ionophore concentrations, of any 3:1 species. Therefore, a compensating process is needed for maintenance of electroneutrality; either anionic cotransport or cationic counter transport is required to complete the transport cycle.

We have checked this by adding picric acid, which indeed facilitates proton equilibration across the membrane. Addition of picric acid (0.4 mM) to a vesicle solution containing X-537A (2×10^{-4} M) increases the Pr^{3+} transport velocity by a factor of 1.8—when picric acid alone is unable to effect Pr^{3+} transport under our experimental conditions, This observation is consistent with operation of a counter transport of protons from the inside to the outside of the vesicles,[28]

The A and B molecules are carboxylic acids, as is the case for all the ionophores studied here (see the formulas), except for M139603 and tetronomycin, which are acyl ylidene tetronic acids and therefore closely related to carboxylic acids. Hence, with all the ionophores studied here, while the A_2 and B_2 systems have each a single pK_a, the AB hybrid has *two* pK_a values, This is a unique distinguishing feature of any AB system, as compared to the A_2 and B_2 cases, Therefore, when a proton migrating outward from the inner compartment of a vesicle encounters such an AB hybrid, the proton transfer A-COOH + B-COO^-, → A-COO^- + B-COOH will assist in the *penetration* of this proton inside the membrane. A similar statement applies to the sodium counterions, and many authors have shown that the rate-determining step, in ionic transport phenomena, occurs at the water–membrane interface,

This hypothesis leads to the prediction that A and B need not be both ionophore antibiotics for synergistic ionic transport across membranes to be set up. Indeed mixtures of lasalocid and crown ether carboxylic acids[29] give rise to similar positive cooperativities[30,31] as reported here. Furthermore, at the pH 6,1 of our experiments, tetronomycin (pK_a = 2.52) and M139603 (pK_a = 1.8 in 1:9 methanol–water) are fully ionized, which is consistent with the high transport rates found with these carriers (Table I). Lasalocid (pK_a = 5.13 in 66% dimethylformamide) differs significantly in acidity from the other ionophores with which it gives rise to synergistic transport (Table II): it is less acidic than the two above-quoted molecules and more acidic than X-206, X-14547A, monensin, and A21387, according to the published pK_a values (obviously, these pK_a's will differ in the lipidic environment, this has been shown for fatty acids,[32] but the sequence of relative acidities should remain the same). Hence, a likely origin for the observed synergistic transport appears to be the pK_a differences that are set as soon as two chemically distinct ionophores are comixed in a membrane environment. The pH dependence of the synergism (Table III) is also consistent with the mechanism implied here for Pr^{3+} transport,

Acknowledgment. We are grateful for ionophore samples to Dr, N. Belcher (Pfizer, Groton, CT), Dr. J. H. Westley (Hoffmann-La Roche, Nutley), Dr. D. H. Davies (ICI, Macclesfield, UK), Dr. A. von Wartburg (Sandoz, Basel, Switzerland), Dr. D. Dorman (Eli- Lilly, Indianapolis , IN), and Dr. B. Vuillemin (Rhône-Poulenc, Vitry, France), We also thank Dr. A. Delville for his help in the minimization procedure. Fonds de la Recherche Fondamentale Collective, Brussels, allocated Grants 2.4504.78 and 21420 D, for the purchase of the NMR spectrometer used in this study, and a grant "Crédit aux chercheurs" No. 1.5.965.80F, which served for updating it. We acknowledge with thanks the useful reviews by the referees, which allowed us to better substantiate the claims made in this article.

Registry No. A23187, 52665-69-7; M139603, 75139-05-8; X-14547A, 66513-28-8; X-537A, 25999-31-9; narasin, 55134-13-9; tetronomycin, 82206-10-8; etheromycin, 59149-05-2; monensin, 17090-79-8; praseodymium, 7440-10-0; sodium, 7440-23-5.

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Oxygen Transfer from Oxaziridines: A Chemical Model for Flavin-Dependent Monooxygenases[1]

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Abstract: The ability of several aryloxaziridines to transfer an oxygen atom to phenolates was examined. 2-(*p*-Nitrophenyl)-3-*tert*-butyloxaziridine (**1**) was found to oxidize potassium 2,6-dialkylphenolates to the corresponding *p*-benzoquinones. Product studies and an observed ESR signal suggest an electron-transfer mechanism for these oxidations. ^{18}O-Labeled oxaziridine **30** was prepared. Oxidations of phenolates with **30** rigorously establish the oxaziridine ring oxygen as the atom that is transferred to substrate. Kinetic studies with oxaziridine **1** and the isomeric nitrone **15** rule out the nitrone as an obligate intermediate in the oxygen-transfer reaction, In the oxidation of substrate, a single electron transfer from phenolate to oxaziridine is thought to generate a phenoxy/nitroxyl radical pair, which upon coupling and fragmentation achieves the oxygen transfer. These oxygen-transfer reactions serve as models for the proposed flavin-based oxaziridine **34** in enzyme-mediated monooxygenations.

