Autocatalytic Radical Ring Opening of *N*-Cyclopropyl-*N*-phenylamines Under Aerobic Conditions − Exclusive Formation of the Unknown Oxygen Adducts, *N*-(1,2-Dioxolan-3-yl)-*N*-phenylamines

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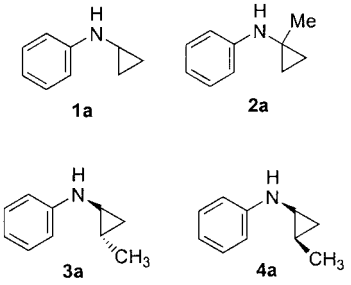
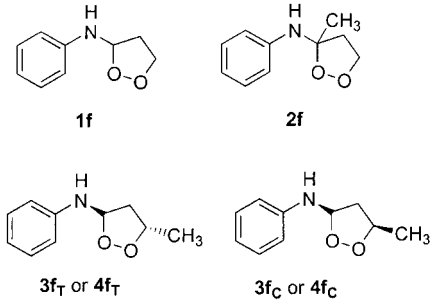
In contrast to the high stability of *N*-alkyl-*N*-cyclopropylamine derivatives, *N*-cyclopropyl-*N*-phenylamine (**1a**) has been found to slowly convert into the hitherto unknown product *N*-(1,2-dioxolan-3-yl)-*N*-phenylamine (**1f**) at room temperature under aerobic conditions. The rate of this conversion was found to be significantly increased by the presence of a catalytic amount of the single-electron oxidizing agent tris(1,10-phenanthroline)Fe^{III} hexafluorophosphate or of the hydrogen-abstracting agents benzoyl peroxide or *tert*-butyl peroxide/UV light. Based on the regio- and stereochemical outcomes of aerobic ring-opening reactions of some specifically ring-methylated derivatives of **1a**, namely *N*-(1-methylcyclopropyl)-*N*-phenylamine (**2a**), *N*-(*trans*-2-methylcyclopropyl)-*N*-phenylamine (**3a**), and *N*-(*cis*-2-methylcyclopropyl)-*N*-phenylamine (**4a**), as well as other experimental evidence, an autocatalytic mechanism analogous to that of the oxygenation of vinylcyclopropanes is proposed for the formation of the 1,2-dioxolane product. The oxidative radical ring opening and related chemistry of these novel derivatives could be valuable in mechanistic studies of heteroatom-oxidizing enzymes.

Introduction

Oxidative radical ring opening and the related chemistry of cyclopropylamine derivatives have been of considerable interest to mechanistic enzymologists and bioorganic chemists.[1] The predictable chemistry of cyclopropylaminium radicals[2] has been used to distinguish between single-electron transfer mechanisms and other types of mechanisms in biological reactions and to design irreversible enzyme inhibitors for therapeutic purposes.[1] Despite this widespread interest, little is known about the oxidative chemistry of these interesting compounds. For example, only a few detailed reports have appeared in the literature concerning the ring opening initiated by the single-electron oxidation of these derivatives.[3] In the present study, we have examined the autocatalytic oxidative ring opening of cyclopropylaminium radicals under aerobic conditions using *N*-cyclopropyl-*N*-phenylamine (**1a**, Scheme 1) as a probe. We report herein the isolation and full characterization of the previously unknown oxygen adduct *N*-(1,2-dioxolan-3-yl)-*N*-phenylamine (**1f**, Scheme 2)[3b,4] as the sole product of the reaction and also propose a plausible mechanism for the transformation.



Scheme 1. Structures of *N*-cyclopropyl-*N*-phenylamines **1a**−**4a**



Scheme 2. Structures of 1,2-dioxolanes **1f**−**4f**

Results and Discussion

We chose *N*-cyclopropyl-*N*-phenylamine (**1a**) as a suitable probe for examining the aerobic ring-opening reaction and related chemistry of cyclopropylaminium radicals for several reasons. Well-characterized oxidants are available for the clean, single-electron oxidation of relatively easily oxidizable *N*-alkyl-*N*-phenylamine derivatives and the ensuing chemistry is well understood.[5] The aminium radical of **1a** is relatively stable and long-lived compared to its *N*-alkyl counterparts and can be expected to undergo efficient ring opening to produce the corresponding carbon-centered rad-

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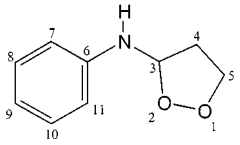
ical.[2] Moreover, since the aminium radical of **1a** contains no readily transferable α-hydrogen atoms on the *N*-alkyl substituents,[6] it should not undergo competitive deprotonation (see, for example, ref.[3a]). Although the synthesis of **1a** has not been reported previously, the recent elegant procedure of Chaplinski and de Meijere[7] allows easy access to the corresponding *N*-benzyl derivative, which was found to be conveniently and cleanly debenzylated by catalytic hydrogenolysis in MeOH containing 0.5% (v/v) glacial acetic acid.

As compared to the behavior of other *N*-(primary, secondary, and tertiary alkyl)-*N*-cyclopropylamine derivatives, **1a** displays unexpected and unique properties. For example, in contrast to the high stability of most other cyclopropylamine derivatives, **1a** was found to be slowly transformed to a single more polar product under aerobic conditions, even at 0 °C (stable at −80 °C). While the rate of this transformation was not significantly affected by the presence of oxidizing agents such as H_2O_2 or *m*-chloroperbenzoic acid, it was found to be considerably increased by the presence of the single-electron oxidant tris(1,10-phenanthroline)Fe^{III} hexafluorophosphate $[(phen)_3Fe^{III}](PF_3)_6]$[8] or of the hydrogen-abstracting reagents benzoyl peroxide $(BzO)_2$ or *tert*-butyl peroxide $(tBuO)_2$/UV light.[5] Moreover, the reaction was found to be strictly dependent on the presence of molecular oxygen, regardless of the reaction conditions used. Mass spectral analysis of the purified product generated from **1a** showed it to have a molecular mass of 165 [MS: *m*/*z* (%) = 165 (12), 132 (32), 105 (49), 93 (37), 86 (43), 77 (44)], suggesting that it is an oxygen adduct of the parent compound. FT-IR analysis of the product indicated the absence of hydroxy, amide, or carbonyl groups (data not shown). Based on the ^1H and ^{13}C NMR spectral analysis of the purified product (Table 1), we propose the previously unknown adduct *N*-(1,2-dioxolan-3-yl)-*N*-phenylamine (**1f**, Scheme 2) as the product of the aerobic oxidative decomposition of **1a**.

