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Promoted by the Quinolinimide-*N*-Oxyl Radical.

A Kinetic and Theoretical Study

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ABSTRACT: A kinetic study of the hydrogen atom transfer (HAT) reactions from a series of organic compounds to the quinolinimide-*N*-oxyl radical (QINO) was carried out in CH_3CN. The HAT rate constants are significantly higher than those observed with the phthalimide-*N*-oxyl radical (PINO) as a result of enthalpic and polar effects due to the presence of the *N*-heteroaromatic ring in

QINO. The relevance of polar effects is supported by theoretical calculations carried out for the reactions of the two *N*-oxyl radicals with toluene which indicate that the HAT process is characterized by a significant degree of charge transfer enabled by the π-stacking that occurs between the toluene and the *N*-oxyl aromatic rings in the transition state structures. An increase of the HAT reactivity of QINO was observed in the presence of HClO$_4$ 0.15 M and Mg(ClO$_4$)$_2$ 0.15 M due to the protonation or complexation with the Lewis acid of the pyridine nitrogen that leads to a further decrease of the electron density in the *N*-oxyl radical. These results fully support the use of *N*-hydroxyquinolinimide (NHQI) as a convenient substitute of *N*-hydroxyphthalimide (NHPI) in the catalytic aerobic oxidations of aliphatic hydrocarbons characterized by relatively high C-H bond dissociation energies.

Introduction

The use of *N*-hydroxyphthalimide (NHPI) as catalyst in the aerobic oxidative functionalization of hydrocarbon has attracted a great attention in recent years. In the presence of metal and nonmetal co-catalysts, the NHPI/O$_2$ system was found to efficiently catalyze the introduction of oxygenated groups in aliphatic and alkylaromatic hydrocarbons.[1]

The key role played in the catalytic cycle by the hydrogen atom transfer from the organic substrate to the phthalimide-*N*-oxyl radical (PINO) (HAT process, Scheme 1) has stimulated several kinetic studies aimed at obtaining quantitative information on the reactivity of PINO and other structurally related short-lived *N*-oxyl radicals towards a variety of C-H bonds.[2,3]
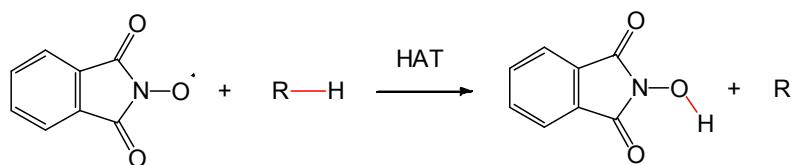

Scheme 1

The HAT reactivity of short-lived *N*-oxyl radicals is strongly dependent on enthalpic effects based on the difference between the O-H bond dissociation energy (BDE) in the *N*-hydroxy derivative and the C-H BDE of the substrates (eq 1). In this respect the high reactivity of PINO is associated with relatively high NO-H BDE in NHPI (87 kcal/mol).[4]

In addition to enthalpic effects, polar effects also play an important role in the HAT reactivity of *N*-oxyl radicals.[6] The HAT transition state (TS) structure is characterized by a partial degree of charge transfer from the substrate to the *N*-oxyl radical (Figure 1). The polar contribution is clearly dependent on the ability of the substrate and the *N*-oxyl radical to stabilize, respectively, the positive and negative charges developing in the transition state (TS).
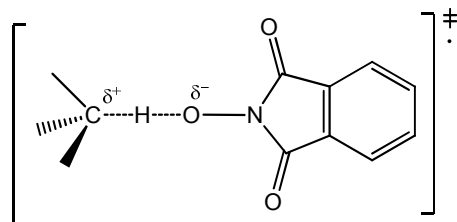
Figure 1. Polar transition state in the HAT process promoted by PINO

On the basis of enthalpic considerations, an increase in the HAT reactivity of *N*-oxyl radicals can be established by an increase of BDE_{NO-H} values of the corresponding *N*-hydroxy derivatives. In aryl substituted *N*-hydroxyphthalimides and other aromatic hydroxylamines an increase of BDE_{NO-H} values is observed with electron withdrawing aryl substituents which destabilize the resonance structure with charge separation shown in Figure 2.[7]
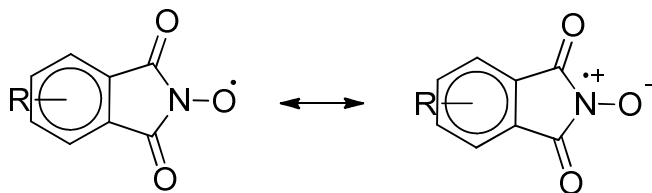
Figure 2. Resonance structures of aryl substituted PINO radicals

Electron withdrawing substituents are also able to increase the reactivity of the *N*-oxyl radical through polar effects on the HAT TS structure as a result of enhanced stabilization of the partial negative charge that develops on the *N*-oxyl radical at the TS.[8] The enhancement of HAT reactivity exerted by electron withdrawing substituents on *N*-oxyl radicals has been reported in several kinetic and product studies of the reaction of aryl substituted PINO and benzotriazole-*N*-oxyl radical with alkylaromatics and benzylic alcohols.[7,9]