The flavin-dependent monooxygenases catalyze the incorporation of one atom of molecular oxygen into a substrate with concomitant reduction of the second atom to water.[2] The binding and activation of molecular oxygen is central to flavin monooxygenase reactivity, yet the nature of the active oxygenating species remains unknown. Recent evidence indicates that 4α-hydroperoxyflavin (**33**, Scheme III) is an initial intermediate in these oxidations; this intermediate and derived species have been offered to explain the flavin, oxygen-transferring systems.[3] We

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(2) (a) Walsh, C. T. *Acc. Chem. Res.* **1980**, *13*, 148. (b) Hemmerich, P. *Prog. Chem. Org. Natl. Prod.* **1976**, *33*, 451. (c) Massey, V.; Hemmerich, P. *Enzymes* **1975**, *3*, 191–252. (d) Flashner, M. S.; Massey, V. In "Molecular Mechanism of Oxygen Activation"; Hayaishi, O., Ed.; Academic Press: New York, 1974; pp 245–283.

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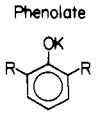
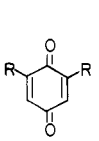
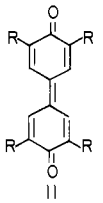
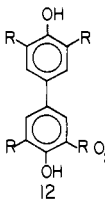
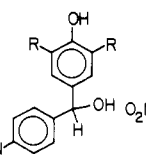
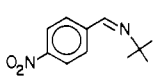
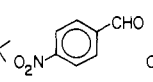
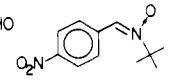
Table I. Oxygenations Effected by Oxaziridine 1 on Phenolate Substrates[a]

Phenolate	Products[b]						
 2	 10	 11	 12	 13	 7	 14	 15
2a (R = t-butyl)	10a, 15%[c]	11a, 30%	12a, 1%	13a, 6%	2%	7%	1%
2b (R = isopropyl)	10b, 38%	–	–	–	11%	5%	–
2c (R = methyl)[d]	10c, 34%	–	–	–	7%	15%	–

[a] Reactions 0.09 M in oxaziridine and phenolate in degassed *tert*-butyl alcohol at 25 °C. [b] Isolated yields based on phenolate. Structures confirmed by ^{1}H NMR, IR, MS, and GLC and TLC coelution with authentic materials. [c] 39% with 5 equiv of 18-crown-6 present (GLC yield, products not isolated). [d] 5 equiv of 18-crown-6 added.

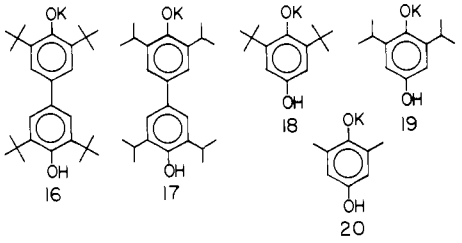


Figure 1. Hydroquinone anions oxidized to quinones by **1** in *tert*-butyl alcohol at 25 °C.

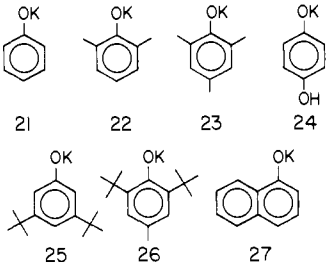
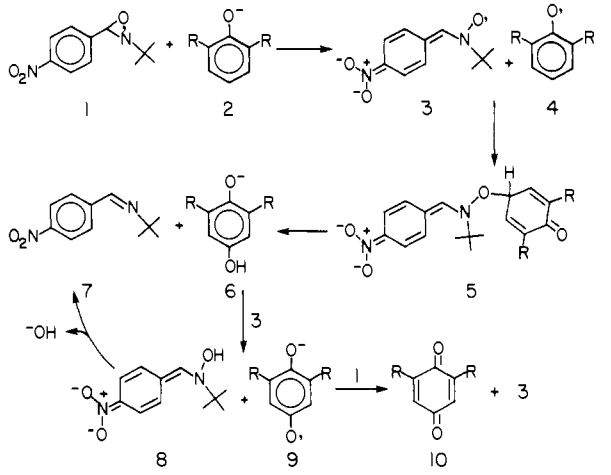


Figure 2. Substrates found unreactive toward oxygenation by oxaziridine **1**. No 18-crown-6 added.

have implicated a flavin N^5-nitroxyl radical in the nonenzymatic transfer of oxygen from flavin N^5-oxides to phenolates, and have speculated on in vivo nitroxyl radical formation by electron transfer to a flavin oxaziridine (i.e., **34** → **36**).[4] We present here our study of aryloxaziridines as electron acceptors and of oxygen transfer from the resulting nitroxyl radical anions to phenoxy radicals. Our results support the viability of the proposed[3b] flavin-based oxaziridine **34** as an activated intermediate in monooxygenase reactions.