Two pieces of chemical evidence provide additional support for the structure of the aerobic oxidative decomposition product **1f**. First, treatment of **1f** with excess $(BzO)_2$ quantitatively produced a more polar product, which was unequivocally identified as the known 3-hydroxy-*N*-phenylpropanamide (**5**) by standard spectroscopic analyses [^1H NMR: δ = 2.62 (t, *J* = 5.3 Hz, 2 H), 2.86−3.01 (br. s, 1 H), 3.98 (t, *J* = 5.5 Hz, 2 H), 7.11 (t, *J* = 7.3 Hz, 1 H), 7.32 (t, *J* = 8.0 Hz, 2 H), 7.51 (d, *J* = 7.7 Hz, 2 H), 7.85−7.91 (br. s, 1 H). − ^{13}C NMR: δ = 39.2 (t), 58.8 (t), 120.0 (d), 124.4 (d), 129.0 (d), 137.6 (s), 170.7 (d). − MS: *m*/*z* (%) = 165 (25), 135 (6), 93 (100), 77 (11), 57 (13), 43 (47)]. A benzoyl-peroxide-mediated transformation of **1f** to **5** is consistent with the expected chemistry of **1f** (Scheme 3). The abstraction of the α-hydrogen atom of **1f** (see below) by the benzoyl peroxide radical (BzO·), followed by homolytic cleavage of the O−O bond, can be expected to produce the corresponding oxygen radical **1h** (Scheme 3). The highly reactive radical **1h** may then abstract a hydrogen atom from the solvent or some other species in the reaction mixture to yield the final product **5**. Second, the catalytic hydrogenation of pure **1f** on 10% Pd/C in MeOH quantitatively produced the corresponding amino alcohol, 3-hydroxy-*N*-phenylpropylamine (**6**; Scheme 4) {^1H NMR: δ = 1.96 (tt, *J* = 5.9, 7.3 Hz, 2 H), 3.47 (t, *J* = 7.3 Hz, 2 H), 3.72 (t, *J* = 5.9 Hz, 2 H), 4.8−5.0 (br. s, 1 H), 7.45−7.60 (m, 5 H). − ^{13}C NMR: δ = 29.6 (t), 51.1 (t), 60.1 (t), 123.3 (d), 130.1 (d), 131.4 (s), 137.6 (d). − MS: *m*/*z* (%) = 152 (100) [M + 1], 134 (25), 106 (85), 94 (20)}. This observation is also consistent with the proposed structure of **1f**, since the carbinolamine intermediate **1j** expected[9] from the reduction of

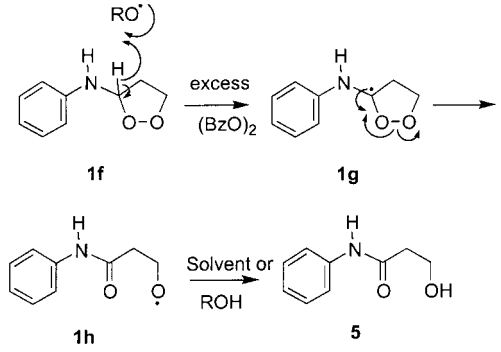
Table 1. ^1H and ^{13}C NMR assignments of **1f**



Proton #	Chemical shift [ppm]	Coupling constant (*J*)[a] [Hz]	Proton #	Chemical shift [ppm]	Coupling constant (*J*) [Hz]
N′	4.50 (br. d)	≈ 9[b]	7′	6.76 (dd)	0.8, 8.6
3′	5.47 (ddd)	3.4, 7.3, 9.3	8′	7.21 (dd)	7.4, 8.6
4′	2.39 (dddd)	3.4, 8.1, 8.4, 12.9	9′	6.84 (tt)	1.1, 7.4
4′′	3.05 (dddd)	3.1, 7.3, 8.1, 12.9	10′	7.21 (dd)	7.4, 8.6
5′	4.01 (dt)	8.4, 8.1	11′	6.76 (dd)	0.8, 8.6
5′′	4.32 (ddt)	0.8[c], 3.1, 8.1			
Carbon #		−	Carbon #		−
3	85.4 (d)	−	8	119.9 (d)	−
4	41.6 (t)	−	9	114.8 (d)	−
5	69.1 (t)	−	10	119.9. (d)	−
6	144.8 (s)	−	11	129.3 (d)	−
7	129.3 (d)	−			

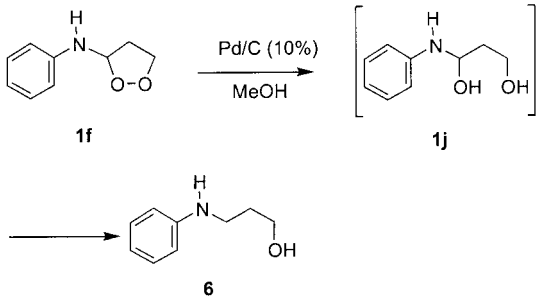
[a] Coupling patterns were determined by two-dimensional NMR experiments. Some of the smaller coupling constants of aromatic protons were not determined. − [b] Coupling between N−H and 3-H was observed only occasionally depending on the purity of the sample. − [c] This small coupling could be due to long-range interactions.

a 1,2-dioxolane ring system should be further reduced to produce the corresponding amino alcohol **6** (Scheme 4). This evidence further supports the conclusion that aerobic single-electron oxidation of *N*-cyclopropyl-*N*-phenylamine produces the oxygen adduct *N*-(1,2-dioxolan-3-yl)-*N*-phenylamine (**1f**).