The decrease of the PINO electron density can also be affected by replacement of the phenyl with an electron withdrawing *N*-heteroaromatic ring (*N*-hydroxyquinolinimide, NHQI, Figure 3). The corresponding *N*-oxyl radical (QINO) should be more reactive than PINO in HAT processes and therefore NHQI may serve as a better catalyst than NHPI in the oxidations of organic compounds using molecular oxygen as terminal oxidant. In this connection, Xia et al. showed that the catalytic activity of NHQI in the aerobic oxidation of toluene is significantly higher than that of NHPI either in the absence or in the presence of a metal cocatalysts.[10] More recently it was reported that NHQI, in combination with 4-carboxyl-*N*-hydroxyphthalimide, showed excellent activity in the aerobic oxidation of ethylbenzene.[11]
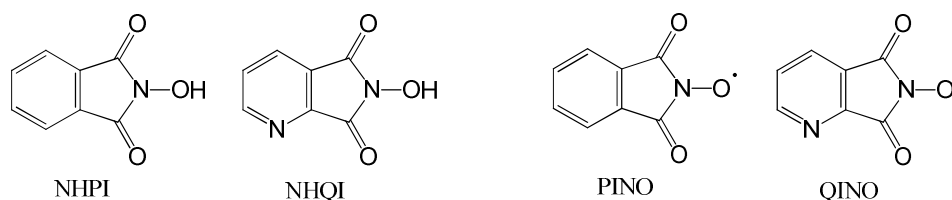
Figure 3. Structures of *N*-hydroxyphthalimide (NHPI), *N*-hydroxyquinolinimide (NHQI), phthalimide-*N*-oxyl radical (PINO) and quinolinimide *N*-oxyl radical (QINO)

In this study we report the ultraviolet-visible (UV-vis) and electron paramagnetic resonance (EPR) spectroscopic characterization of QINO and a kinetic investigation of the HAT reactivity of

QINO with a series of organic substrates including aliphatic hydrocarbons, alkylaromatics, alcohols, ethers, aldehydes and amides. The results were compared with those found in the HAT processes promoted by PINO. Theoretical calculations using a density-functional theory (DFT) based technique was carried out for the HAT reactions of PINO and QINO with toluene, selected for the industrial relevance of the HAT from alkylaromatics to *N*-oxyl radicals,[1] in order to gain an insight into the energetics of the HAT process involving these species. Since an increase of the QINO reactivity in HAT process may result from the protonation or complexation with metal cations of the heteroaromatic nitrogen, kinetic studies have been also investigated in the presence of Brønsted and Lewis acids ($HClO_4$ and $Mg(ClO_4)_2$) employed at 0.15 M concentration.

Results

Generation and characterization of QINO

The QINO radical was generated in a quartz cuvette by adding a 0.5 M solution of cerium(IV) ammonium nitrate in acetonitrile to a 1.0 M solution of NHQI at 25 °C, after which the UV-vis spectrum was obtained. This method was used previously to characterize spectroscopically PINO and other transient *N*-oxyl radicals (Figure 4).[3,12]
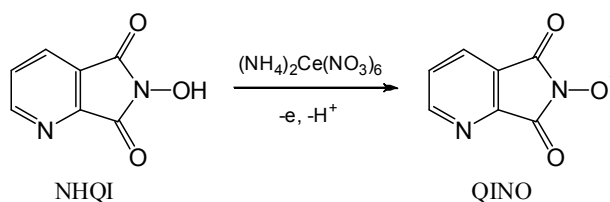
Figure 4. Generation of QINO by oxidation of NHQI with cerium(IV) ammonium nitrate

The UV-vis spectrum so-obtained has an absorption band centred at 380-390 nm. This band overlaps with the absorbance region of cerium salts (see Figure S1 in the SI). Better UV-vis spectroscopic characterization of QINO was obtained in a laser flash photolysis (LFP) experiment as described in Scheme 2.[13,14] Cumyloxyl radical (CumO•), generated by LFP at 355 nm of a 1 M

solution of dicumyl peroxide in N_2-saturated acetonitrile at 25 °C, abstracts a hydrogen atom from NHQI (5 nM) yielding QINO (eq 2 in Scheme 2).[15] This hydrogen atom abstraction reaction occurs in competition with the β-scission of CumO[•] which leads to the formation of acetophenone and a methyl radical (eq 3 in Scheme 2, $k_\beta \sim 6.5 \times 10^5$ s^{-1} in CH_3CN).[13] Figure 5 shows the time-resolved spectra obtained. The first-order decay of the cumyloxyl radical recorded at its maximum absorption wavelength (485 nm)[14] is accompanied by the build-up of the QINO absorption at 390 nm.
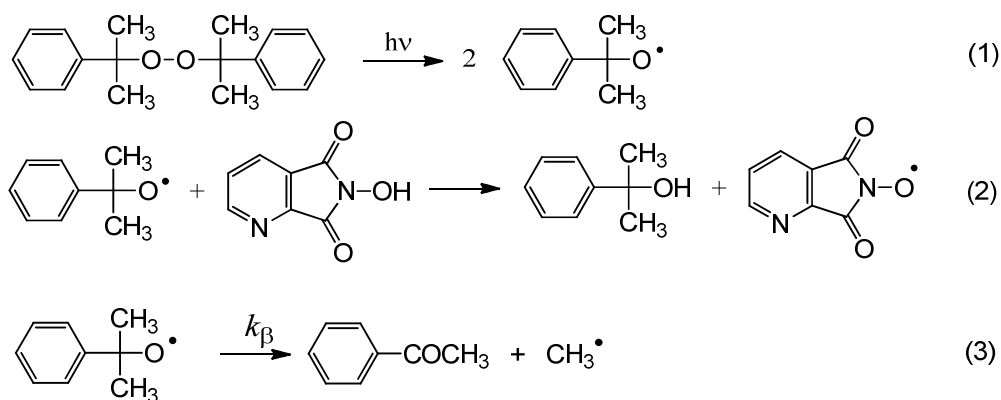
Scheme 2
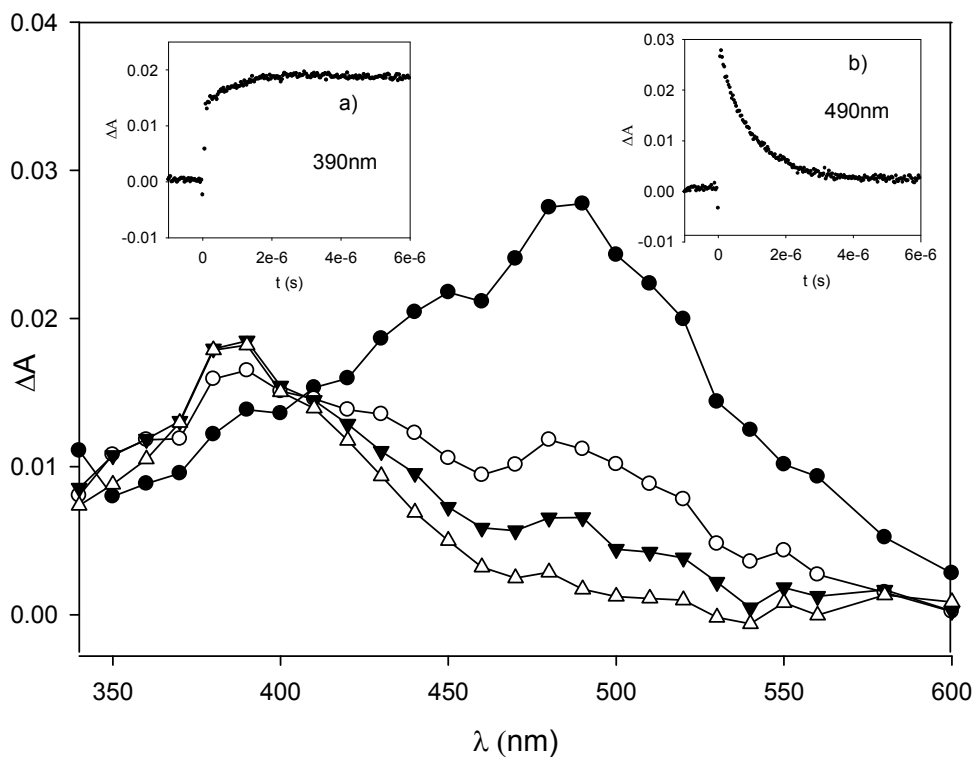
Figure 5. Transient absorption spectra measured 98 ns (●), 288 ns (○), 1 μs (▼) and 2 μs (Δ) after 355 nm laser excitation of a solution of dicumyl peroxide (1 M) and NHQI (5 mM) in CH$_3$CN at 25 °C under N$_2$. Inset **a**: first-order buildup of the QINO absorption at 390 nm. Inset **b**: first-order decay of the absorption of the cumyloxyl radical at 490 nm