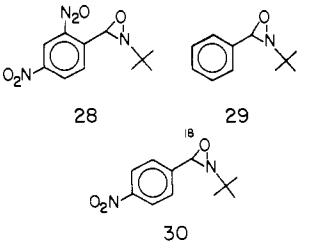
Model Reactions. 2-(*p*-Nitrophenyl)-3-*tert*-butyloxaziridine (**1**)[5] oxidizes several 2,6-dialkylphenolates to *p*-benzoquinones

Scheme I



(Table I) at ambient temperature in anhydrous *tert*-butyl alcohol. Addition of 18-crown-6 is essential for oxidation of potassium 2,6-dimethylphenolate (**2c**) and increases the yield of benzoquinone formation from potassium 2,6-di-*tert*-butylphenolate (**2a**). Facile oxidation of hydroquinone anions **16**–**20** (Figure 1) to the corresponding quinones is effected by oxaziridine **1**. The slow oxidation of anion **20** is greatly accelerated by addition of 18-crown-6 (5 equiv). Figure 2 shows substrates found unreactive toward oxaziridine **1**.

Dinitro-substituted oxaziridine **28** has been prepared by MCPBA oxidation of (2,4-dinitrobenzylidene)-*tert*-butylamine,



the product of the condensation of 2,4-dinitrobenzaldehyde and *tert*-butylamine. When allowed to react with phenolate **2a**, a 44% yield of *p*-benzoquinone **10a** is observed (GLC) after 1 h (cf. **1** + **2a**, Table I; 15% yield of **10a** after 8 h).

The mechanism of Scheme I is consistent with oxygenation of phenolates by **1**. Electron transfer from phenolates to oxaziridine (**1** + **2** → **3** + **4**) followed by coupling (**3** + **4** → **5**) and fragmentation (**5** → **6** + **7**) affords hydroquinone anion **6**. Subsequent

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(4) (a) Rastetter, W. H.; Gadek, T. R.; Tane, J. R.; Frost, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 2228. (b) Frost, J. W.; Rastetter, W. H. *Ibid.* **1981**, *103*, 5245.

(5) Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5739.

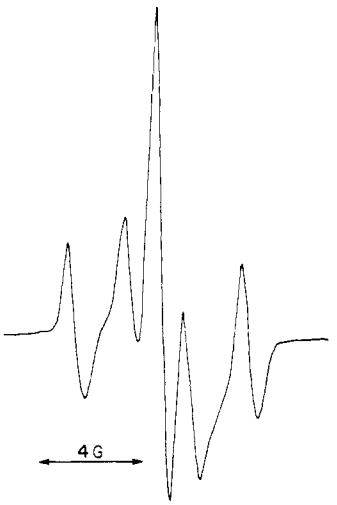


Figure 3. ESR spectrum observed in reaction mixture of phenolate **2a** with oxaziridine **1** in anhydrous *tert*-butyl alcohol at 25 °C. a_H = 1.1 and 2.2 G, g = 2.00. This same pattern was observed in reaction mixtures of **2a** with oxaziridine **29** and nitrone **15** (see text).

oxidation of hydroxylated product (**6**) by sequential hydrogen atom abstraction (**6** + **3** → **9**) and electron transfer (**9** + **1** → **10** + **3**) yields *p*-benzoquinone (**10**). This mechanism finds precendent in the phenolic oxidations effected by Fremy's salt[6] and other nitroxyl radicals.[4b,7]

Reactions of phenolate with oxaziridine is facilitated by increase in the steric bulk of the 2- and 6-position substituents[8] and/or complexation of potassium counterion. Increased separation of potassium cation from phenolate anion increases (or determines, cf. **2c**) the reactivity of the substrate toward oxaziridine, likely by lowering the activation barrier to electron transfer (i.e., **1** + **2** → **3** + **4**).[9]