1f **1g** **1h** **5**

Scheme 3. Reaction of *N*-(1,2-dioxolan-3-yl)-*N*-phenylamine (**1f**) with benzoyl peroxide



1f **1j** **6**

Scheme 4. Hydrogenolysis of *N*-(1,2-dioxolan-3-yl)-*N*-phenylamine (**1f**)

In order to examine the mechanism of the above transformation, we synthesized and characterized *N*-(1-methylcyclopropyl)-*N*-phenylamine (**2a**; Scheme 1), *N*-(*trans*-2-methylcyclopropyl)-*N*-phenylamine (**3a**), and (*cis*-2-methylcyclopropyl)-*N*-phenylamine (**4a**), and examined their aerobic oxidation products under various reaction conditions. The data presented in Table 2 clearly show that all these compounds are quantitatively converted into the corresponding 1,2-dioxolane products (**2f**−**4f**; Scheme 2) within 1−2 h in the presence of catalytic amounts of $[(phen)_3Fe^{III}](PF_6)_3$ (0.6−1.0 mol %) under aerobic conditions.[10] As expected, under rigorously anaerobic conditions in the presence of catalytic amounts of $[(phen)_3Fe^{III}](PF_6)_3$, these amines did not react to produce detectable amounts (by ^1H NMR) of the 1,2-dioxolanes or any other products (Table 2), confirming the strict oxygen dependence of the process (see below, however). Furthermore, the starting materials recovered from similar anaerobic reaction mixtures of the 2-methyl derivatives **3a** and **4a** were found to have retained their original *trans* or *cis* configurations, respectively, suggesting that reversible opening and closing of the cyclopropyl ring does not occur to any significant extent in the presence of catalytic amounts of $[(phen)_3Fe^{III}](PF_6)_3$. Moreover, the pure *cis* and *trans* isomers, **3a** and **4a**, produced identical mixtures of 45% *cis* (**3f$_C$**) and 55% *trans* (**3f$_T$**) 1,2-dioxolane products (as estimated by ^1H NMR spectroscopy), demonstrating that the insertion of oxygen is not concerted with the opening of the cyclopropyl ring.

Treatment of the amines **1a**−**4a** (Scheme 1) with stoichiometric amounts of $[(phen)_3Fe^{III}](PF_6)_3$ under anaerobic conditions resulted in the complete consumption of the amine and the catalyst (as indicated by a color change from blue to red) in about 2 h. However, these reactions produced uncharacterizable complex mixtures of polymeric and other oxidized products, suggesting that excess $[(phen)_3Fe^{III}](PF_6)_3$ is capable of further oxidation of the initial intermediates of the reaction pathway under these conditions. Furthermore, when similar reactions were carried out under aerobic conditions, while traces of the corresponding 1,2-dioxolanes and 15−25% of the amides **5** were produced, within about 1 h most of the starting materials had again been converted into a mixture of uncharacterizable products similar to that seen in the anaerobic reactions. These results indicate that the controlled generation of the initial oxidation product of the amine is necessary for efficient formation of 1,2-dioxolane products under aerobic conditions.

Reactions of *N*-alkyl-*N*-phenylamines with the outer-sphere single-electron oxidant $[(phen)_3Fe^{III}](PF_6)_3$ have been extensively studied.[5] These studies have shown that $[(phen)_3Fe^{III}](PF_6)_3$ abstracts a single electron from the nitrogen atom to produce the corresponding nitrogen cation radical.[6] Therefore, we believe that $[(phen)_3Fe^{III}](PF_6)_3$ also abstracts a single electron from the nitrogen atoms of **1a**−**4a** to generate the corresponding aminium radicals **1b**−**4b** (Scheme 5). This notion is also consistent with the immediate conversion of blue $[(phen)_3Fe^{III}](PF_6)_3$ to red $[(phen)_3Fe^{II}](PF_6)_2$ upon its addition to the amine. Moreover, the observation that the products are exclusively derived from the opening of the C-1−C-2 bonds of **3a** and **4a** indicates that, as expected, the direction of ring opening of the initially formed aminium radical is determined by the stability of the resulting carbon radical. This observation further suggests that the carbon-centered radical is a discrete intermediate along the reaction pathway (i.e. the ring opening and the insertion of molecular oxygen are not concerted). Furthermore, the observation that only a catalytic amount (less than 1 mol %) of $[(phen)_3Fe^{III}](PF_6)_3$ is sufficient for the complete transformation of **1a**−**4a** (Scheme 1) to the corresponding 1,2-dioxolane products **1f**−**4f** (Scheme 2) suggests that the reaction must also be autocatalytic. However, since no detectable ring-opened or any other products were formed under strictly anaerobic conditions in the presence of catalytic amounts of $[(phen)_3Fe^{III}](PF_6)_3$, we conclude that the species responsible for the chain propagation must be one of the oxygen-bound species (see Scheme 5). Furthermore, the predominant formation of polymeric and other oxidized products in the presence of excess catalyst, in contrast to the exclusive formation of the

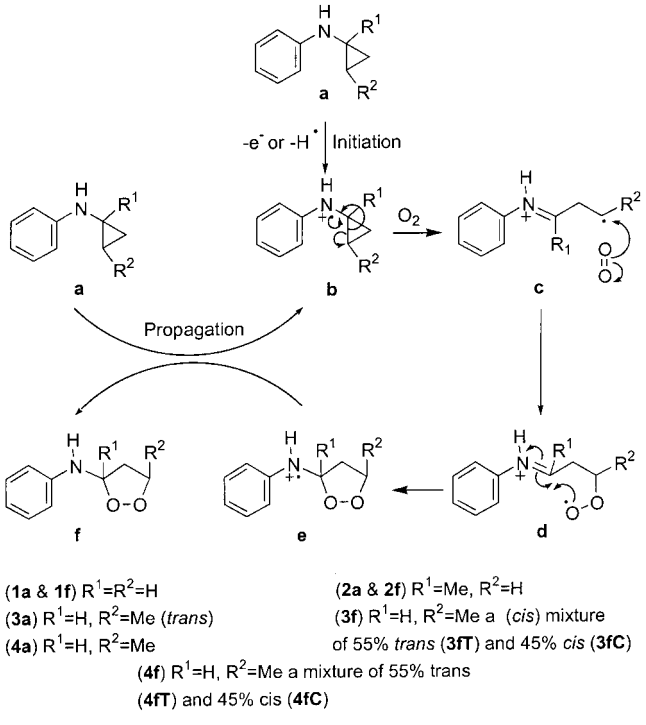
Table 2. Oxidation of *N*-cyclopropyl-*N*-phenylamine derivatives with benzoyl peroxide, *tert*-butyl peroxide, and tris(1,10-phenanthroline)-Fe^{III} hexafluorophosphate under various reaction conditions