The electron spin resonance spectrum of QINO was obtained at 298 K by UV photolysis of a CH$_3$CN solution containing NHQI 10 mM and 10% (v/v) of di-*tert*-butyl peroxide. The spectrum (see Figure 6) shows three main lines due to the coupling of the unpaired electron with nitroxidic nitrogen (a_N= 4.57 G).[16] Each lines shows also unresolved hyperfine structure due to small coupling of the unpaired electron with the nitrogen and hydrogen aromatic nuclei. A similar EPR spectrum of QINO was obtained by oxidation of NHQI with cerium(IV) ammonium nitrate (CAN) in CH$_3$CN at 25 °C (see Figure S2 in the Supproting Information). The 2nd derivative spectrum clearly showed unresolved hyperfine structure due to small coupling of the unpaired electron with the nitrogen and hydrogen aromatic nuclei.
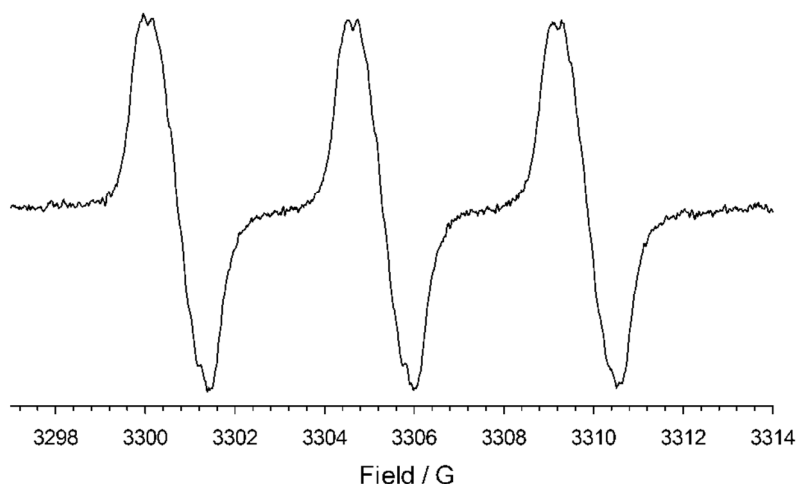
Figure 6. EPR spectrum of QINO recorded at 298 K during UV photolysis of a CH_3CN solution containing NQHI 10 mM and di-*tert*-butyl peroxide (10% v/v)


NO-H Bond dissociation enthalpies (BDE) of NHQI

The BDE_{NO-H} of NHQI is a parameter of fundamental importance for the analysis of the HAT reactivity of QINO. Its value, determined both experimentally and by theoretical calculations was compared with the BDE_{NO-H} value of NHPI previously determined with the same methodologies.[2c,7a,d,8,17] The experimental determination of O-H BDE was carried out by the EPR radical equilibration technique. For this purpose, we measured the equilibrium constant (K_{eq}) for the hydrogen atom transfer reaction between NHQI and a NHPI derivative whose OH BDE was already known (Scheme 3). As a reference we choose 4-CH_3OCO-NHPI which is characterized by an O-H BDE of 87.8 kcal/mol.[18]

$$NHQI + 4\text{-}CH_3OCO\text{-}PINO\cdot \xrightleftharpoons{K_{eq}} QINO\cdot + 4\text{-}CH_3OCO\text{-}NHPI$$
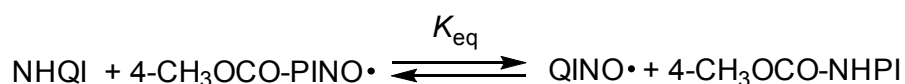
Scheme 3

The initial concentration of *N*-hydroxyimides were used to calculate K_{eq}, while the relative radical concentration were determined by means of EPR spectroscopy (see details and Figure S3 in the