The mechanism of Scheme I is supported by the observation of a strong ESR signal attributable to the stable 2,6-di-*tert*-butyl-*p*-semiquinone radical (**9**). A five-line pattern (Figure 3) is observed upon mixing oxaziridines **1** or **29**[10] with phenolate **2a** in anhydrous, degassed *tert*-butyl alcohol at 25 °C. This pattern is typical of semiquinone radicals in this solvent.[11] As precedented,[11] these spectra collapse from five to three lines (g = 2,007, a_H = 1.4 G) upon changing the solvent to anhydrous ethanol, a better solvating medium.[11,12]

Product studies further support radical intermediates. In addition to *p*-benzoquinones, products indicative of phenoxy radical dimerization[13] have been isolated from reactions of **1** with phenolates. Formation of phenol dimers **11a** and **12a** in the oxidation of phenolate **2a** by oxaziridine **1** suggests diffusion of some phenoxy radical out of the solvent cage prior to the coupling reaction (**3** + **4** → **5**). The more highly oxidized diphenoquinone **11a** arises by in situ oxidation of **12a**, e.g., by a second equivalent

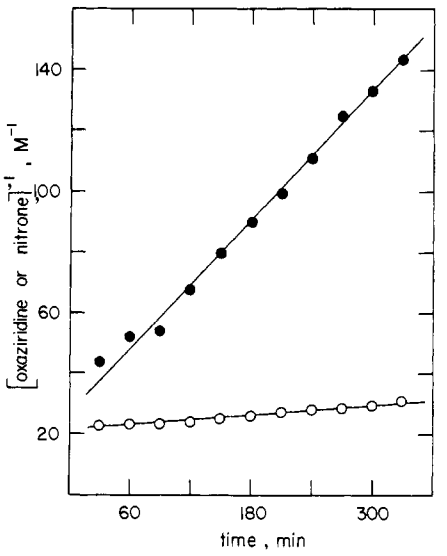
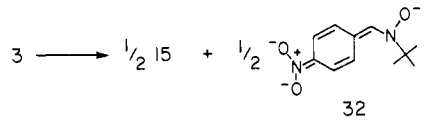


Figure 4. Rate of disappearance of oxaziridine **1** (●) and nitrone **15** (○) in reactions with phenolates **2a** in *tert*-butyl alcohol at 25 °C. 10^3k: oxaziridine, 6.42 ± 0.07 M^{-1} s^{-1}; nitrone, 0.37 ± 0.03 M^{-1} s^{-1}. Error limits represent 95% confidence.

Scheme II



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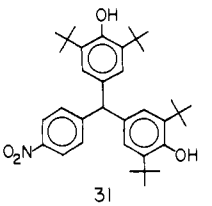
of **1**.[3] The observation of diphenoquinone only in the reactions of phenolate **2a** may reflect relative phenoxy radical stabilities.[14] The product, *p*-nitrobenzaldehyde (**14**) is believed to result from base hydrolysis of **7** (the reaction **8** → **7** liberates HO^-, see Scheme I). Condensation of **14** and phenolate **2a** in the reaction mixture affords benzhydrol **13**. A control reaction of **14** and **2a** in *tert*-butyl alcohol at 25 °C yields **13** (6%) and **31** (4%). Similar



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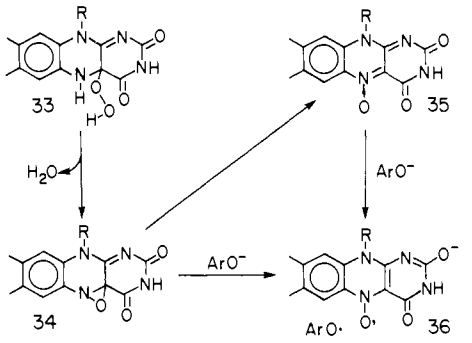
reactions of phenols and aromatic aldehydes under basic conditions have been reported.[13a]

The dimerization of phenoxy radicals (e.g., see **11a** and **12a**) raises the question of the fate of the coincident nitroxyl radical anions (**3**) not participating in adduct formation (i.e., **3** + **4** → **5**). Disproportionation of **3** is believed to yield nitrone **15** (Table I) and hydroxylamine anion **32** (Scheme II). Protonation and elimination of HO^- from **32** affords imine **7**. Nitrone **15**[5] has been isolated in 1% yield in the reaction of phenolate **2a** and oxaziridine **1**.

