Synthetic Methods

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Hydrogen Abstraction and Electron Transfer with Aminoxyl Radicals: Synthetic and Mechanistic Issues

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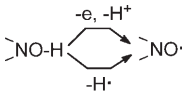
bond energy · electron transfer · hydrogen transfer · oxidations · radicals

Aminoxyl radicals ($R_2NO^{\bullet}$) are a valuable class of reactive intermediates with interesting synthetic and reactivity properties. This Minireview summarizes salient synthetic results obtained in radical oxidations using aminoxyl radicals, and then focuses on reactivity issues arising from recent literature surveys. The structural and reactivity features of the aminoxyl radical and substrate provides a possible explanation of the double reactivity of the aminoxyl radicals. This mechanistic dichotomy between H-atom abstraction and electron-abstraction routes is highlighted in this Minireview.

The synthetic value of environmentally benign and selective oxidations by abstraction of a hydrogen atom with aminoxyl radicals is well known.[1–3] In principle, aminoxyl radicals ($R_2NO^{\bullet}$) can be obtained from the parent hydroxylamines (R_2NO-H) by either abstraction of a hydrogen atom or by abstraction of an electron followed by deprotonation (Scheme 1).



Scheme 1. Possible pathways for the generation of aminoxyl radicals.

Both persistent and short-living aminoxyl radicals are known.[1] An example of such a persistent radical is 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO), but its numerous reactions will not be considered here because no hydrogen-abstraction or electron-transfer steps are involved.[1b] Among the short-living aminoxyl radicals, phthalimide *N*-oxyl (PINO) is a prominent example. This radical is easily generated from its precursor *N*-hydroxyphthalimide (HPI) by the action of O_2 and $Co(OAc)_2$,[3,4] or by means of other oxidants, such as $Pb(OAc)_4$[5a] or $[Bu_4N]VO_3$,[5b] or even enzymes.[6] Once generated, the aminoxyl radical abstracts a hydrogen atom from a given substrate, thereby enabling subsequent interaction with O_2 and the oxidation outlined in Scheme 2.[3,4,7,8]

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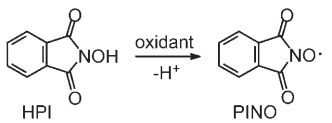
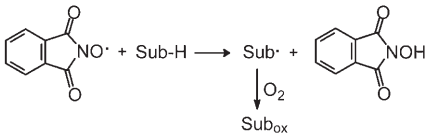
Aminoxyl Radicals as Hydrogen-Abstracting Species

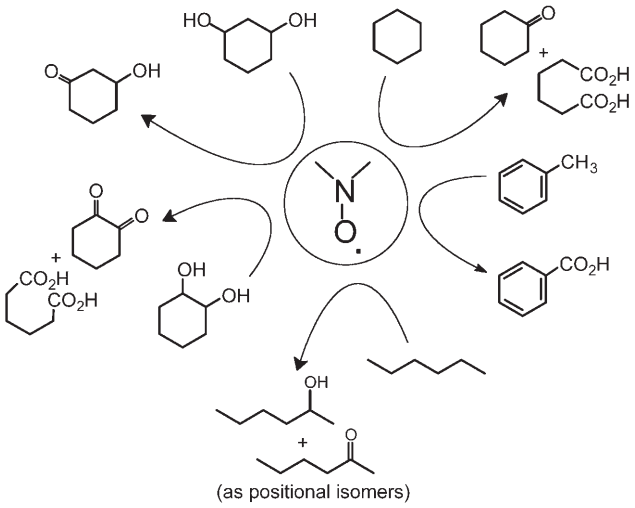
In the first reports by Ishii et al.,[9,10] oxidations were carried out with O_2 in benzonitrile or acetic acid at 100 °C in the presence of catalytic amounts of HPI and cobalt(II) acetylacetonate [$Co(acac)_2$]. Alcohols and diols were converted into carbonyl compounds efficiently by this method; however, the great appeal of this procedure lies in oxidizing simple hydrocarbons, a fundamental goal in organic synthesis (Scheme 3). Cycloalkanes afforded a mixture of cyclic ketones plus open-chain α,ω-bicarboxylic acids, linear alkanes gave significant amounts (40–80 %) of the corresponding alcohols and ketones as mixtures of positional isomers, and alkyl benzenes were oxidized in almost quantitative yields.[4]

