spectra showed $(M + 1)^+$ peaks at m/z 531, 499, and 515 for **10**, **11**, and **12**, respectively, with no appreciable, higher m/z values in any of the spectra. The molecular formulas were confirmed by high-resolution FAB mass spectra.

Thus, we have accomplished the total synthesis of three representative compounds which have a high degree of complexity (five N-heteroaromatic rings containing a total of eight nitrogens; ribosyl or deoxyribosyl groups on the appropriate nitrogens for cross-sectional analogy; and, pro forma, eight, six, or seven asymmetric carbons). The synthesis requires only three steps from ribo- or deoxyribonucleosides plus initial O-protection and final O-deprotection. The compounds represent respectively a covalently linked RNA cross section, 1,9-di-(β-D-ribofuranosyl)-3*H*-pyrimido[1″,6″:1′,2′]imidazo[4′,5′:4,5]imidazo[2,1-*i*]purin-8(9*H*)-one (**10**); a covalently linked DNA cross section, 1,9-bis-(2′-deoxy-β-D-ribofuranosyl)-3*H*-pyrimido[1″,6″:1′,2′]imidazo[4′,5′:4,5]-imidazo[2,1-*i*]purin-8(9*H*)-one (**11**);[15] and a covalently linked DNA/RNA hybrid cross section, 1-(2′-deoxy-β-D-ribofuranosyl)-9-(β-D-ribofuranosyl)-3*H*-pyrimido[1″,6″:1′,2′]-imidazo[4′,5′:4,5]imidazo[2,1-*i*]purin-8(9*H*)-one (**12**). These highly fluorescent molecules are worthy of further chemical and biological investigations.

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(15) The pyrimidine methyl group is lacking in this initial model in the bis(deoxyribosyl) series.

Oxidation of 3,5,5-Trimethyl-2-oxomorpholin-3-yl (TM-3) with Molecular Oxygen. Generation of a Persistent Aminyl Radical[1]

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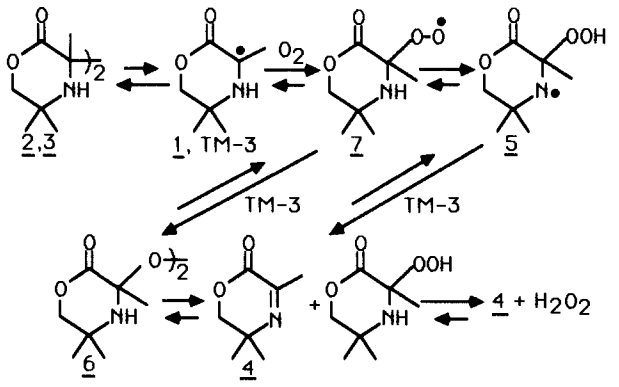
The captodative free radical 3,5,5-trimethyl-2-oxomorpholin-3-yl (**1**, TM-3) from bond homolysis of *meso*- and *dl*-bi(3,5,5-trimethyl-2-oxomorpholin-3-yl) (**2** and **3**) is oxidized to 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) by molecular oxygen.[2] Because the oxomorpholinyls have pharmaceutical potential as mild one-electron reducing agents for in vivo manipulation of quinone antitumor drugs,[3] we initiated a study of the mechanism of their oxidation by molecular oxygen including determination of the reduced oxygen species produced. Earlier studies of other redox reactions of TM-3 suggested that reduction occurred by single electron transfer.[4]