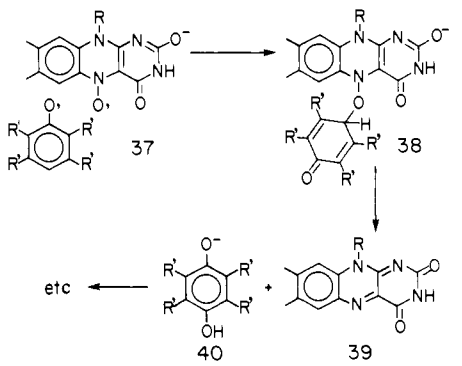
Nitrone **15** has been prepared[5] and is found reactive toward phenolate **2a** in a manner analogous to oxaziridine **1** (vide supra). In the presence of phenolate **2a**, rate constants for the disappearance of **1** and **15** are significantly different (Figure 4; 10^3k: oxaziridine, 6.42 ± 0.07 M^{-1} s^{-1}; nitrone, 0.37 ± 0.03 M^{-1} s^{-1}). This greater than 10-fold rate difference excludes nitrone **15** as an obligate intermediate in the oxidations of phenolates by oxaziridine **1** and implicates direct electron transfer from phenolate to oxaziridine in the rate-determining step of oxygen transfer. Electron transfer to either **1** or **15** apparently yields, albeit at

(6) Teuber, H.-J.; Dietz, K. H. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 871.
(7) Forrester, A. R.; Thompson, R. H. *J. Chem. Soc. C* **1965**, 1224; **1966**, 1844.
(8) Similar reactivity differences of 2,6-dialkylphenols in other reactions have been noted: see ref 12a.
(9) Bruice has noted the effect of *tert*-butyl substitution on the electron density and reactivity of phenolates toward flavin hydroperoxides; see: Kemal, C.; Bruice, T. C. *J. Am. Chem. Soc.* **1979**, *101*, 4017.
(10) No product studies have been conducted using oxaziridine **29**.
(11) The observed spectra have been interpreted as the superposition of two triplets arising from a tightly bound ion pair and a free or weakly associated anion and cation. See the following: (a) Lucken, E. A. C. *J. Chem. Soc.* **1964**, 4234. (b) Oakes, J.; Symons, M. C. R. *Trans Faraday Soc.* **1968**, *64*, 2579. (c) Pannell, J. *Chem. Ind. (London)* **1962**, 1797. More likely, the triplets arise from two, nonequilibrating, isomeric, tight ion pairs, i.e., with the cation bound at each of two nonequivalent oxygen atoms.
(12) Swain, C. G.; Swain, M. S.; Powell, A. L.; Alunni, S. *J. Am. Chem. Soc.* **1983**, *105*, 502.
(13) (a) Coffield, T. H.; Filber, A. H.; Ecke, G. G.; Kolka, A. J. *J. Am. Chem. Soc.* **1957**, *79*, 5019. (b) Walling, C.; Hodgdon, R. B., Jr. *Ibid.* **1958**, *80*, 228. (c) Nonhebel, D. C.; Walton, J. C. "Free Radical Chemistry"; Cambridge University Press: New York, 1974; pp 326–410.
(14) (a) Buchachenko, A. L. "Stable Radicals"; Consultants Bureau: New York, 1973; pp 57–59. (b) Ingold, K. U. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973.

Scheme III



Scheme IV



different rates, the same nitroxyl radical (i.e., **3**). A mixture of nitrone **15** and phenolate **2a** in anhydrous *tert*-butyl alcohol (25 °C) displays the same five-line, semiquinone ESR signal observed in reactions of **2a** with oxaziridines **1** or **29** (Figure 3, vide supra).

^{18}O-Labeled oxaziridine **30** (38% ^{18}O) has been prepared by oxidation of *N*-(*p*-nitrobenzylidene)-*tert*-butylamine (**13**) by ^{18}O-labeled MCPBA.[15] Oxaziridine **30** is efficient in label transfer in the oxidation of phenolate **2a** to *p*-benzoquinone **10a** ($(M + 2)^+/M^+ = 0{,}37$). The efficient transfer of ^{18}O label rigorously establishes the oxaziridine ring oxygen as the atom that is transferred. Similar ^{18}O-labeling experiments have been used to study phenolic oxidations by nitroxides.[16]

Discussion

The study of oxygen transfer from oxaziridines is of interest, per se and as a model for biochemical monooxygenations. Davis et al. have examined oxygen transfer from 2-sulfonyloxaziridines in the oxidations of sulfides and disulfides,[17] olefins,[18] carbanions,[19] sulfenic acids,[20] and selenides.[21] The intermediacy of a flavin-based oxaziridine **34** in monooxygenase hydroxylations was first proposed by Orf and Dolphin[3b] and has been extensively modified by Rastetter et al.[4]

Our previous studies have demonstrated nonenzymatic oxygen transfer to phenols from excited-state flavin N^5-oxide[4a] and to phenolates from ground-state flavin N^5-oxide (**35**, Scheme III),[4b]

In the ground-state reaction of N^5-oxide **35** and phenolate, a nitroxyl radical anion (see **36**) has been characterized by ESR.[4b] The products formed by reaction of phenolate and ^{18}O-labeled N^5-oxide **35** point to the nitroxyl radical anion as the active, oxygen-transferring species.