Sheldon and co-workers obtained comparable results for the oxidation of hydrocarbons or cycloalkanes by using the HPI/[$Co(acac)_2$]/O_2 system in $PhCF_3$ solution at 80 °C.[1,11] Ishii et al. later found that the addition of small amounts of an additive, such as *m*-chlorobenzoic acid (MCBA), to the HPI/[$Co(acac)_2$]/O_2 system enabled the oxidation to be carried out at room temperature, with good selectivity for the oxidation of a secondary alcohol in the presence of a



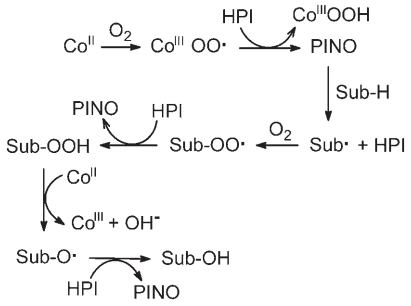


Scheme 2. The H-atom transfer (HAT) mechanism for the oxidation of a substrate (Sub-H) by the aminoxyl radical PINO.



Scheme 3. Oxidation reactions with aminoxyl radicals.

primary alcohol (Table 1).[4,8,12] PINO is produced from HPI in a catalytic cycle involving $Co^{II} \rightarrow Co^{III}$ oxidation and a short-living $Co^{III}OO^{\cdot}$ species (Scheme 4), whereas MCBA



Scheme 4. Catalytic cycle for oxidation with the HPI/Co^{II}/O_2 system.

possibly enhances the solubility of the cobalt salts, thereby ensuring better efficiency for the redox decomposition of a hydroperoxide intermediate of the substrate en route to the products.[13–16]

Minisci et al. used a variant of the procedure developed by Ishii et al., in which $Co(OAc)_2$ was used instead of [Co-(acac)$_2$], and achieved the oxidation of benzylic alcohols to benzaldehydes in almost quantitative yields.[17] *N*,*N*-dimethyl-

Carlo Galli was born in Rome in 1949, where he studied Chemistry (Laurea, 1972). After postdoctoral research with Joe Bunnett at the University of California, Santa Cruz (1978–1979), he returned to Italy, where for 12 years he was a Research Fellow of the National Council of Research (CNR). He was appointed Associate Professor of the University "La Sapienza" in Rome in 1987, and since 1990 has been Professor of Organic Chemistry. He was awarded the Ciamician Medal of the Italian Chemical Society (1985). His research interests include ring-closing reactions, radical and electron-transfer processes, and mechanistic features of enzymatic oxidations.

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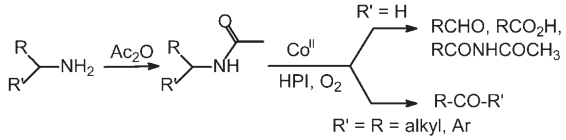
Table 1: Selected examples of oxidations with PINO.