Supporting Information).[19] On the assumption that the entropic term can be neglected $BDE_{NHQI}=BDE_{4-CH_3OCO-NHPI}-RT\ln(K_{eq})$. From the experimentally determined radical concentrations, we obtained $K_{eq}=1.20$, from which, an O-H BDE of 87.7 ± 0.6 kcal/mol for NHQI was calculated.[20]

Theoretical calculations

Density-functional theory (DFT) based calculations were performed to model the reactions of QINO and PINO radicals with toluene. The B3LYP/6-31+G(2d,2p)[21] level of theory was used as the underlying method. The effects of noncovalent interactions in the reacting systems were modeled with the dispersion-correcting potentials (DCPs) approach described previously.[22] Although there exists a number of more common approaches to correcting for the absence of dispersion in the B3LYP (and other) methods, we elected to use the DCP approach in order to obtain results comparable with those previously published for computational studies of the reactions between PINO and phenols. The method we applied is abbreviated as B3LYP-DCP/6-31+G(2d,2p).

We computed the energy-optimized structures of the reactants, pre- and post-reaction (noncovalently bound) complexes and the cisoid (π-stacked) and transoid (non-stacked) transition state (TS) structures in an implicit solvent field (acetonitrile) using the SMD model of Marenich et al.[23] All non-TS structures were verified to have only positive vibration frequencies and the TS structures had a single imaginary frequency that lead to the corresponding pre- and post-reaction species. The gas- and solvent-phase energy-optimized Cartesian coordinates of the reactants, pre- and post-reaction complexes, transition states and products are provided in the Supporting Information.

The O-H BDEs for NHQI and NHPI O-H BDEs were computed using the restricted open-shell (RO) version of CBS-QB3.[24] All calculations were performed using the Gaussian-09 program package.[25]

The (RO)CBS-QB3 method predicts the gas-phase O-H BDEs in NHQI and NHPI to be 84.0 and 83.1 kcal mol^{-1} respectively,[26] with a difference of 0.9 kcal mol^{-1} which is in line with the experimentally determined ΔBDE_{NO-H} (0.7 kcal mol^{-1}). The same approach predicts the C-H BDE

of the methyl group in toluene to be 89.7 kcal/mol. For comparison, the B3LYP-DCP/6-31+G(2d,2p) approach predicts the analogous BDEs in NHQI, NHPI, and toluene to be 80.0, 79.0, and 88.8 kcal/mol, respectively. We attribute the lack of agreement between the (RO)CBS-QB3 and B3LYP-DCP BDEs for NHQI and NHPI to delocalization errors associated with the underlying B3LYP functional. This suggests that the B3LYP-derived barrier heights and reaction endergonicity will be higher than the actual values (see below).

The calculated solvent phase free energies associated with the reaction of QINO and PINO with toluene in acetonitrile solvent are shown in Table 1. In the gas-phase, the reactants form fairly strongly bound pre-reaction complexes, with enthalpies of association of 8.4 (QINO) and 7.8 kcal/mol (PINO). However, the inclusion of entropic correction results in pre-reactions complex formation that are endergonic (2.6 kcal/mol in both cases, see Tables S1-S2 in the SI). The inclusion of estimates of the solvent effects increase the endergonicity of pre-reaction complex formation to 5.5 (QINO) and 4.6 (PINO) kcal/mol. These results are consistent with both the relatively high polarity of the radicals and the differential in the polarity between the radicals.

Table 1. Reaction free energies, relative to reactants, of the hydrogen atom transfer from toluene to QINO and PINO in acetonitrile solvent. The data were obtained using B3LYP-DCP/6-31+G(2d,2p) with the SMD solvation (acetonitrile) model. All values are in kcal/mol

Reaction step	QINO + Toluene	PINO + Toluene
Pre-reaction complex	5.5	4.6
Cisoid TS complex	19.6	20.6
Transoid TS complex	21.8	23
Post-reaction complex	13.3	14.4
Products	10.3	11.4

The TS structures associated with the HAT reaction of QINO and PINO with toluene were found to be π-stacked, or "cisoid" (Figure 7), rather than a "transoid" structure (i.e. non-stacked, or open, see Figure S43 in the SI). This finding is consistent with the calculated structure for the HAT identity reaction for the toluene/benzyl[27] and the phenol/phenoxyl[28] couples. As was discussed in ref. 7, the overlap of the aromatic moieties results in some degree of noncovalent bonding interaction between them within the TS structure, thereby stabilizing the cisoid TS structure preferentially to the transoid structure. In the case of the QINO/PINO reactions with toluene, the cisoid transition state structures are 3.2 kcal/mol lower in free energy relative to transoid structures in the gas-phase (see Tables S1-S2 in the SI). The preferential stabilization of the cisoid TS structures persist in solvent but the differential between the cisoid and transoid structures is reduced by ca. 1 kcal/mol (see Tables S3-S4 in the SI), presumably because the transoid TS structures are more stabilized by interactions with the solvent field.

The calculated free energy barrier height for the reaction between QINO and toluene is 19.6 kcal/mol. As expected on the basis of the arguments made above, this barrier is found to be 1 kcal/mol lower than that associated with the PINO reaction. Both barriers are expected to be over-estimated by ca. 2-3 kcal/mol on the basis that B3LYP predicts a larger differential between the NHQI/NHPI O-H BDEs and the toluene methyl group C-H BDE than does (RO)CBS-QB3.

The lower free energy barrier in the QINO-toluene HAT reaction is consistent with the fact that there is a higher degree of charge transfer between the reactants in this system as compared to that in the PINO-toluene reaction. For example, our solvent-phase calculations indicate that 0.47 electrons are transferred from toluene to QINO-toluene in the cisoid TS complex, which is 0.06 electrons higher than in the analogous PINO-toluene complex. For comparison, the degree of charge transfer system in the transoid TS structures is 2-4 fold lower. This supports the notion that the ring stacking interactions in the TS facilitates charge transfer and promotes HAT.