As precedented by the model studies reported herein, oxaziridines may give rise to nitroxyl radical anions upon single electron transfer from phenolates. Thus, flavin oxaziridine **34**, were it isolable in the laboratory,[22] might accept an electron from phenolate to give the previously generated (see **35** → **36**) radical pair, **36**. The generation of the flavin N^5-nitroxyl radical from either flavin N^5-oxide **35** or flavin oxaziridine **34** parallels the similar reactivities of nitrone **15** and oxaziridine **1**. The mechanism envisaged for monooxygenase-mediated phenolate oxygenation (Scheme IV) utilizes radical coupling (**37** → **38**) and adduct formation (**38** + **39** → **40**) reactions analogous to the processes (**3** + **4** → **5** and **5** → **6** + **7**, respectively) of Scheme I.

In enzyme-mediated monooxygenations, the Orf–Dolphin oxaziridine **34** may arise from putative 4α-hydroperoxyflavin **33** by N^5-displacement at the proximal hydroperoxy oxygen atom. This dehydration is directly precedented by the conversion of other α-hydroperoxyamines into oxaziridines.[23]

The present model study shows that appropriately conjugated oxaziridines are viable oxygen-transferring ring systems for oxygenation of phenols. Kinetic studies (vide supra) indicate that nitrones are less reactive toward phenolate anions than are the oxaziridines. Hence, in the biological reaction, isomerization of flavin oxaziridine to flavin N^5-oxide (i.e., **34** → **35**) need not precede electron transfer. Indeed, relief of ring strain in the homolysis of the oxaziridine C–O bond may serve to drive the one-electron reduction (**34** → **36**, cf. **1** → **3**).[24] The possibility that nitrone **35** represents the active flavin nitroxyl precursor has been examined. Riboflavin N^5-oxide (cf. **35**) bound to *p*-hydroxybenzoate hydroxylase and other monooxygenase apoenzymes failed to oxygenate substrates.[25] These results and our present kinetic studies appear to rule out the nitrone as the active oxygenating intermediate.

In its simplicity, the flavin-based oxaziridine is attractive, especially in light of other, more exotic mechanistic proposals.[3,26] The oxidation of phenolates by oxaziridines demonstrated here serve as models[27] for the enzymatic reactions of the proposed[3b] flavin oxaziridine intermediate.

Experimental Section

^1H NMR spectra were obtained on a Varian T-60 (60 MHz) or Bruker WM-270 (270 MHz) spectrometer. Chemical shifts are reported downfield from tetramethylsilane (Me_4Si) on the δ scale. Internal Me_4Si was utilized at 60 MHz and residual $CHCl_3$ reference was utilized at 270 MHz. Infrared spectra were recorded on a Perkin-Elmer 283B grating infrared spectrometer. Mass spectra were recorded on a MAT-44 spectrometer. ESR spectra were obtained on a Varian E-Line spectrometer. Gas-liquid chromatographic (GLC) analyses were carried out on a Varian Series 3700 chromatograph using He as carrier gas. An 8 ft × 1/8 in. 4.1% Carbowax or Zonyl E-7 column on Chromosorb G and a flame-ionization detector were used. Peaks were identified by coinjection with authentic materials. Melting points are uncorrected.

All solvents were distilled from appropriate drying agents and stored over activated 4-Å molecular sieves under N_2. *tert*-Butyl alcohol was degassed through 3 freeze-pump-thaw cycles to an ultimate pressure of 2×10^{-2} mmHg.

Phenols were purchased and purified by recrystallization or distillation prior to use. When not commercially available, authentic quinones,

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diphenoquinones, and bis(phenols) were prepared according to literature procedures. 18-Crown-6 was obtained from Aldrich Chemical Co. and dried by azeotropic distillation. Potassium *tert*-butoxide was purified by sublimation.

All glassware used was flame dried and cooled under a N_2 stream immediately prior to use.