Reaction system	Substrate	Product(s) (yield in %)	Ref.
HPI/[Co(acac)$_2$]/O_2 in AcOH at 100 °C	cyclohexane	cyclohexanone (30) and adipic acid (35)	[10]
HPI/[Co(acac)$_2$]/O_2 in AcOH at 100 °C	octane	octanols (55) and octanones (15)	[10]
HPI/[Co(acac)$_2$]/O_2 in AcOH at 100 °C	toluene	benzoic acid (90)	[10]
HPI/[Co(acac)$_2$]/MCBA/O_2 in AcOEt or MeCN at RT	2-octanol	2-octanone (80)	[12]
HPI/[Co(acac)$_2$]/MCBA/O_2 in AcOEt or MeCN at RT	1-phenylethanol	acetophenone (98)	[12]
HPI/[Co(acac)$_2$]/MCBA/O_2 in AcOEt or MeCN at RT	2,3-octanediol	2,3-octanedione (70) and hexanoic acid (15)	[12]
HPI/[Co(acac)$_2$]/MCBA/O_2 in AcOEt or MeCN at RT	1,2-cyclohexanediol	1,2-cyclohexanedione (25) and adipic acid (30)	[12]
HPI/[Co(acac)$_2$]/MCBA/O_2 in AcOEt or MeCN at RT	1,3-butanediol	4-hydroxy-2-butanone (60)	[12]
HPI/$Co(OAc)_2$/O_2 in MeCN at 35 °C	$PhCH_2NMe_2$	benzaldehyde (60)	[3]
HSI/$Co(OAc)_2$/O_2 in MeCN at 35 °C	$PhCH_2NMe_2$	benzaldehyde (40)	[3]
HPI/$Co(OAc)_2$/MCBA/O_2 in MeCN at RT	$PhCH_2NHCOCH_3$	benzaldehyde (20) and $PhCONHCOCH_3$ (75)	[3]

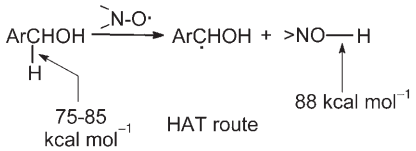
benzylamines were converted into aldehydes in good yields by the use of catalytic amounts of either HPI or *N*-hydroxysuccinimide (HSI) for the formation of the corresponding aminoxyl radical intermediates. The attempted oxidation of primary and secondary amines caused degradation ofthe HPI catalyst, and thus the amino groups in those substrates were protected by acetylation. This approach led to the aerobic oxidation of *N*-alkyl- or *N*-benzylamides or even lactams under mild conditions to give carbonyl products in good yields as mixtures of imides, carboxylic acids, or aldehydes (Scheme 5).[13,17]



Scheme 5. Strategy for the oxidation of amines via the amide. Redrawn with permission from Minisci et al.[13] Copyright (2002) American Chemical Society.

These experimental approaches, which use oxygen rather than more conventional, but polluting inorganic oxidants, testify of the efforts made by chemists to develop new synthetic strategies that are environmentally friendly.[1,18,19]

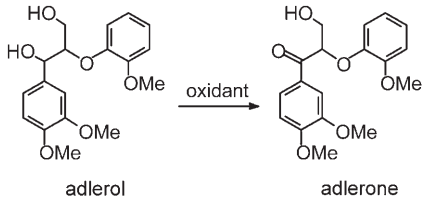
The synthetic value of the oxidations accessible through the use of aminoxyl radicals, most notably PINO, has led to a more detailed investigation of the underlying reactivity issues. A key feature of PINO is the high energy of the NO–H bond (88 kcal mol^{-1}) in the precursor HPI.[16,20,21] This thermodynamic feature dominates the radical reactivity of PINO by H-atom transfer (HAT), as outlined in Scheme 6 for the



Scheme 6. The thermodynamic driving force for H-atom transfer (HAT) between an R_2N-O$^{\bullet}$ species and a C–H donor substrate results from the relative bond dissociation energies (BDEs).