Reactant	Conditions	Products [% conversion][a]
1a	$(BzO)_2$, dark, ambient temp., 1 h[b]	**1f/5** (7:3) [100%]
1a	$(BzO)_2$, dark, −20 °C, 3 d	**1f** [100%]
1a	$(BzO)_2$, dark, ambient temp., anaerobic, 1 h	No new products [0%]
1a	$(t\text{BuO})_2$, dark, ambient temp., 5 h	No new products [0%]
1a	$(t\text{BuO})_2$/UV, ambient temp., 2 h	**1f** [100%]
1a	$(t\text{BuO})_2$/UV, ambient temp., anaerobic, 2 h	No new products [0%]
1a	$[(phen)_3Fe^{III}(PF_6)_3]$ (cat. amt.), ambient temp., 1 h	**1f** [100%]
2a	$(t\text{BuO})_2$/UV, ambient temp., 2 h	**2f** [100%]
3a	$(t\text{BuO})_2$/UV, ambient temp., 2 h	$\mathbf{3f_C/3f_T}$ (45:55) [100%]
4a	$(t\text{BuO})_2$/UV, ambient temp., 2 h	$\mathbf{3f_C/3f_T}$ (45:55) [100%]
3a	$(t\text{BuO})_2$/UV, ambient temp., anaerobic, 2 h	No new products [0%]
4a	$(t\text{BuO})_2$/UV, ambient temp., anaerobic, 2 h	No new products [0%]
3a	$(phen)_3Fe(PF_6)_3$ (cat. amt.), ambient temp., 1 h	$\mathbf{3f_C/3f_T}$ (45:55) [100%]
4a	$(phen)_3Fe(PF_6)_3$ (cat. amt.), ambient temp., 1 h	$\mathbf{3f_C/3f_T}$ (45:55) [100%]

[a] The percent conversions were determined by ^1H NMR analysis of the crude reaction mixtures. Isolated yields are generally lower than % conversions and could not be accurately determined due to the instability of the products under rigorous purification conditions. However, estimated isolated yields are in the range of 60−80% of the % conversions for most reactions. − [b] The dioxolane products were found to be converted into the corresponding 3-hydroxy-*N*-phenylpropionamides [$PhNHCOCH_2CH_2OH$ (**5**)] in the presence of excess $(BzO)_2$ at ambient temperatures. However, in the presence of excess $(t\text{BuO})_2$ or catalytic amounts of $[(phen)_3Fe^{III}](PF_6)_3$, the dioxolanes were converted into the corresponding amides only slowly with longer reaction times. The introduction of an equivalent amount of $[(phen)_3Fe^{III}](PF_6)_3$ under similar experimental conditions (both anaerobic and aerobic) led to the generation of a complicated polymeric mixture of unidentifiable products (see Results and Discussion).

1,2-dioxolane under catalytic conditions, strongly suggests that the catalyst behaves primarily as an initiator under the catalytic aerobic reaction conditions.

Based on the above information, a plausible mechanism for the $[(phen)_3Fe^{III}](PF_6)_3$-catalyzed transformation of *N*-cyclopropyl-*N*-phenylamines to the corresponding *N*-(1,2-dioxolan-3-yl)-*N*-phenylamine under aerobic conditions is shown in Scheme 5. The salient mechanistic features of the reaction are: (1) a single-electron abstraction by $[(phen)_3Fe^{III}](PF_6)_3$ to generate the corresponding initial aminium cation radical **b**;[5] (2) a fast and efficient irreversible ring opening of the aminium radical to produce the most stable carbon-centered radical **c** (we have no experimental evidence to allow a distinction to be made as to whether it is the protonated or the unprotonated aminium radical that undergoes the ring-opening reaction); (3) reaction of the carbon radical with molecular oxygen to generate the corresponding peroxy radical **d**, akin to that proposed for the oxygenolysis of vinylcyclopropanes[11] (for a similar proposal, see also ref.[2d]); (4) ring closure of the peroxy radical to produce the corresponding 1,2-dioxolanylaminium radical **e**[12] (again, we believe that ring closure occurs in this step, in analogy to the mechanism proposed for the oxygenolysis of vinylcyclopropanes[11]); (5) abstraction of an electron from the original amine **a** by the 1,2-dioxolanylaminium radical to propagate the chain reaction and to produce the final 1,2-dioxolane product **f** (see Scheme 5). However, we note that a mechanism involving the abstraction of an electron from the original amine **a** by peroxy radical **d** to give the peroxy anion, followed by nucleophilic addition to the iminium species to generate the corresponding 1,2-dioxolane **f**, would be equally possible (see, for example, ref.[13]).