Preparation of Oxaziridine 30. Imine **7**[5] (787 mg, 3.82 mmol) was dissolved in CH_2Cl_2 (2 mL). ^{18}O-Labeled *m*-chloroperoxybenzoic acid[14] (800 mg, 39% labeled, 4.59 mmol active oxygen) was dissolved in CH_2Cl_2 (18 mL). The solutions were cooled to 0 °C and combined. The mixture was stirred at 0 °C for 2 h, then sequentially washed with $NaHSO_3$ (saturated aqueous, 25 mL), $NaHCO_3$ (saturated aqueous, 2 × 25 mL), and H_2O (25 mL). Drying ($MgSO_4$) and evaporation of solvent in vacuo yielded a slightly yellow solid, which was chromatographed on silica gel (20% EtOAc/pentane). The resulting crystals were recrystallized (petroleum ether) to yield oxaziridine **30** (651 mg, 76%) as white needles (mp 62–63 °C): ^1H NMR (60 MHz, $CDCl_3$) 1.23 (9 H, s), 4.85 (1 H, s), 7.65 (2 H, d, J = 9 Hz), 8.33 (2 H, d, J = 9 Hz); IR ($CHCl_3$) 2980, 2875, 1790, 1765, 1725, 1605, 1515, 1470, 1420, 1345, 1295 cm^{-1}. The ratio of the m/e 225 [$(M + 1)^+$, [^{18}O]oxaziridine] to m/e 223 [$(M + 1)^+$, [^{16}O]oxaziridine)] mass peaks was 0.38.

Preparation of Oxaziridine 28. 2,4-Dinitrobenzaldehyde (1.13 g, 5.8 mmol) and *tert*-butylamine (848 mg, 11.6 mmol) were dissolved in Et_2O (10 mL) over activated 4-Å sieves (4.5 g). The mixture was allowed to stand for 16 h. The solution was filtered and evaporated in vacuo to yield (2,4-dinitrobenzylidene)-*tert*-butylamine as a brown solid (1.45 g, 95%, mp 74.5–75.5 °C): ^1H NMR (60 MHz, $CDCl_3$) 1.32 (9 H, s), 8.20 (1 H, s), 8.30 (1 H, d, J = 2 Hz), 8.55 (1 H, S), 8.75 (1 H, d, J = 2 Hz); IR (KBr pellet) 2960, 2870, 1605, 1535, 1350, 1225, 1195, 905, 835, 740, 720 cm^{-1}.

(2,4-Dinitrobenzylidene)-*tert*-butylamine (1.04 g, 4.10 mmol) was dissolved in CH_2Cl_2 (5 mL). *m*-Chloroperoxybenzoic acid (853 mg, 4.90 mmol active oxygen) was dissolved in CH_2Cl_2 (50 mL). The two solutions were cooled to 0 °C, combined, and allowed to stir at 0 °C for 5 h. The resulting solution was filtered and sequentially washed with $NaHSO_3$ (saturated aqueous, 2 × 25 mL), $NaHCO_3$ (saturated aqueous, 2 × 25 mL), and H_2O (25 mL). Evaporation in vacuo afforded a brown oil. Trituration (petroleum ether, 0 °C) of the oil yielded **30** (422 mg, 39%) as a yellow solid (mp 57–59 °C): ^1H NMR (60 MHz, $CDCl_3$) 1.30 (9 H, s), 5.60 (1 H, s), 7.98 (1 H, d, J = 8 Hz), 8.58 (1 H, dd, J = 2, 8 Hz), 9.00 (1 H, d, J = 2 Hz); IR (KBr pellet) 3125, 3100, 3060, 2975, 1620, 1610, 1580 (br), 1350 (br), 1270, 1250 cm^{-1}. Anal. Calcd for $C_{11}H_{13}N_3O_5$: C, 49.43; H, 4.91; N, 15.72. Found: C, 49.61; H, 5.07; N, 15.51.

Reaction of *p*-Nitrobenzaldehyde and Potassium 2,6-Di-*tert*-butylphenolate. 2,6-Di-*tert*-butylphenol (543 mg, 2.62 mmol) and potassium *tert*-butoxide (294 mg, 2.62 mmol) were dissolved in *tert*-butyl alcohol (5 mL) under N_2 atmosphere. *p*-Nitrobenzaldehyde (396 mg, 2.62 mmol) was dissolved in *tert*-butyl alcohol (5 mL) and $CHCl_3$ (0.5 mL) in a separate flask under N_2. The phenolate solution was transferred via cannula into the aldehyde solution and allowed to stir at room temperature for 72 h. The mixture was concentrated in vacuo, eluted through a small silica plug (15% EtOAc/pentane), and chromatographed on silica (silica gel PTLC, 15% EtOAc/pentane) to yield two compounds, **31** (51 mg, 4%) and **13** (55 mg, 6%) as orange semisolids.