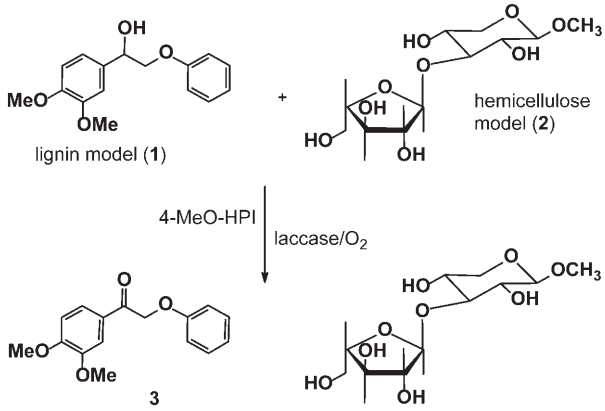
selective oxidation of benzyl alcohols to aldehydes.[6] Hydroxylamine precursors of other aminoxyl radicals which contain NO–H bonds of lower energy than HPI[6] are accordingly less proficient than HPI in HAT routes, as exemplified by the case of the aminoxyl radical TEMPO.[1b] The NO–H bond of the hydroxylamine group of TEMPO (TEMPOH: 69 kcal mol^{-1})[6,22] is so low that TEMPO hardly performs as an H-abstracting species.[6]

In keeping with this thermodynamic issue, the presence of C–H bonds of dissimilar energy in a substrate may enable an aminoxyl radical to perform as a selective HAT oxidant. For example, adlerol (1-(3,4-dimethoxyphenyl)-3-hydroxy-2-(2-methoxyphenoxy)-propan-1-ol) is a well established model compound of lignin,[23] and contains both a benzyl alcohol and a primary alkanol functionality. The selective oxidation of the benzylic alcohol of adlerol to the ketone derivative adlerone (1-(3,4-dimethoxyphenyl)-3-hydroxy-2-(2-methoxyphenoxy)-propan-1-one) has been taken as a benchmark reaction (Scheme 7) to evaluate the selectivity of several oxidizing agents.[24] Good selectivity has indeed been achieved in oxidations performed with aminoxyl radicals.[25]



Scheme 7. Selective oxidation of adlerol.

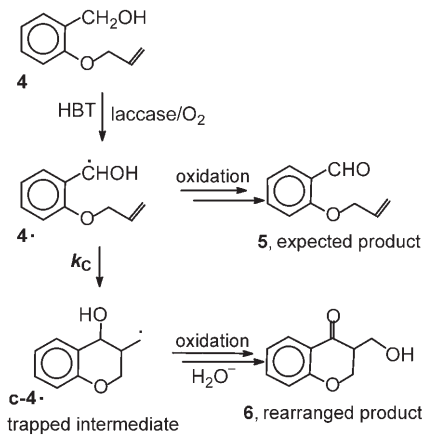
The selective oxidation of the adlerol-like model compound **1** in the presence of the dimeric model compound of hemicellulose **2** has been achieved through a chemoenzymatic approach.[6] The enzyme laccase in the presence of O_2 oxidizes the R_2N-OH precursor and produces the aminoxyl radical, which subsequently carries out the HAT oxidation. 4-MeO-substituted HPI was employed in this case as the hydroxylamine mediator of the enzyme for the oxidation of a 1:1 mixture of **1** and **2** at room temperature over 24 h (Scheme 8).[6] This approach led to the selective oxidation of alcohol **1** to the carbonyl derivative **3** (58% yield), while the aliphatic alcohol groups of **2** were left unchanged.[6] The lower bond dissociation energy (BDE) of benzylic C–H bonds (ca. 79–84 kcal mol^{-1}),[22] compared to aliphatic C–H bonds (ca. 92–97 kcal mol^{-1}),[22] drives the R_2N-O$^{\bullet}$ radical ($BDE_{O\text{-}H}$ of 4-MeO-HPI = 87 kcal mol^{-1})[20] to abstract the *weaker* benzylic C–H bond geminal to the OH bond in **1**, but not the *stronger* aliphatic C–H bond geminal to the OH bonds in **2**. Thus, a selective HAT process, and consequently a



Scheme 8. Competitive chemoenzymatic oxidation of model compounds of lignin (**1**) and a polysaccharide (**2**). Reprinted with permission from Ref. [6]. Copyright (2005) The Royal Society of Chemistry.