After the hydrogen atom transfer is completed, the calculations predict that the species involved in the reaction will not remain complexed in acetonitrile. The enthalpies/free energies associated with

complexation within the post-reaction complex are predicted to be +3.4/+13.3 kcal/mol for NHQI-benzyl and +4.7/+14.4 kcal/mol for NHPI-benzyl, relative to the reactants in solvent. The final dissociated products of the HAT reaction in solvent are 10.3 (QINO) and 11.4 (PINO) kcal/mol higher in free energy than the reactants. On the basis of the differences between the B3LYP and (RO)CBS-QB3 bond dissociation energies, our expectation is that the free energies of the two reactions are closer to 7-8 kcal/mol.
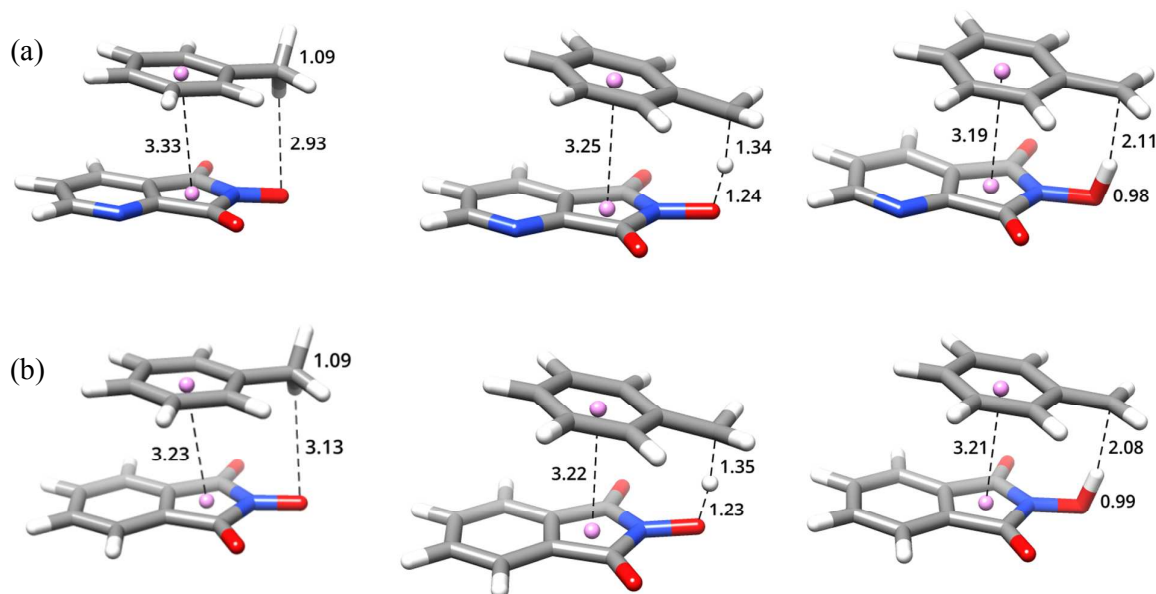

Figure 7. Optimized structures for the pre-reaction, transition state, and post-reaction structures for the reaction of (a) QINO and (b) PINO with toluene. Structures were obtained using the B3LYP-DCP/6-31+G(2d,2p) with the SMD solvation (acetonitrile) model. Key distances shown are in Angstroms. Key: Carbon = grey; Hydrogen = White; Oxygen = red; Nitrogen = blue. The geometric centers of the five- and six membered rings are shown as purple spheres.

Kinetic study of the HAT from C-H bonds to QINO and PINO

Kinetic studies were carried out by UV-vis spectrophotometry generating QINO and PINO by oxidation of NHQI and NHPI with cerium(IV) ammonium nitrate in CH_3CN at T = 25 °C.[3,12,29] The decay of the *N*-oxyl radicals was recorded at 390 nm and 380 nm for QINO and PINO, respectively.
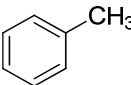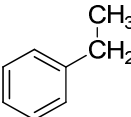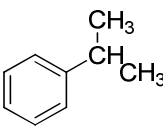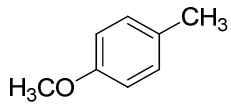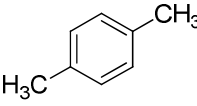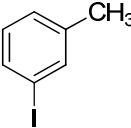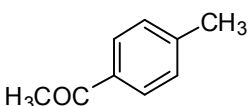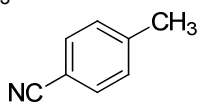
Using an excess of substrates (at least 10-fold) to attain pseudo first-order conditions, clean first

order decays were observed with the H-abstraction rate faster than the spontaneous decay of the *N*-

oxyl radicals and excellent linear fits were obtained by plotting the pseudo-first order rate constants

(k_{obs}) as a function of the concentration of hydrogen donors. From the slope of these plots, the

second order rate constants for HAT (k_H) were determined, as shown in Figure 8 for the reactions of