Here we report that oxidation of TM-3 with molecular oxygen gives a quantitative yield of **4** and hydrogen peroxide at least in part via covalent bond formation and with the generation of a persistent aminyl radical. Quantitative or near quantitative (95 ± 5%) formation of **4** was observed for oxidation in chloroform, acetonitrile, ethanol containing 0.32 M magnesium perchlorate, and methanol solvents as indicated by UV and ^{1}H NMR spectroscopy. Quantitative formation of hydrogen peroxide, 1 equiv per radical dimer, was observed in the latter three media; the best yield in chloroform, where hydrogen peroxide was not stable, was 58%. Hydrogen peroxide analyses were performed initially by HPLC/peroxychemiluminescence spectroscopy[5] and subsequently by spectrophotometric analysis of the product of reaction with titanium tetrachloride.[6] Oxidation of TM-3 dimer **2** or **3** followed first-order kinetics, monitoring formation of **4** spectrophotometrically at its maximum, 320 nm. The rate constant was the rate constant for bond homolysis of **2** or **3**;[7] at 25.0 ± 0.1 °C, k = (3.1 ± 0.2) × 10^{-6} (**2** in chloroform), (1.82 ± 0.004) × 10^{-5} (**2** in acetonitrile), (2.22 ± 0.01) × 10^{-3} (**2** in ethanol containing 0.32 M magnesium perchlorate), (2.38 ± 0.02) × 10^{-3} (**2** in methanol), and (4.49 ± 0.03) × 10^{-3} s^{-1} (**3** in methanol). TM-3 also reacted with hydrogen peroxide with formation of oxazinone **4**, but the rate was more than 2 order of magnitude lower.

Scheme I



The initial observation which indicated that oxidation of TM-3 by molecular oxygen might involve covalent bond formation was the observation of a paramagnetic species giving a three-line 1:1:1 EPR signal with g = 2.0060 and a_N = 14 G and g = 2.0057 and a_N = 15 G in air-saturated chloroform and ethanol containing 0.32 M magnesium perchlorate solutions of radical dimers **2** or **3**, respectively; the 24-line signal characteristic of TM-3 was absent. With solutions of **2** at high concentration (e.g., 0.1 M), the three-line signal increased in intensity with time and then abruptly disappeared after a period approximately equal to the time necessary for reduction of at least 95% of the dissolved oxygen, calculated from the rate constant for bond homolysis and the solubility of oxygen which is in the range of 1.5 × 10^{-3} M.[8] At this point the 24-line TM-3 EPR signal appeared. Shaking with air restored the three-line signal and destroyed the 24-line signal. The cycle could be repeated several times. The three-line EPR signal suggested the formation of either an aminyl or nitroxide bonded to unprotonated carbons. A nitroxide structure was eliminated because the EPR signal still appeared as a 1:1:1 pattern with 80% enriched $^{17}O_2$ as the oxidant. The hydrogen peroxide formed contained ^{17}O, detected by using the hydrogen peroxide to oxidize 4-oxo-2,2,6,6-tetramethylpiperidine to its [^{17}O]nitroxide and subsequent EPR analysis.[9,10]

A mechanism for the oxidation of TM-3 with the intermediacy of aminyl **5** is shown in Scheme I. Two pathways to oxazinone **4** and hydrogen peroxide are proposed because the rise in the concentration of **5** is not synchronous with the formation of **4** and hydrogen peroxide. The nonsynchronous behavior was observed when the oxidation was conducted with an excess of oxygen in ethanol containing 0.32 M magnesium perchlorate. In fact, under these conditions **5** could be easily observed even at low initial

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concentration of radical dimer **2**; magnesium cation stabilizes the aminyl radical analogous to its stabilization of TM-3.[11] With an excess of oxygen, **5** reached its maximum concentration long after 99% of **2** had been oxidized to **4**.[12] At this point addition of **2** resulted in the rapid disappearance of the three-line EPR signal of **5** and the appearance of the 24-line signal of TM-3. Although peroxide **6** was not visible by ^1H NMR, its formation is consistent with the formation of peroxides from reaction of triphenylmethyl with oxygen.[13]

The reversibility of oxidation of **2** is proposed because reaction of oxazinone **4** with hydrogen peroxide gave a persistent radical showing a three-line EPR signal identical with the signal assigned to aminyl **5**. The intensity of the signal was comparable to the intensity observed for the air oxidation of **2** at equivalent concentrations, and the same EPR signal was observed by using hydrogen peroxide labeled with ^{17}O.[14] Mixing of solutions containing equal concentrations of the persistent radical from oxidation of **2** with oxygen and reaction of hydrogen peroxide with **4** gave a solution showing a single three-line EPR signal with the same intensity. Furthermore, freeze, pump, thaw degassing of solutions of aminyl **5** formed from **2** and oxygen after consumption of **2** increased the rate of disappearance of the aminyl EPR signal.[12] The reversible formation of bis(triarylmethyl) peroxides has been established.[15]