selective oxidation of lignin model **1** in the presence of polysaccharide model **2**, results. This is an example of an environmentally friendly oxidation strategy that occurs in aqueous solution,[1,19] and may present applications in the pulp and paper industry.[2,6,19,26]

The fleeting formation of radical R· in the HAT oxidation of a RH substrate by an aminoxyl radical has been investigated by using 2-allyloxybenzyl alcohol (**4**) as a probe substrate (Scheme 9).[6] In fact, although the expected oxidation product, namely, 2-allyloxybenzaldehyde (**5**), was obtained in the aerobic chemoenzymatic oxidation catalyzed by laccase and mediated by 1-hydroxybenzotriazole (HBT), as the precursor of the R_2N-O· species, the intermediate benzyl radical (**4**·) was in part trapped (as **6**) through fast formation of a six-membered ring by an intramolecular *6-exo-trig* process (k_c)[6,27] and ensuing O_2-dependent functionalization.



Scheme 9. Interception of the radical intermediate of the HAT oxidation. Reprinted with permission from Ref. [6]. Copyright (2005) The Royal Society of Chemistry.

Generation of the aminoxyl radical PINO by oxidation of HPI with $Pb(OAc)_4$ in AcOH solution at 25 °C (see Scheme 2) was adopted by Espenson and co-workers for kinetic reactivity studies.[5a] The rate of hydrogen abstraction from a number of H-donor substrates was studied (RH, in Table 2)[5a,16] by following the time-dependent depletion of the absorption band of PINO ($\lambda_{max} = 382$ nm; $\varepsilon = 1360\ M^{-1}cm^{-1}$) by spectrophotometry. The substrates were mostly benzylic and allylic alcohols or hydrocarbons, in which the energy of the scissile C–H bond was expected to be low enough for the H-abstraction power of PINO; in fact there was a reasonable correlation between increasing values of the rate constant k_H and decreasing C–H bond energies.[16,28] The reactivity of PINO appears, therefore, to be dominated by enthalpic factors, as is reasonable for a process where the homolytic cleavage of the C–H bond is rate-determining. Comparison of the reactivity of toluene and [D_8]toluene led to a kinetic isotope effect k_H/k_D of 27,[5a] thus confirming the H-abstraction step as rate-determining and showing the relevance of tunneling effects. Analysis of the rate constants for hydrogen abstraction for a set of *p*-substituted benzyl alcohols according to the Hammett equation gave $\rho = -0.41$ versus σ^+.[5a,16]

Table 2: Comparison of the rate constants (at 25 °C) of hydrogen abstraction (k_H in $M^{-1}s^{-1}$) by PINO, $(CF_3)_2NO$·, and BTNO.

Substrate, RH (BDE_{C-H} in kcal mol^{-1})[a]	k_H, PINO[b] (in AcOH)	k_H, $(CF_3)_2NO$·[c] (in freon)	k_H, BTNO[d] (in MeCN)
$PhCH_2OH$ (80)	12	n.d.	1.9
p-MeO-$C_6H_4CH_2OH$ (ca. 79)	45	n.d.	6.2
$PhCH_3$ (89)	0.62	8.8×10^{-3}	0.27[e]
$PhCH_2CH_3$ (85)	5.4	0.3	0.70[e]
$PhCHMe_2$ (84)	27	0.3	0.55[e]
Ph_2CHOH (79)	58	n.d.	3.2
Ph_2CH_2 (84)	13	0.48	0.72
Ph_3CH (81)	59	8.8	2.3
fluorene (82)	40	n.d.	3.8
tetrahydrofuran (92)	n.d.	0.35	n.d.

[a] From Ref. [22]. [b] Generated by oxidation of HPI with $Pb(OAc)_4$.[5a,16] [c] From Ref. [29]. [d] From Ref. [31]; generated by oxidation of HBT with Ce^{IV}. [e] As *p*-MeO derivatives. n.d.: not determined.