Scheme 5. Proposed mechanism for the formation of *N*-(1,2-dioxolan-3-yl)-*N*-phenylamines from the autocatalytic aerobic radical ring opening of *N*-cyclopropyl-*N*-phenylamines [Note: our results do not distinguish whether the aminium radical intermediates are protonated or unprotonated in the above scheme; while only the protonated intermediates are shown, a similar mechanism involving the unprotonated intermediates could also be envisaged; moreover, we also note that a mechanism involving electron abstraction from the original amine **a** by peroxy radical **d** to give the peroxy anion (and radical-propagating species **b**) followed by nucleophilic addition to the iminium species to generate the corresponding 1,2-dioxolane **f** would be equally possible (see, for example, ref.[13])]

As mentioned above, besides $[(phen)_3Fe^{III}](PF_6)_3$, both $(tBuO)_2$/UV (254 nm) and $(BzO)_2$ were also found to be effective in catalyzing the transformations of **1a**−**4a** to the corresponding 1,2-dioxolanes under aerobic conditions. The data presented in Table 2 indicate that these reactions are also strictly oxygen-dependent and that they are initiated by $tBuO^{\cdot}$ and $BzO^{\cdot}$ radicals. The data also show that 1,2-dioxolane products were further oxidized to the corresponding hydroxyamides, especially by $(BzO)_2$, suggesting that these agents are less specific than $[(phen)_3Fe^{III}](PF_6)_3$. However, as for the $[(phen)_3Fe^{III}](PF_6)_3$-catalyzed reactions, sub-stoichiometric amounts (10 mol %) of these agents were also found to be effective in the quantitative transformation of the above amines to the corresponding 1,2-dioxolanes at longer reaction times (data not shown). The requirement for relatively high concentrations of the reagents and longer reaction times than the $[(phen)_3Fe^{III}](PF_6)_3$-catalyzed reactions could be due to several reasons: (a) the $tBuO^{\cdot}$ or $BzO^{\cdot}$ radicals may only be present at very low levels in the reaction medium due to the mild reaction conditions used; (b) the low concentrations of these radicals may be rapidly quenched by competing reactions with the solvent, reaction intermediates, and/or the products; (c) the rates of the initial reactions of the $tBuO^{\cdot}$ or $BzO^{\cdot}$ radicals with the substrates could be slower than the rates of electron abstractions by $[(phen)_3Fe^{III}](PF_6)_3$. Therefore, in order to reduce the reaction times, most experiments (Table 2) were carried out using excess or stoichiometric amounts of these reagents. However, more than 80−90% of the unchanged peroxides were recovered on workup of the relevant reaction mixtures, again confirming that only sub-stoichiometric amounts of these reagents are necessary to bring about complete transformation and that the reactions are again autocatalytic. The absence of detectable ring-opened or any other products under anaerobic conditions, even using excess reagents [within the standard reaction time frame (1−2 h)], suggests that the rate of quenching of low levels of $tBuO^{\cdot}$ and $BzO^{\cdot}$ radicals by the side reactions must be faster than the rate of the initial N−H proton abstraction from the amines.

The above results suggest that $(tBuO)_2$/UV- and $(BzO)_2$-mediated transformations of **1a**−**4a** to the corresponding 1,2-dioxolanes may also follow the same autocatalytic pathway as $[(phen)_3Fe^{III}](PF_6)_3$-mediated reactions. However, recent studies have shown that peroxide radicals are inefficient in abstracting an electron from amine nitrogen atoms to produce the corresponding iminium radicals.[5] In fact, experimental and theoretical studies have shown that peroxide radicals are more likely to abstract an α-C- or N-proton than to abstract an electron from the nitrogen atom.[5c] Therefore, $(tBuO)_2$/UV- or $(BzO)_2$-mediated reactions are most likely to be initiated by the abstraction of the hydrogen atom from the nitrogen atom.[5c] The possibility that abstraction of an α-ring-H (cyclopropyl-proton) might initiate these reactions was ruled out by the observation that both $(tBuO)_2$/UV and $(BzO)_2$ promote the quantitative production of the corresponding 1,2-dioxolane from **2a**, which does not possess α-ring-protons. Once the initial aminium radical is generated, the reaction may follow the same course as in the single-electron-transfer pathway (Scheme 5). Moreover, based on the similarities between the chemistries of active oxygen species and peroxides, we believe that autooxidation of these amines may also follow a pathway similar to that of the $(tBuO)_2$/UV- or $(BzO)_2$-mediated reactions.

Conclusions

The above results clearly show that the aerobic oxidative ring opening of *N*-cyclopropyl-*N*-phenylamine derivatives quantitatively produces relatively stable, hitherto unknown 3-amino-1,2-dioxolane derivatives. Structure−reactivity studies suggest that the reaction proceeds by an efficient autocatalytic pathway, similar to that proposed for the oxygenation of vinylcyclopropanes.[11] The quantitative oxidative ring-opening chemistry described herein might be useful in modeling the mechanisms of heteroatom oxidations in biological reactions and in the design of effective suicide inhibitors for the relevant enzymes. We are currently examining the scope and limitations of this novel reaction and its potential applications in the mechanistic enzymology of monooxygenases.

Experimental Section

General: NMR spectra were recorded at 300 MHz for ^1H and 75.4 MHz for ^{13}C (proton-coupled and -decoupled), or at 400 MHz for ^1H and 100.5 MHz for ^{13}C (proton-coupled or -decoupled) at 25 °C. All NMR spectra were recorded with samples in $CDCl_3$, using TMS as an internal standard. − All UV irradiations were carried out with light from a 254-nm UV lamp. Products were purified by normal-phase column chromatography using 200−424 mesh silica gel. − TLC analyses were carried out on precoated silica gel plates. All reagents and chemicals used were obtained from various commercial sources and were used without further purification. Although several attempts were made, analytically pure samples of *N*-cyclopropyl-*N*-phenylamines and the corresponding dioxolanes could not be obtained due to their instability under rigorous purification conditions. However, the spectral properties are consistent with their structures.

***N*-Benzylformanilide:** A mixture of formanilide (18.5 g, 0.15 mol), benzyl chloride (18.5 g, 0.15 mol), K_2CO_3 (30.66 g, 0.23 mol), and DMSO/THF (200 mL; 1:2, v/v) was refluxed for 3 days. The reaction mixture was then filtered, concentrated, diluted with CH_2Cl_2 (100 mL), and washed 3 times with water. The crude product was purified by column chromatography on silica gel and crystallized from hexane/CH_2Cl_2. Yield 50%. − ^1H NMR (400 Hz): δ = 5.00 (s, 2 H), 7.09−7.36 (m, 10 H), 8.56 (s, 1 H). − ^{13}C NMR (100.5 MHz): δ = 48.7 (t), 123.9 (d), 126.7 (d), 136.6 (s), 140.9 (s), 162.2 (d).