QINO with alkylaromatics.[30]
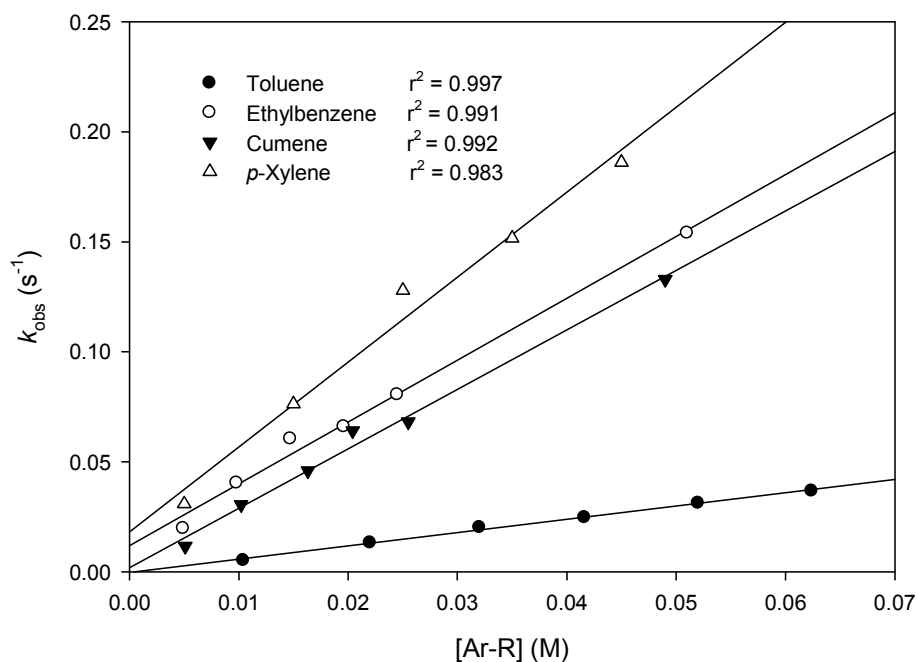
Figure 8. Dependence of the observed rate constants (k_{obs}) against [substrate] for the reactions of
QINO with alkylaromatics measured in CH_3CN solution at T = 25°C by following the decay of
QINO at 390 nm.
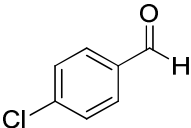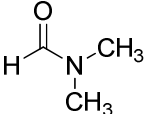
The k_H values are collected in Table 2 for the reactions of QINO and PINO with

alkylaromatics and in Table 3 for the other hydrogen atom donors. In Table 2 are also reported the

k_H values for the HAT reactions of QINO with alkylaromatics in the presence of either 0.15 M

$HClO_4$ or 0.15 M $Mg(ClO_4)_2$ in CH_3CN. Linear plots of k_{obs} against [substrate] are reported in

Figures S4-S39 in the Supporting Information.

Table 2. Second order rate constants (k_H) for hydrogen atom transfer (HAT) from alkylaromatics to QINO and PINO measured in CH$_3$CN at T = 25 °C.

Substrate	k_H (M^{-1}s^{-1}) [a]	
	QINO	PINO
CH$_3$ (toluene)	0.2 2.8[b] 0.33[c]	0.11
CH$_3$–CH$_2$ (ethylbenzene)	1.5 28[b] 2.4[c]	0.95[d] 1.17[d,e]
CH$_3$–CH–CH$_3$ (cumene)	2.9 57[b] 3.7[c]	1.3
H$_3$CO–C$_6$H$_4$–CH$_3$	1.3	0.93
H$_3$C–C$_6$H$_4$–CH$_3$	0.65 9.7[b] 1.2[c]	0.57[d] 0.68[d,e]
I–C$_6$H$_4$–CH$_3$	0.15 1.9[b]	0.11
H$_3$COC–C$_6$H$_4$–CH$_3$	0.11 0.45[b]	0.07
NC–C$_6$H$_4$–CH$_3$	0.036 0.11[b]	0.022

[a] Average of at least three independent determinations. Error ± 5%. Statistically corrected for the number of labile hydrogens. Correlation coefficients 0.982<r^2<0.999. [b] In the presence of 0.15 M HClO$_4$. [c] In the presence of 0.15 M Mg(ClO$_4$)$_2$. [d] See Ref. 12. [e] In the presence of 0.1 M HClO$_4$.

Table 3. Second order rate constants (k_H) for hydrogen atom transfer (HAT) from aliphatic hydrocarbons, alcohols, aldehydes, ethers and amides to QINO and PINO measured in CH$_3$CN at T = 25 °C.

Substrate	k_H $(M^{-1}s^{-1})$ [a]	
	QINO	PINO
(cyclohexane)	0.034	0.014
(adamantane)	0.54	0.15
CH_3OH	0.032	0.012
CH_3CH_2OH	0.55	0.29
$(CH_3)_2CHOH$	3.8	2.1
(4-chlorobenzaldehyde)	0.55	0.19
(tetrahydrofuran)	2.2	1.0
(N,N-dimethylformamide)	0.19	0.14[b]

[a] Average of at least three independent determinations. Error ± 5%. Correlation coefficients $0.972 < r^2 < 0.999$. [b] See ref. 12.

Discussion

The data shown in Tables 2-3 indicate that the presence of the *N*-heteroaromatic ring in QINO results in a significant increase in HAT rate constants involving all the substrates. The higher reactivity of QINO compared to PINO can be rationalized on the basis of both enthalpic and polar effects. We found that the BDE_{NO-H} value for NHQI determined experimentally by the EPR radical equilibration technique is ca 0.7 kcal/mol higher than that of NHPI, and 1.1 kcal/mol by the B3LYP-DCP approach in solvent. The introduction of an electron-withdrawing nitrogen atom into

the aromatic ring of NHQI results in a destabilization of the charge-separated resonance structure of the *N*-oxyl radical (see Figure 2),[2c] thereby increasing the BDE_{NO-H}.

The reactivity of *N*-oxyl radicals in the HAT processes is determined by both the enthalpic requirements of the C-H and NO-H bond dissociation energies and by the polar effects that may stabilize the activated complex.[6] The introduction of an N atom in the aromatic ring of QINO leads to a stabilization of the activated complex by increasing the electron density on QINO. Figure 7 shows an example of these stabilizing effects in the TS for the HAT from substituted toluenes.

The computational modelling of the benzylic hydrogen abstraction from toluene by QINO and PINO provides additional insights on the role of charge transfer stabilization of TS structures. The hydrogen transfer occurs by the same mechanism described in the previous study on the reactions of activated phenols with PINO and other *N*-oxyl radicals.[6g,8] The pre-reaction complex that is formed between the reactants has a cisoid structure that is stabilized through π-stacking interactions (see Figure 7). Relative to the separated reactants, the complexes have free energies of 5.5 (QINO) and 4.6 (PINO) kcal/mol. The cisoid arrangements are maintained in the TS structures, allowing a charge transfer contribution to the HAT process through the π-overlap between the benzylic and QINO aromatic rings.[31] The calculations support the expectation that the inclusion of a nitrogen atom in the aryl ring of the abstracting radical, as in QINO, allows for a greater degree of charge transfer in the TS. Specifically, 0.06 more electrons are transferred between the QINO and benzyl moieties in the TS structure than in the analogous TS structure involving PINO.