This value further supports that H-abstraction oxidation of the substrates by PINO is the rate-determining step. Finally, the reactivity of PINO was found to be higher than that of the aminoxyl radical $(CF_3)_2NO$· (Table 2),[29] which is in keeping with the BDE_{O-H} value of the two parent hydroxylamines, which is larger for the more reactive HPI (88 versus 84 kcal mol^{-1}).[21,29]

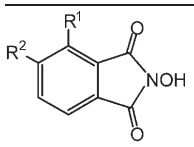
This finding is consistent with the reactivity of the abstraction of the benzylic hydrogen atom (k_H, in $M^{-1}s^{-1}$, at 300 ± 5 K) from ethylbenzene (BDE_{C-H} 85.5 kcal mol^{-1})[22] by a series of oxygen-centered radicals (BDE_{O-H} in kcal mol^{-1}, in parenthesis):[22,29] HO· (119), *t*BuO· (104), *t*BuOO· (89), $(CF_3)_2NO$· (84), and TEMPO (69). The decreasing values of BDE_{O-H} correlate nicely with the decreasing k_H values of 2×10^9, 1×10^6, 0.2, 0.3, and ca. 10^{-9}, respectively.[29,30] This finding confirms the close relationship between thermodynamic and reactivity features in the HAT route: the weaker the O–H bond formed by the abstracting radical, the lower the H-abstraction reactivity.

As an experimental alternative to the use of $Pb(OAc)_4$ for the oxidation of HPI to PINO, the HPI/$Co(OAc)_2$/MCBA/O_2 system (see Scheme 4) was also studied. The H-abstraction proficiency of PINO was assessed in competitive oxidations of *p*-X-substituted benzyl alcohols in MeCN solution at 25 °C.[20] From the amount of the aldehydes produced, the relative reactivity (k_X/k_H) could be calculated, and a Hammett constant $\rho = -0.68$ versus σ^+ obtained;[20] this value is in close agreement with the above kinetic determination by Espenson and co-workers.[5a] A remarkably good agreement with this ρ value was found by another investigation, in which competition experiments performed with a larger set of both *m*- and *p*-X-substituted benzyl alcohols and the same HPI/Co^{II}/MCBA/O_2 system gave $\rho = -0.69$.[3,14] The competitive oxidation of $PhCH_2OH$ and $PhCD_2OH$ by HPI/$Co(OAc)_2$/MCBA/O_2 was also investigated, and gave an intermolecular kinetic isotope effect $k_H/k_D = 16$.[20]

This study was expanded through the use of six X-aryl-substituted *N*-hydroxyphthalimides (X-HPIs) containing electron-withdrawing (4-MeOCO, 3-F) or electron-donating (X = 4-Me, 4-MeO, 3-MeO, 3,6-$(MeO)_2$) groups.[20] The BDE_{O-H} of these X-HPIs was determined by the EPR radical

equilibration technique (Table 3).[20,21,32] Pairwise competition experiments for the oxidation of substituted benzyl alcohols led to Hammett correlations for each X-HPI, in addition to the k_H/k_D ratios determined from deuteriated substrates

Table 3: Bond dissociation energy values for the NO–H bond of X-aryl-substituted *N*-hydroxyphthalimides (X-HPIs), k_H/k_D ratios, and Hammett ρ values determined in competition experiments for the oxidation of substituted benzyl alcohols by the X-HPIs/Co^{II}/MCBA/O_2 system in MeCN solution at 25 °C.[a]

	BDE_{O-H} [kcal mol^{-1}][b]	ρ	k_H/k_D
HPI ($R^1=R^2=H$)	88.1	−0.68	16
$R^1=H$, $R^2=CO_2Me$	88.9	−0.70	14
$R^1=F$, $R^2=H$	88.6	−0.69	n.d.
$R^1=OMe$, $R^2=H$	87.9	−0.60	n.d.
$R^1=H$, $R^2=Me$	88.2	−0.67	n.d.
$R^1=H$, $R^2=OMe$	87.3	−0.60	18