***N*-Benzylacetanilide:** The same procedure as described for *N*-benzylformanilide was used, except that formanilide was replaced with acetanilide. Yield 45%. − ^1H NMR (400 MHz): δ = 1.89 (s, 3 H), 4.89 (s, 2 H), 6.97−7.32 (m, 10 H). − ^{13}C NMR (100.5 MHz): δ = 22.6 (q), 52.7 (t), 127.2 (d), 127.8 (d), 128.1 (d), 128.5 (d), 128.7 (d), 137.4 (s), 142.8 (s), 170.2 (s).

***N*-Benzyl-*N*-cyclopropyl-*N*-phenylamine:** This compound was synthesized according to the procedure of Chaplinski and de Meijere[7] with minor modifications. A solution of *N*-benzylformanilide (5.1 g, 21.2 mmol) in freshly distilled THF (125 mL) was treated with $Ti(OiPr)_4$ (8 mL, 27.1 mmol) and the resulting mixture was stirred under N_2 for 5 min. A 2.0 M solution of ethylmagnesium bromide in THF (20 mL, 40 mmol) was then added dropwise and the mixture was stirred for 24 h. The reaction was then quenched by the addition of saturated aqueous ammonium chloride solution (75 mL). The resulting mixture was filtered and the filtrate was extracted with CH_2Cl_2. The combined organic layers were concentrated in vacuo and the residue was subjected to chromatography yielding 3.8 g (80%) of the product. − ^{1}H NMR (300 MHz): δ = 0.64−0.70 (m, 2 H), 0.77−0.84 (m, 2 H), 2.59 (tt, *J* = 3.8, 6.5 Hz, 1 H), 4.60 (s, 2 H), 6.73 (t, *J* = 7.3 Hz, 1 H), 6.92 (d, *J* = 8.7 Hz, 2 H), 7.12−7.29 (m, 7 H). − ^{13}C NMR (75.4 MHz): δ = 8.9 (t), 32.7 (d), 56.2 (t), 113.9 (d), 117.4 (d), 126.3 (d), 126.6 (d), 128.4 (d), 128.8 (d), 139.9 (s), 149.8 (s). − $C_{16}H_{17}N$ (223.32): calcd. C 86.06, H 7.67; found C 86.27, H 7.72.

***N*-Benzyl-*N*-(1-methylcyclopropyl)-*N*-phenylamine:** This compound was synthesized according to a procedure analogous to that described above for *N*-benzyl-*N*-cyclopropyl-*N*-phenylamine using *N*-benzylacetanilide; it was obtained in 40% yield after purification. − ^{1}H NMR (400 MHz): δ = 0.96−0.98 (br. s, 2 H), 0.99−1.01 (br. s, 2 H), 1.37 (s, 3 H), 4.51 (br. s, 2 H), 6.68 (t, *J* = 7.3 Hz, 1 H), 6.80 (dd, *J* = 1.10, 8.8 Hz, 2 H), 7.12−7.22 (m, 5 H), 7.24−7.30 (m, 2 H). − ^{13}C NMR (100.5 MHz): δ = 18.8 (q), 21.9 (t), 29.7 (t), 38.1 (s), 54.6 (t), 113.7 (d), 116.5 (d), 127.7 (d), 128.5 (d), 128.8 (d), 140.2 (s), 147.8 (s). − $C_{17}H_{19}N$ (237.34): calcd. C 86.03, H 8.07; found C 86.16, H 8.11.

***N*-Benzyl-*N*-(*cis*- and *trans*-2-methylcyclopropyl)-*N*-phenylamine:** This compound was synthesized as a mixture of *cis* and *trans* isomers according to a procedure analogous to that described above for *N*-benzyl-*N*-cyclopropyl-*N*-phenylamine using propylmagnesium bromide; it was obtained in 68% yield after purification. The two isomers were separated by column chromatography on silica gel. − ***cis* Isomer:** ^{1}H NMR (400 MHz): δ = 0.30 (dt, *J* = 5.9, 4.8 Hz, 1 H), 0.90 (ddd, *J* = 5.5, 7.3, 8.4 Hz, 1 H), 1.10 (d, *J* = 5.9 Hz, 3 H), 1.16 (dddq, *J* = 4.8, 6.5, 8.4, 5.9 Hz, 1 H), 2.61 (ddd, *J* = 4.4, 6.6, 7.3 Hz, 1 H), 4.52 (d, *J* = 17.2 Hz, 1 H), 4.70 (d, *J* = 16.9 Hz, 1 H), 6.74 (tt, *J* = 1.1, 7.3 Hz, 1 H), 6.97 (dd, *J* = 1.1, 7.7 Hz, 2 H), 7.16−7.30 (m, 7 H). − ^{13}C NMR (100.5 MHz): δ = 12.7 (q), 13.3 (t), 15.7 (d), 38.3 (d), 56.5 (t), 114.3 (d), 117.5 (d), 126.50 (d), 126.8 (d), 128.3 (d), 139.9 (s), 150.7 (s). − ***trans* Isomer:** ^{1}H NMR (400 MHz): δ = 0.57 (dt, *J* = 6.6, 5.5 Hz, 1 H), 0.84 (ddd, *J* = 3.7, 4.8, 8.8 Hz, 1 H), 1.02 (dddq, *J* = 3.3, 5.9, 8.8, 6.2 Hz, 1 H), 1.16 (d, *J* = 6.2 Hz, 3 H), 2.28 (dt, *J* = 6.6, 3.3 Hz, 1 H), 4.54 (d, *J* = 16.9 Hz, 1 H), 4.62 (d, *J* = 16.9 Hz, 1 H), 6.73 (tt, *J* = 1.1, 7.3 Hz, 1 H), 6.85 (dd, *J* = 1.1, 8.8 Hz, 2 H), 7.14−7.23 (m, 5 H), 7.24 (m, 2 H). − ^{13}C NMR (100.5 MHz): δ = 16.6 (q), 16.7 (t), 17.2 (d), 40.7 (d), 55.9 (t), 113.7 (d), 117.2 (d), 126.3 (d), 126.6 (d), 128.4 (d), 128.8 (d), 139.9 (s), 149.7 (s). − $C_{17}H_{19}N$ (237.34; analyzed as *cis*/*trans* mixture): calcd. C 86.03, H 8.07; found C 86.19, H 8.07.