The k_H values for the HAT from alkylaromatics to QINO reported in Table 2 show an increase along the series cumene > ethylbenzene > toluene, as expected from the series of decreasing C-H BDEs from the tertiary C-H bond of cumene (BDE = 83.2 ± 1 kcal mol^{-1})[32] to the primary C-H bond in toluene (BDE = 89.7 ± 1.2 kcal mol^{-1})[32] and is in line with the HAT promoted by PINO in acetic acid[2b] and in CH_3CN (see Table 2). For the series of substituted toluenes, as expected for a HAT process promoted by electrophilic radicals and in accordance with the enthalpic and polar effects discussed above, the k_H values increase with the electron donating strength of the aryl

substituent. When the $\log(k_H^X/k_H^H)$ values for the reactions of QINO with substituted toluenes were

plotted against the Okamoto-Brown substituent constants σ^+, good Hammett-type correlations was

obtained (Figure 9).[33] The negative ρ value (-0.99),[34] as well as the better linearity obtained with the

σ^+ rather than the σ constants, are in accordance with the significant polar effects associated to the

development of a partial positive charge on the benzylic position in the HAT TS.
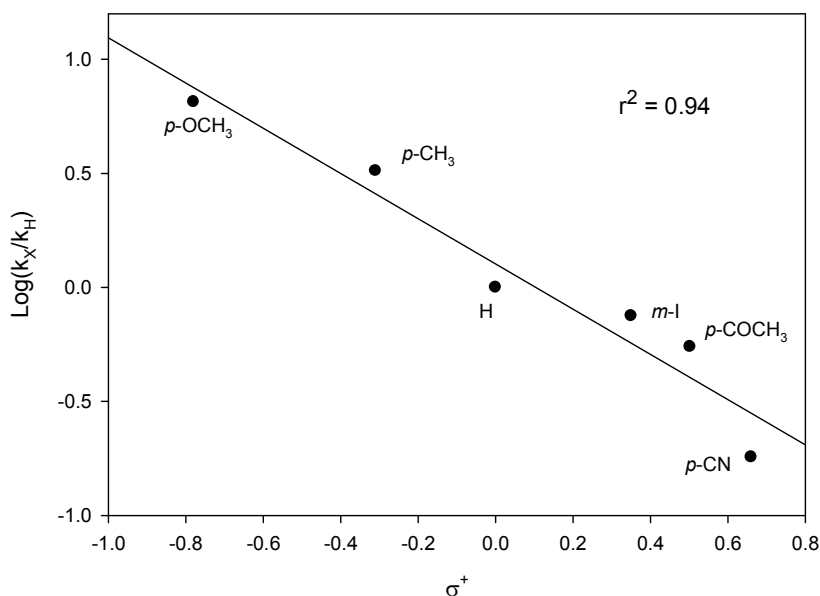
Figure 9. Hammett plot for the reaction of substituted toluenes with QINO in CH_3CN at 25°C.

Table 3 shows the rate constants for the HAT from a series of hydrogen atom donors. Rate

constants for the HAT from C-H bonds in unactivated aliphatic hydrocarbons (cyclohexane and

adamantane), as expected, are significantly lower than those determined with alkylaromatics. The

increase in reactivity observed for QINO as compared to PINO is of fundamental importance with

these substrates which are characterized by relatively high C-H BDE values (99.5 kcal/mol for

cyclohexane, 96.2 and 98.4 kcal/mol for tertiary and secondary C-H bonds respectively in

adamantane).[32]

The higher reactivity observed in HAT from alcohols, ethers (THF), amides (DMF) is in line with

the enthalpic and polar effects associated with electron rich C-H bonds in α position to heteroatoms,

able to stabilize the partial positive charge that develops on carbon in the HAT.

The presence of the heteroaromatic nitrogen in NHQI allows a further activation of the corresponding *N*-oxyl radical in HAT processes by adding Brønsted or Lewis acids in fact the protonation or coordination of the N atom decreases the electron density on QINO (Figure 10).[35]

An increased electrophilicity of QINO would result as a consequence of the destabilization of the charge separated resonance structures shown in Figure 10. In this context, it should be mentioned that through complexation of NHQI with cobalt and copper ions it was possible to improve the activity of NHQI in the oxidation of toluene. This activating effect has been interpreted on the basis of an electron-withdrawing effect produced by the complexation of the *N*-heteroaromatic ring with the metal salts. The complexation of NHQI with $CuCl_2$ has been also confirmed through real time *in situ* FTIR spectral analysis.[10]
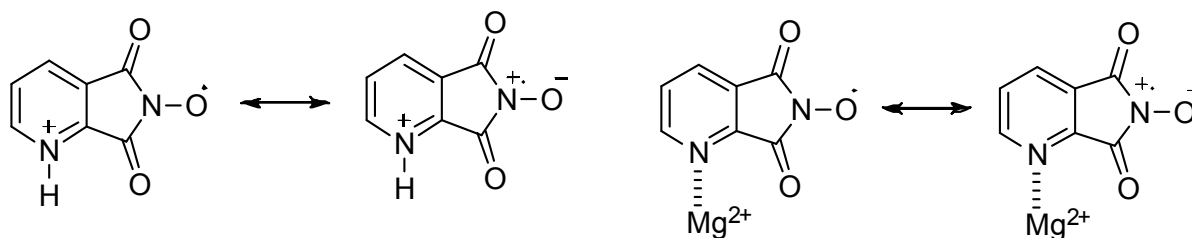
Figure 10. Resonance structures of QINO in the presence of Brønsted or Lewis acids

In order to investigate the effect of acid additives on the QINO reactivity in HAT process, kinetic studies with alkylaromatics were also investigated in the presence of 0.15 M $HClO_4$ and 0.15 M $Mg(ClO_4)_2$.