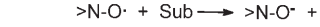
[a] From Ref. [20]. [b] Determined at −10 °C in MeCN[20] by the EPR radical equilibration technique.[32]

(Table 3).[20] Once again, the sizeable k_H/k_D values supported that H-atom transfer from the benzyl alcohol to the X-PINOs was the rate-determining step, while the Hammett ρ values confirmed the above determination with parent PINO.[5a,14,16,20]

Another relevant aminoxyl radical, namely, BTNO (benzotriazole-*N*-oxyl), was generated by oxidation of 1-hydroxybenzotriazole (HBT) with either $Pb(OAc)_4$ in AcOH or cerium(IV) ammonium nitrate in MeCN. The reactivity of BTNO in abstracting hydrogen from appropriate substrates (RH) was studied spectrophotometrically in MeCN solution at 25 °C.[31] The rate constants k_H were uniformly smaller by at least one order of magnitude than those with PINO (Table 2) for the same substrates. This result is in keeping with the lower energy of the NO–H bond of HBT than HPI (85 versus 88 kcal mol^{-1}, respectively).[6] Moreover, the k_H data in Table 2 confirm that the reactivity of the aminoxyl radicals is decidedly lower than that of oxygen-centered radicals such as tBuO$^\bullet$ or HO$^\bullet$, the k_H values of which approach the diffusion limit.[30] This finding reflects that the O–H bonds formed with the oxygen-centered radicals in the rate-determining HAT step are stronger[22] than the NO–H bonds formed with the aminoxyl radicals.[6] Additional studies to evaluate the reactivity of other aminoxyl radicals in the H-abstraction reaction is in progress so as to widen the scope of this comparison.

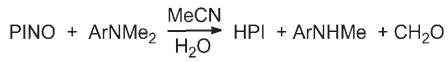
Aminoxyl Radicals as One-Electron Oxidants

Another facet of the reactivity of aminoxyl radicals has been recognized by recent studies on the oxidation of substrates with low redox potentials. In principle, an aminoxyl radical, depending on its $R_2N\text{-}O^\bullet/R_2N\text{-}O^-$ reduction potential, could perform as a one-electron abstractor towards substrates having a matching redox potential. This reactivity feature, outlined in Scheme 10, has been realized by the oxidation of aniline derivatives,[33] whose redox potentials lie in the range 0.5–1.1 V/NHE,[34] and therefore is accessible to the reduction potential of the PINO/$PINO^-$ couple (0.92 V/NHE in MeCN).[33]



Scheme 10. Electron-transfer oxidation of a substrate by an aminoxyl radical.

PINO, generated from HPI by either oxidation with $Pb(OAc)_4$ or laser flash photolysis of $(t\text{BuO})_2$ at 266 nm, was found to be effective in promoting the oxidative N demethylation of 4-X-substituted-*N*,*N*-dimethylanilines (X-DMAs) in MeCN at 25 °C (Scheme 11).[33]



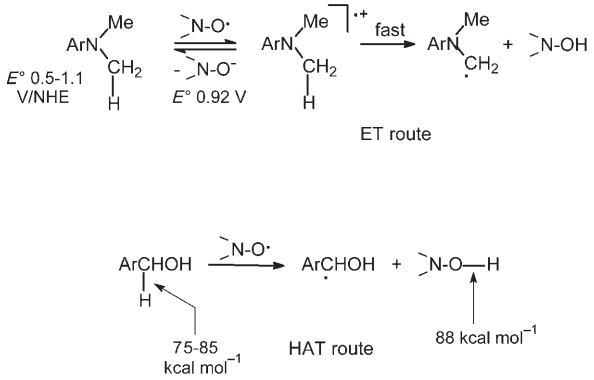
Scheme 11. PINO-induced oxidative N demethylation through electron transfer.

