−CO, α-C−H (trans), and α-C−H (cis), respectively).[22a]

It is interesting to note that the k_H value for DMF (**7**) is significantly lower than that measured for *N*,*N*-dimethylacetamide (**8**), a result that can be rationalized on the basis of the lower C−H BDEs for the latter compound (92.5 and 94.7 kcal mol^{-1} for the α-C−H (trans) bonds calculated for **8** and **7**, respectively). With the more reactive and less selective cumyloxyl radical, similar k_H values were instead determined.[22a]

In the reaction with *N*,*N*-diethylformamide (**9**), the measured k_H value (0.19 M^{-1} s^{-1}) is higher than that obtained with *N*,*N*-dimethylformamide (**7**) (0.14 M^{-1} s^{-1}), indicating that with the former substrate HAT occurs preferentially from the ethyl α-C−H bonds. The different regioselectivity can be reasonably attributed to the ca. 2 kcal mol^{-1} lower BDE calculated for the α-amido C−H bonds in *N*,*N*-diethylformamide (**9**) as compared to those in *N*,*N*-dimethylformamide (**7**).[22b] The higher k_H value measured for HAT from *N*,*N*-diethylacetamide (**10**) (0.43 M^{-1} s^{-1}) can be explained on the basis of the above-mentioned decrease in BDEs of the C−H bonds that are α to nitrogen caused by the replacement of the formyl with an acetyl group.

The k_H values measured for HAT from the cyclic amides *N*-formylpyrrolidine (**11**) and *N*-acetylpyrrolidine (**12**) to PINO (k_H = 1.9 and 5.9 M^{-1} s^{-1}, respectively) were much higher (ca. 10-fold) than those measured for HAT from structurally comparable acyclic substrates *N*,*N*-diethylformamide (**9**) and *N*,*N*-diethylacetamide (**10**). This result is in accordance with those observed in HAT reactions from cyclic amides promoted by other radical species[22b,23c] and reflects the operation of stereoelectronic effects. In *N*-formylpyrrolidine (**11**) and *N*-acetylpyrrolidine (**12**), optimal overlap between the ring α-C-H bonds and the amide π-system can be achieved (Scheme 7a),

Scheme 7



resulting in a weakening of these bonds and in a more efficient stabilization of the intervening carbon radical formed following HAT. In the acyclic *N*,*N*-diethylformamide (**9**) and *N*,*N*-diethylacetamide (**10**), instead, a similar conformation of the α-C−H bond is disfavored by the free rotation around the N−C bonds resulting in significantly lower k_H values.

On the same line, the lower reactivity of *N*-formylpiperidine (**13**) (k_H = 0.44 M^{-1} s^{-1}) as compared to *N*-formylpyrrolidine (**11**) can be also explained with the same argument, since the α-C-H bonds cannot be collinear with the amide π-system due to geometrical restrictions imposed by the six-membered ring (Scheme 7b).

A decrease in k_H following addition of Brønsted and Lewis acids is confirmed for all the tertiary amides investigated. In the presence of 0.1 M $HClO_4$, a k_H value could be measured only for the most reactive *N*-formylpyrrolidine (**11**) and *N*-acetylpyrrolidine (**12**), where a lowering of more than 2 orders of magnitude was observed. For the other amides, the decrease in reactivity was such that HAT occurred in competition with the self-decay of PINO and only an upper limit for the k_H values could be obtained (<3 × 10^{-3} M^{-1} s^{-1}). With the weaker trifluoroacetic acid, the k_H values could be determined for most of the tertiary amides, and a 3−30-fold decrease in k_H was observed. The larger decrease in k_H found for *N*-formylpyrrolidine (**11**) can be explained in terms of a reduced importance of the stereoelectronic effects occurring when the amide group is protonated. For the same substrate in the presence of 0.1 M $Mg(ClO_4)_2$, the k_H value was significantly lower than that observed in 0.1 M CF_3COOH, a result that might be interpreted with an even minor contribution of stereoelectronic effects when the amide is coordinated to the Lewis acid.

In conclusion, the results reported in this study clearly indicate that HAT from amides to PINO is strongly influenced by structural and medium effects. The effect of acid additives is similar to those observed in related HAT processes from amides to alkoxyl radicals and lead to a strong deactivation of C−H bonds of these substrates. These results suggest that such deactivating effects might be exploited to control the C−H functionalization selectivity in the aerobic oxidation of amides, an aspect that is currently under investigation in our laboratories.

EXPERIMENTAL SECTION

Materials. Acetonitrile (HPLC grade), *N*-hydroxyphthalimide, cerium(IV) ammonium nitrate $(NH_4)_2Ce(NO_3)_6$, $Mg(ClO_4)_2$, CF_3CO_2H, and $HClO_4$ were commercially available and used as received. *N*,*N*-Dimethylformamide (**7**), *N*,*N*-dimethylacetamide (**8**), *N*,*N*-dimethylformamide-d_1, *N*,*N*-dimethylformamide-d_6, *N*,*N*-dimethylformamide-d_7, *N*,*N*-diethylformamide (**9**), *N*,*N*-diethylacetamide (**10**), *N*-formylpyrrolidine (**11**), *N*-formylpiperidine (**12**), acetanilide, acetamide, ethylbenzene, *p*-xylene, and *p*-methoxytoluene were commercially available at their highest purity and used as received. *N*-Acetylpyrrolidine and *N*-(4-X-benzyl)acetamides (**1**−**6**) were prepared following procedures reported in the literature.[22b,23d]

Kinetic Studies. PINO was generated by oxidation of NHPI (1 mM) with cerium(IV) ammonium nitrate (CAN, 0.5 mM) in CH_3CN at 25 °C in the absence of acid additives or in the presence of $HClO_4$ (0.1 M), CF_3CO_2H (0.1 M), or $Mg(ClO_4)_2$ (0.1 M). After the

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J. Org. Chem. 2016, 81, 11924−11931

generation of PINO, an excess of substrate was added in order to operate under pseudo-first-order conditions (final concentration 1.8−300 mM), and the absorbance change was monitored at 380 nm. For all the substrates investigated, each kinetic trace obeyed a first-order kinetic. Second-order rate constants were obtained from the slopes of plots of the observed rate constants k_{obs} vs substrate concentration. Rate constants are reported as an average of at least three independent determinations with an error ±5%.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02482.

Instrumentation; mathematical treatment of kinetic data for the HAT process from DMF, DMF-d_1, DMF-d_6, and DMF-d_7 to PINO in CH_3CN; and plots of k_{obs} vs [substrate] for the reactions of PINO with *N*-(4-X-benzyl)acetamides, tertiary amides, acetanilide, and alkyl aromatics (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: osvaldo.lanzalunga@uniroma1.it.

ORCID

Massimo Bietti: 0000-0001-5880-7614

Osvaldo Lanzalunga: 0000-0002-0532-1888

Notes

The authors declare no competing financial interest.

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(33) On the basis of the results of product studies on the reaction of PINO with *p*-xylene (ref 9), where formation of the adduct between the *p*-methylbenzyl radical and PINO was observed ($CH_3C_6H_4CH_2$−PINO), an analogous product can be expected following HAT from the *p*-methyl group of *N*-(4-methylbenzyl)acetamide to PINO, namely, the adduct of the benzylic radical thus formed with PINO ($CH_3CONHCH_2C_6H_4CH_2$−PINO).

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