Considering the electron withdrawing effect of the two imidic carbonyls, the pK_a value for piridinium cation (pK_a = 12.3 in CH_3CN)[36] is much higher than that of $HClO_4$ (pK_a = 2.0 in CH_3CN),[36] thus the protonation of QINO to give $QINOH^{+\bullet}$ in 0.15 M $HClO_4$ should be almost quantitative. Accordingly, a variation of the UV-vis spectra of QINO, generated by oxidation of NHQI (1.0 mM) with CAN (0.5 mM) in CH_3CN, was observed as a function of increasing the

[HClO$_4$] up to the value of 0.15 M (see Figure S40 in the SI).

The data reported in Table 2 indicate increases in reactivity of more than one order of magnitude, in the presence of 0.15 M HClO$_4$ for all the alkylaromatics tested. This is consistent with the previsions based on the favorable enthalpic and polar effects associated with the protonation of QINO. It should be noted that a smaller increase of the k_H value for the HAT from alkylaromatics (ethylbenzene and *p*-xylene, see Table 2) in the presence of HClO$_4$ was also observed for PINO in a previous study.[12] The increase of reactivity with PINO has been attributed to the protonation of imidic carbonyl groups.

Compared to HClO$_4$ a lower degree of activation was observed in the presence of 0.15 M MgClO$_4$. For example the k_H value for the HAT from toluene to QINO increased from 0.2 M^{-1}s^{-1} to 0.33 M^{-1}s^{-1} by addition of the Lewis acid. This behavior reflects a minor decrease of electron density in QINO as compared to the perchloric acid.

The increase of QINO electrophilicity caused by the protonation of the heteroaromatic nitrogen is in accordance with the more negative ρ value (-1.8) determined in the Hammett correlation (see Figure S42 in the SI) for the HAT process from substituted toluenes to QINO observed in the presence of 0.15 M HClO$_4$.

In conclusion the results reported in this study clearly indicate that QINO has greater hydrogen abstracting ability than PINO in HAT processes from all the classes of organic compounds investigated. This supports the use of *N*-hydroxyquinolinimide (NHQI) as a convenient substituted for *N*-hydroxyphthalimide (NHPI) in the catalytic aerobic oxidations of substrates such as aliphatic hydrocarbons that have relatively high C-H bond dissociation energies.

Experimental Section

Materials

Acetonitrile (HPLC grade), *N*-hydroxyphthalimide (NHPI), $(NH_4)_2Ce(NO_3)_6$, $Mg(ClO_4)_2$ and $HClO_4$ were commercially available and used as received. *N*-hydroxyquinolinimide (NHQI) was synthesized by reaction of pyridine-2,3-dicarboxylic acid anhydride[37] with hydroxylamine hydrochloride following a procedure reported in the literature.[10]

Toluene, ethylbenzene, cumene, *p*-xylene, *p*-methoxytoluene, *m*-iodotoluene, 4-methylacetophenone, *p*-tolunitrile, cyclohexane, adamantane, methanol, ethanol, 2-propanol, tetrahydrofuran, *N,N*-dimethylformamide, *p*-chlorobenzaldehyde were commercially available at their highest purity and used as received.

Kinetic Studies

QINO and PINO were generated by oxidation of the corresponding *N*-hydroxyimides (NHQI and NHPI) (1 mM) with cerium(IV) ammonium nitrate (CAN) 0.4 mM in CH_3CN at 25 °C.

HAT reactions of QINO with alkylaromatics were investigated either in the absence of acid additives or in the presence of $HClO_4$ (0.15 M) or $Mg(ClO_4)_2$ (0.15 M). After the generation of the *N*-oxyl radicals, 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 390 nm for QINO and 380 nm for PINO. For all the substrates investigated each kinetic trace obeyed a first-order kinetics. 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 the average of at least three independent determinations with an error ± 5%.

Supporting Information Available: Instrumentation. Determination of the O-H BDE values by EPR measurements. UV-vis spectroscopic characterization of QINO. EPR spectrum of QINO obtained by oxidation of NHQI with cerium(IV) ammonium nitrate (CAN) in CH_3CN at 25 °C. EPR spectrum of irradiated CH_3CN solution containing di-*tert*-butyl peroxide, NHQI and 4-CH_3OCO-NHPI. Plots of k_{obs} vs [substrate] for the reactions of QINO and PINO with alkylaromatics, aliphatic hydrocarbons, alcohols, aldehydes, ethers and amides. UV-vis spectra of QINO in MeCN/[$HClO_4$] (0-0.2 M). Hammett plot for the HAT process from substituted toluenes to PINO in CH_3CN and to QINO in $CH_3CN/HClO_4$ 0.15 M. Gas- and solvent-phase (acetonitrile) computational results for HAT reaction of QINO/PINO with toluene. Optimized structures of the transition states for the reaction of QINO and PINO with toluene. Cartesian coordinates of the optimized structures of the reaction steps. This material is available free of charge via the Internet at http://pubs.acs.org.

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(30) The pseudo first-order rate constant for the decay of QINO is described by the equation $k_{obs} = k_d + k_H$ [Ar-R] where k_d is the QINO self decay rate constant. Thus in the plot of k_{obs} vs [Ar-R] the intercept on the k_{obs} axis ([Ar-R] = 0) should not be on the origin but should be equal to k_d. Since the extrapolated intercept value is always subjected to significant errors, a precise k_d determination using this approach is not allowed.

(31) It is rather difficult to determine with accuracy the contribution of charge transfer from π-stacking between the aryl rings of PINO/QINO and aromatic substrates to the HAT process since it is summed to the enthalpic and other polar effects, also present in the non-aryl hydrocarbons. On these basis a direct comparison of the relative weight of these effects with different substrates is not possible.

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Table of Contents Graphic

PINO   X=CH
QINO   X=N

NHPI   X=CH
NHQI   X=N