Data for **31**: ^1H NMR (270 MHz, $CDCl_3$) 1.37 (36 H, s), 5.13 (2 H, s), 5.40 (1 H, s), 6.89 (4 H, s), 7.28 (2 H, $^1/_2$AB q, J = 6.9 Hz), 8.12, (2 H, $^1/_2$AB q, J = 6.9 Hz); IR ($CHCl_3$) 3625, 2050, 2960, 2875, 1655, 1595, 1520, 1430, 1350, 1320, 1235, 1155, 1120, 1070, 895, 860 cm^{-1}; MS, m/e 545 (M^+).

Data for **13**: ^1H NMR (270 MHz, $CDCl_3$) 1.41 (18 H, s), 5.27 (1 H, s), 5.85 (1 H, s), 6.47 (1 H, s), 7.58 (2 H, s), 7.60 (2 H, $^1/_2$AB q, J = 8.6 Hz), 8.21 (2 H, $^1/_2$AB q, J = 8.6 Hz); IR ($CHCl_3$) 3625, 2050, 2960, 2880, 1595, 1520, 1425, 1345, 1245, 1180, 1070, 885, 860 cm^{-1}; MS, m/e 357 (M^+).

Reactions of Oxaziridine 1 with Phenolates. Oxaziridine 1 (200 mg, 0.90 mmol) was placed in a 25-mL round-bottomed flask and sealed under N_2. The phenol (0.090 mmol) and potassium *tert*-butoxide (101 mg, 0.90 mmol) were placed in separate flasks and sealed under N_2. *tert*-Butyl alcohol (10 mL) was charged into the flask containing the phenol, and the solution was degassed through three freeze–pump–thaw cycles. This phenolic solution was transferred via cannula to the flask containing the *tert*-butoxide and stirred until the mixture became homogeneous. This solution was transferred via cannula to the stirred oxaziridine. Solutions of reactive phenolates (see text) turned dark green; no color change was observed with unreactive phenolates (see Figure 2). Reactions were monitored by GLC and worked up after 72 h. Products were isolated by concentration in vacuo and silica gel column chromatography (5–10% EtOAc/pentane). All products were identified by ^1H NMR, IR, MS, and TLC comparisons with authentic materials, purchased or prepared by literature procedures. Yields are found in Table I.

Reaction of Oxaziridine 28 with Phenolate 2a The reaction of ^{18}O-labeled oxaziridine **28** (100 mg, 0.45 mmol) and potassium 2,6-di-*tert*-butylphenolate (120 mg, 0.49 mmol) in *tert*-butyl alcohol (10 mL) was conducted as previously described for the reaction of **1** and **2a** (vide supra). The reaction mixture was allowed to stir at room temp for 4 days. Concentration in vacuo and chromatography (2-mm silica gel PTLC, 15% EtOAc/pentane) afforded ^{18}O-labeled 2,6-di-*tert*-butylbenzoquinone (19.5 mg, 18%). Data for quinone: NMR, IR, and mp same as that for quinone **10a**; MS ratio, m/e 220/222 ($M^+/(M + 2)^+$) 0.37.

Reaction of 1 and 15 with Phenolate 2a: Rate Determination. The reaction of oxaziridine **1** and nitrone **15** (20.0 mg, 0.09 mmol) with potassium 2,6-di-*tert*-butylphenolate (22.1 mg, 0.09 mmol) in *tert*-butyl alcohol (2 mL) was conducted as previously described (vide supra). The disappearances of **1** and **15** were monitored by GLC (SE-30 for **1**, Zonyl E-7 for **15**; decane internal standard) over 6 h. The reciprocal of the concentration of **1** or **15** vs. time was plotted (Figure 4) to determine the rate constants.

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Registry No. 1, 26378-36-9; **2a**, 24676-69-5; **2b**, 88343-91-3; **2c**, 58425-33-5; **7**, 718-36-5; **10a**, 719-22-2; **10b**, 1988-11-0; **10c**, 527-61-7; **11a**, 2455-14-3; **12a**, 128-38-1; **13a**, 88343-92-4; **14**, 555-16-8; **15**, 3585-88-4; **16**, 88343-93-5; **17**, 88343-94-6; **18**, 81882-94-2; **19**, 88343-95-7; **20**, 88343-96-8; **28**, 88343-97-9; **30**, 84279-01-6; **31**, 77621-69-3; *m*-chloroperoxybenzoic acid, 937-14-4; 2,4-dinitrobenzaldehyde, 528-75-6; *tert*-butylamine, 75-64-9; (2,4-dinitrobenzylidene)-*tert*-butylamine, 88343-98-0; *p*-nitrobenzaldehyde, 555-16-8; monooxygenase, 9038-14-6; oxygen, 7782-44-7.