The rate constants for the oxidation were highly dependent on the electron-donating power of the X substituents ($\rho=-2.5$ versus σ^+; Table 4),[33] as well as on the oxidation potential of the substrates. An intermolecular kinetic isotope effect $k_H/k_D=1$ was determined with an appropriately deuteriated *p*-MeO-*N*,*N*-dimethylaniline.[33] These experimental findings differ greatly from the results obtained in the radical HAT oxidation of X-substituted benzyl alcohols by PINO or PINO congeners (see Table 3).[20] They are, however, compatible with a two-step mechanism involving a reversible electron transfer (ET) from the DMAs to PINO, followed by the fast cleavage of a proton from the N-(α)C–H bond of an anilinium radical-cation intermediate (Scheme 12). This situation gives an α-amino carbon radical and ultimately the *N*-demethylated product (Scheme 11), as confirmed by product analyses.[33]

Table 4: Oxidation potentials of 4-X-substituted *N*,*N*-dimethylanilines (X-DMAs) and rate constants for their reaction with PINO at 25 °C in MeCN.[a]

X-DMA	$E°$ (V/NHE) in MeCN[a]	k_H [M^{-1} s^{-1}]
X=CN	1.29	4.5×10^2
X=CF_3	1.25	1.4×10^3
X=CO_2Et	1.21	3.5×10^3
X=OPh	0.80	3.0×10^5
X=OMe	0.69	3.7×10^6

[a] Data from Ref. [33].



Scheme 12. Different reaction pathways for the aminoxyl radical PINO, depending on the substrate.

The DMAs have lower oxidation potential values (0.5–1.1 V) than substituted benzyl alcohols ($E° > 1.4$ V/NHE),[35] while their NC–H bonds are stronger (90–92 kcal mol^{-1})[22] than the C–H bonds of benzyl alcohols (ca. 75–85 kcal mol^{-1})[22] (Scheme 12). Both factors disfavor the operation of a radical HAT mechanism during the reaction of PINO with the DMAs, and results in a change to an ET mechanism.

Consistent with these results is the oxidation of 4-X-substituted phenols, which have similarly low redox potentials (in the 0.4–0.9 V/NHE range), by PINO. The substantial k_H/k_D value (in the 3.1–3.7 range) in these reactions led to a proton-coupled electron-transfer (PC-ET) mechanism being suggested, where a partial electron transfer from the phenolic ring to PINO occurs in the transition state during hydrogen abstraction.[36] The reaction of other readily oxidizable substrates (for example, substituted ferrocenes: 0.5–0.9 V/NHE) with PINO or other aminoxyl radicals is under investigation,[37] to further confirm the mechanism outlined in Scheme 10.

Conclusions

Studies dealing with the synthetic and reactivity properties of the aminoxyl radicals have been reviewed. Most of the cases pertain to the oxidation of H-donor substrates by hydrogen abstraction. Benzyl alcohols and alkyl arenes are typical reducing substrates, which are extensively oxidized and—depending on the energy of the C–H bond being cleaved by the aminoxyl radical—can be discriminated in terms of their H donicity: the weaker the C–H bond of the substrate, the faster the H abstraction. The Hammett correlations and kinetic isotope effects endorse H abstraction as the rate-determining step of the oxidation. Whenever the comparison is possible, the increasing reactivity of various aminoxyl radicals correlates with the increasing energy of the NO–H bond in the hydroxylamine precursors. Finally, a new alternative reaction pathway involving the aminoxyl radicals as electron-abstracting species towards electron-donor substrates has been outlined. The aminoxyl radicals emerge as an important class of reactive intermediates, and the investigated reactivity features will allow their use in environmentally friendly oxidations to be optimized and, therefore, synthetic applications to be fostered.

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