***N*-Cyclopropyl-*N*-phenylamine (1a):** A solution of *N*-benzyl-*N*-cyclopropyl-*N*-phenylamine (1.0 g) in methanol (200 mL) and glacial acetic acid (1 mL) was hydrogenated (4 bars) for 4 h in the presence of 10% Pd/C catalyst (100 mg). The reaction mixture was filtered, concentrated, basified, and extracted with CH_2Cl_2. Purification of the crude product by column chromatography on silica gel yielded 62% of *N*-cyclopropyl-*N*-phenylamine (**1a**). − ^{1}H NMR (400 MHz): δ = 0.48−0.52 (m, 2 H), 0.69−0.74 (m, 2 H), 2.41 (tt, *J* = 3.3, 6.6 Hz, 1 H), 4.10−4.20 (br. s, 1 H), 6.73 (t, *J* = 7.3 Hz, 1 H), 6.79 (dd, *J* = 1.1, 8.4 Hz, 2 H), 7.19 (dd, *J* = 7.3, 8.4 Hz, 2 H). − ^{13}C NMR (100.5 MHz): δ = 7.4 (t), 25.2 (d), 113.1 (d), 117.7 (d), 129.1 (d), 148.7 (s).

***N*-(1-Methylcyclopropyl)-*N*-phenylamine (2a):** This compound was obtained in 58% yield by catalytic debenzylation of *N*-benzyl-*N*-(1-methylcyclopropyl)-*N*-phenylamine according to the same procedure as that described above for *N*-cyclopropyl-*N*-phenylamine. − ^{1}H NMR (400 MHz): δ = 0.62 (dd, *J* = 4.4, 6.2 Hz, 2 H), 0.77 (dd, *J* = 4.4, 6.2 Hz, 1 H), 1.35 (s, 3 H), 4.09 (br. s, 1 H), 6.69 (tt, *J* = 1.1, 7.3 Hz, 1 H), 6.73 (dd, *J* = 1.1, 8.4 Hz, 2 H), 7.17 (ddd, *J* = 1.8, 7.3, 8.4 Hz, 2 H). − ^{13}C NMR (100.5 MHz): δ = 15.2 (t), 21.7 (q), 30.2 (s), 113.5 (d), 117.1 (d), 129.1 (d), 147.1 (s).

***N*-(*trans*-2-Methylcyclopropyl)-*N*-phenylamine (3a):** This compound was obtained in 45% yield by catalytic debenzylation of *N*-benzyl-*N*-(*trans*-2-methylcyclopropyl)-*N*-phenylamine according to the same procedure as that described above for *N*-cyclopropyl-*N*-phenylamine. − ^{1}H NMR (400 MHz): δ = 0.49 (ddd, *J* = 5.1, 5.5, 6.6 Hz, 1 H), 0.67 (ddd, *J* = 3.7, 4.8, 8.8 Hz, 1 H), 0.84 (dddq, *J* = 2.9, 5.9, 8.8, 6.2 Hz, 1 H), 1.14 (d, *J* = 6.2 Hz, 3 H), 2.09 (dt, *J* = 6.6, 3.3 Hz, 1 H), 4.05−4.15 (br. s, 1 H), 6.70−6.74 (m, 3 H), 7.18 (dddd, *J* = 1.1, 1.8, 7.3, 8.1 Hz, 2 H). − ^{13}C NMR (100.5 MHz): δ = 15.5 (d), 15.5 (t), 17.1 (q), 33.3 (d), 113.0 (d), 117.5 (d), 129.1 (d), 148.5 (s).

***N*-(*cis*-2-Methylcyclopropyl)-*N*-phenylamine (4a):** This compound was obtained in 55% yield by catalytic debenzylation of *N*-benzyl-*N*-(*cis*-2-methylcyclopropyl)-*N*-phenylamine according to the same procedure as that described above for *N*-cyclopropyl-*N*-phenylamine. − ^{1}H NMR (400 MHz): δ = 0.13 (dt, *J* = 5.5, 4.4 Hz, 1 H), 0.91 (dt, *J* = 4.8, 7.0 Hz, 1 H), 1.00 (ddpent, *J* = 6.6, 6.2, 5.9 Hz, 1 H), 1.10 (d, *J* = 5.9 Hz, 3 H), 2.42 (dt, *J* = 4.0, 7.0 Hz, 1 H), 3.09−4.05 (br. s, 1 H), 6.72 (t, *J* = 7.3 Hz, 1 H), 6.78 (d, *J* = 8.3 Hz, 2 H), 7.18 (dd, *J* = 7.3, 8.4 Hz, 2 H). − ^{13}C NMR (100.5 MHz): δ = 11.9 (q), 12.5 (t), 13.5 (d), 29.8 (d), 112.9 (d), 117.4 (d), 129.1 (d), 149.1 (s).

Oxidation of *N*-Cyclopropyl-*N*-phenylamine and Its Derivatives with *tert*-Butyl Peroxide: A solution of *N*-cyclopropyl-*N*-phenylamine (20 mg, 0.15 mmol) and *tert*-butyl peroxide (50 mg, 0.34 mmol) in $CHCl_3$ (25 mL) was stirred for 1−2 h in a vessel open to the atmosphere while irradiating with light of wavelength 254 nm from a 4-W UV lamp. The solution was subsequently concentrated in vacuo and its composition was analyzed by ^{1}H NMR spectroscopy.