The reversibility of the oxidation of **2** was consistent with the relative maximum EPR signal intensities for **5** resulting from different initial concentrations of **2**. The mechanism in Scheme I predicts that $[\mathbf{5}] = K_c[\mathbf{4}][H_2O_2]^{1/2}$ where K_c is a composite equilibrium constant. Solutions of **2**, 0.06, 0.08, and 0.12 M, in ethanol containing 0.32 M magnesium perchlorate were reacted with oxygen to completion; the EPR signal heights were measured; and the resulting concentrations of **4** and hydrogen peroxide were determined. The measured and calculated relative signal intensities were 1:2.5:5.7 and 1:2.1:4.8, respectively. The signal intensity starting with 0.08 M **2** indicated that the maximum concentration of **5** was approximately 1×10^{-5} M by comparison with standard solutions of 4-oxo-2,2,6,6-tetramethylpiperidinoxy.

The formation and persistence of **5** appears to be anomalous. Aminyl radicals are in general less persistent than **5** unless resonance stabilized, show g values in the range of 2.004-2.005 with a_N = 12.5-16 G, and react with molecular oxygen.[16] The half-life of 2,2,6,6-tetramethylpiperidinyl at 24 °C is less than 35 s.[10] Gas-phase N-H and O-H bond energies for simple secondary amines and hydrogen peroxide suggest that $\mathbf{7} \Rightarrow \mathbf{5}$ would be slightly endothermic.[17] Possibly, intramolecular hydrogen bonding to the hydroperoxy functional group provides some additional stabilization of **5** and gives rise to the high g value. 2-Aminophenoxy, *o*-semiquinones and -semidiones,[18] and *tert*-butyl(2-hydroxy-1-phenylethyl)nitroxide[19] have been shown to exhibit intramolecular hydrogen bonding. Although aminyl radicals generally react with oxygen to give nitroxides, an example which does not is 4-oxo-2,2,6,6-tetramethylpiperidinyl.[20]

In summary, we report evidence that oxidation of TM-3 with molecular oxygen yields stoichiometric quantities of hydrogen peroxide with generation of an unusually persistent aminyl radical. We have also found that other radicals of this type, including 3,5-dimethyl-5-hydroxymethyl-2-oxomorpholin-3-yl,[3] 3,5,5-trimethyl-2-oxopiperizin-3-yl,[21] and the oligomers of the diradical bi(3,5,5-trimethyl-2-oxomorpholin-6-yl)-3,3′-diyl,[22] produce persistent aminyl radicals upon exposure to air. The mechanism in Scheme I for oxidation of TM-3 is related to the mechanisms proposed for the air oxidation of dicyclohexylamine,[23] indoles including tryptophan to kynurenine,[24] tetrahydrofolate,[25] and reduced flavins.[26]

Registry No. 1, 57765-64-7; *meso*-**2**, 53153-52-9; (±)-**3**, 53153-53-0; **4**, 53153-46-1; **5**, 103150-35-2.

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Molecular and Electronic Structure of $Cu(tet\text{-}b)SSCH_2CO_2 \cdot 3CH_3OH$, a Novel Copper(II) Alkyl Persulfide Complex

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A few Cu(II) aromatic[1-5] and aliphatic[6,7] thiolate complexes have been structurally characterized; most are transient species having varied decomposition pathways,[8-11] some of which may be blocked. We have crystallized a *cis*-$Cu^{II}N_2S_2$ complex[7] ligated by a linked L-cysteine ester [$^-SCH_2(CO_2CH_3)NHCH_2^-$]$_2$ (**2**); the parent Cu(cysteine)$_2$ complex[11] and ternary Cu(cysteine) complexes[8-10] are quite unstable. We report here a novel Cu(II) thiolate redox reaction that yields a stable Cu(II)-alkyl persulfide complex and provides new structural and spectroscopic guideposts for mechanistic studies.

In an attempt to prepare the mercaptoacetate analogue of $Cu(tet\text{-}b)SCH_2CH_2CO_2$ (**3**),[6] ether was vapor diffused at 6 °C into a filtered solution of 0.5 mM $Cu(tet\text{-}b)^{2+}$,[2] 1.3 mM KOH, and 0.65 mM $HSCH_2CO_2H$ or its dicyclohexylamine salt[12] in 8 mL of methanol. Complex **1** crystallized as thin green plates in

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