Oxidation of *N*-Cyclopropyl-*N*-phenylamine and Its Derivatives with Benzoyl Peroxide: A solution of *N*-cyclopropyl-*N*-phenylamine (15 mg, 0.11 mmol) and benzoyl peroxide (27.3 mg, 0.11 mmol) in $CHCl_3$ (10 mL) was stirred in the dark for 45 min in a vessel open to the atmosphere. The solution was subsequently washed with aqueous Na_2CO_3 solution, concentrated in vacuo, and analyzed by ^{1}H NMR spectroscopy.

Oxidation of *N*-Cyclopropyl-*N*-phenylamine and Its Derivatives with Tris(1,10-phenanthroline)iron(III) Hexafluorophosphate: A solution of *N*-cyclopropyl-*N*-phenylamine (25 mg, 0.19 mmol) and a catalytic amount of $[(phen)_3Fe^{III}](PF_6)_3$ (ca. 1 mg, 0.6 mol %) in $CHCl_3$ (25 mL) was stirred for 1 h in a vessel open to the atmosphere at room temperature. The solution was subsequently filtered through a plug of silica, concentrated in vacuo, and analyzed by ^{1}H NMR spectroscopy.

***N*-(1,2-Dioxolan-3-yl)-*N*-phenylamine (1f):** ^{1}H NMR (400 MHz): δ = 2.39 (dddd, *J* = 3.4, 8.1, 8.4, 12.9 Hz, 1 H), 3.05 (dddd, *J* =

3.1, 7.3, 8.1, 12.9 Hz, 1 H), 4.01 (dt, J = 8.4, 8.1 Hz, 1 H), 4.32 (ddt, J = 0.8, 3.1, 8.1 Hz, 1 H), 4.50 (br. d, $J \approx 9$ Hz, 1 H), 5.74 (ddd, J = 3.4, 7.3, 9.3 Hz, 1 H), 6.76 (dd, J = 0.8, 8.6 Hz, 2 H), 6.84 (tt, J = 1.1, 7.4 Hz, 1 H), 7.21 (dd, J = 7.4, 8.6 Hz, 2 H). − ^{13}C NMR (100.5 MHz): δ = 41.6 (t), 69.1 (t), 85.4 (d), 114.8 (d), 119.9 (d), 129.3 (d), 144.8 (s). − MS: *m*/*z* (%) = 165 (12), 132 (32), 105 (49), 93 (37), 86 (43), 77 (44).

***N*-(3-Methyl-1,2-dioxolan-3-yl)-*N*-phenylamine (2f):** ^{1}H NMR (400 MHz): δ = 1.69 (s, 3 H), 2.60 (ddd, J = 4.6, 8.3, 12.6 Hz, 1 H), 2.75 (ddd, J = 7.2, 8.0, 12.6 Hz, 1 H), 4.21 (ddd, J = 7.2, 8.0, 8.3 Hz, 1 H), 4.34 (dt, J = 4.6, 8.0 Hz, 1 H), 6.91 (tt, J = 1.1, 7.5 Hz, 1 H), 6.95 (ddd, J = 1.1, 2.0, 7.5 Hz, 1 H), 7.19−7.24 (m, 3 H). − ^{13}C NMR (100.5 MHz): δ = 23.0 (q), 46.5 (t), 70.2 (t), 119.4 (d), 120.9 (d), 128.9 (d), 141.9 (s).

***N*-(*cis*- and *trans*-5-Methyl-1,2-dioxolan-3-yl)-*N*-phenylamine ($3f_T$ + $3f_C$ and $4f_T$ + $4f_C$). − *N*-(*cis*-5-Methyl-1,2-dioxolan-3-yl)-*N*-phenylamine:** ^{1}H NMR (400 MHz): δ = 1.31 (d, J = 6.3 Hz, 3 H), 2.28 (ddd, J = 3.7, 7.5, 12.9 Hz, 1 H), 2.62 (ddd, J = 4.3, 6.9, 12.9 Hz, 1 H), 4.49−4.55 (br. s, 1 H), 4.58 (dddq, J = 0.6, 4.6, 6.9, 6.3 Hz, 1 H), 5.71 (dd, J = 4.3, 7.5 Hz, 1 H), 6.72−6.76 (m, 2 H), 6.82 (dq, J = 7.5, 1.2 Hz, 1 H), 7.17−7.21 (m, 2 H). − ^{13}C NMR (100.5 MHz): δ = 16.5 (q), 47.5 (t), 76.21 (d), 85.84 (d), 114.57 (d), 119.66 (d), 144.75 (s). − MS: *m*/*z* (%) = 179 (63), 146 (51), 132 (100), 93 (81), 77 (28), 43 (28). − **N-(*trans*-5-Methyl-1,2-dioxolan-3-yl)-*N*-phenylamine:** ^{1}H NMR (400 MHz): δ = 1.36 (d, J = 6.0 Hz, 3 H), 1.89 (ddd, J = 4.0, 8.6, 12.9 Hz, 1 H), 3.11 (ddd, J = 6.9, 7.2, 12.9 Hz, 1 H), 4.31 (ddq, J = 8.6, 6.6, 6.0 Hz, 1 H), 4.47−4.50 (br. s, 1 H), 5.68 (dd, J = 4.0, 7.2 Hz, 1 H), 6.72−6.76 (m, 2 H), 6.82 (dq, J = 7.5, 1.2 Hz, 1 H), 7.17−7.21 (m, 2 H). − ^{13}C NMR (100.5 MHz): δ = 19.8 (q), 48.5 (t), 77.0 (d), 86.7 (d), 114.4 (d), 119.7 (d), 129.2 (d), 144.8 (s). − MS: *m*/*z* (%) = 179 (63), 146 (51), 132 (100), 93 (81), 77 (28), 43 (28).

Supporting Information: ^{1}H-NMR spectra of compounds **1a**−**4a** (Scheme 1) and **1f**−**4f** (Scheme 2) and 2D ^{1}H-NMR spectrum of **1f**.

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