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Selective Autoxidation of Electron-Rich Substrates under Elevated Oxygen Pressures

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We report here the observation of a novel autoxidation pathway which occurs with electron-rich substrates. Tertiary amines, dialkyl thioethers, olefins, and alkynes under high oxygen pressures (>20 bars of O_2), in polar solvents, and at elevated temperatures (>90 °C) yield in good to excellent selectivity amine oxides, sulfoxides, and *site-specific* olefin and alkyne cleavage products, respectively. The results of mechanistic studies, including high oxygen pressure electrochemical studies, are discussed. A mechanism for this novel oxygenation reaction pathway that is consistent with the observed results is proposed. It involves an initial unfavorable electron transfer from the electron-rich substrate to oxygen to yield superoxide and the radical cation, which reacts with triplet oxygen to yield the oxygenated radical cation intermediate, a suspected potent oxidant. Electron transfer to the oxygenated radical cation from additional substrate (chain reaction) or superoxide yields a zwitterionic intermediate. This intermediate either reacts with additional substrate (O-atom transfer) to yield product (sulfoxide and *N*-oxide, in the case of thioethers and tertiary amines) or is converted with unimolecular reactivity to dioxetane-like (in the case of alkenes) or dioxetene-like (in the case of alkynes) derived products.

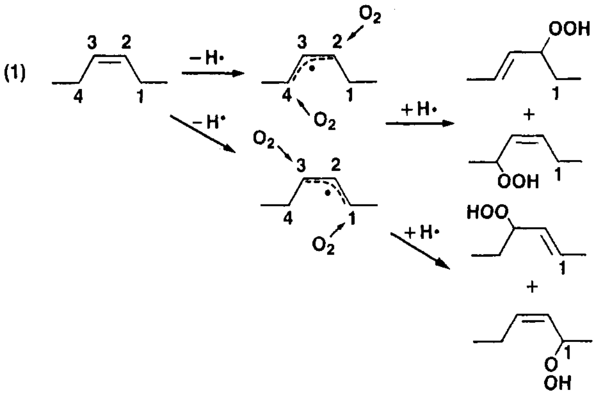
Introduction

The air-induced oxidation (autoxidation) of organic substances is a well-known reaction,[1-3] in which great progress in the discovery and study of natural free-radical processes has been made.[4] The ubiquitous presence of oxygen in our environment has fed this interest since autoxidation processes can have such a profound effect chemically, e.g., rancidity, diseases, etc. Consequently, studies of ambient O_2 pressure autoxidations of various organic substrates have led to a reasonable understanding of such processes and, in particular, the types of products such processes yield. For example, olefin autoxidations yield allylic hydroperoxides,[5,6] where as many as four isomers can be formed in statistically equal amounts (Scheme I),[3] and their reaction with additional olefin yields epoxides and alcohols. The intermediate hydroperoxy radicals themselves can react in a bimolecular fashion to yield ketone, alcohol, and oxygen.[5,6] The autoxidation of alkynes also yields products which result from preferential attack at the C–H bonds α to the triple bond.[7] As a consequence, propargylic hydroperoxides and their corresponding alcohol and ketone decomposition products are observed under ambient pressures.[3,7]

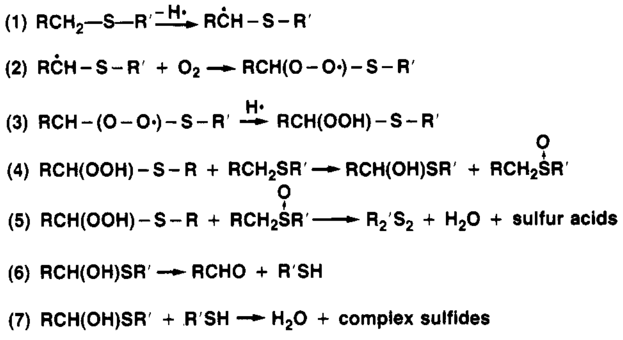
The autoxidation of thioethers (R_2S) under ambient O_2 pressures has also been intensively studied. These autoxidations also occur primarily by abstraction of the α-hydrogens to yield intermediate α-hydroperoxy compounds and ultimately acids (aldehydes), mercaptans, disulfides, and thiohemiacetals (Scheme II).[8-12]

Tertiary amines have also been studied,[13] and in common with these other organic substrates, the autoxidation chemistry is dominated by α-CH abstraction. Although initial electron transfer to form the amminium radical cation likely occurs, loss of a proton to form the α-CH radical followed by oxygenation results in the α-hydroperoxy species. This hydroperoxide is capable of oxidizing additional tertiary amine to its *N*-oxide. Indeed, varying amounts of *N*-oxide are observed (up to 40%) during the autoxidation of tertiary amines under ambient conditions.[13]

Scheme I



Scheme II



$$(1)\ RCH_2{-}S{-}R' \xrightarrow{-H\cdot} R\dot{C}H{-}S{-}R'$$

$$(2)\ R\dot{C}H{-}S{-}R' + O_2 \rightarrow RCH(O{-}O\cdot){-}S{-}R'$$

$$(3)\ RCH{-}(O{-}O\cdot){-}S{-}R' \xrightarrow{H\cdot} RCH(OOH){-}S{-}R'$$

$$(4)\ RCH(OOH){-}S{-}R + RCH_2SR' \rightarrow RCH(OH)SR' + RCH_2\overset{O}{S}R'$$

$$(5)\ RCH(OOH){-}S{-}R + RCH_2\overset{O}{S}R' \rightarrow R_2'S_2 + H_2O + \text{sulfur acids}$$

$$(6)\ RCH(OH)SR' \rightarrow RCHO + R'SH$$

$$(7)\ RCH(OH)SR' + R'SH \rightarrow H_2O + \text{complex sulfides}$$

Our studies of selective metal ion catalyzed oxygen oxidations at elevated temperatures and pressures have prompted us to investigate the liquid-phase reaction of molecular oxygen with these electron-rich organic substrates under conditions of *high* oxygen concentration

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(1) Lyons, J. E. *Hydrocarbon Process.* **1980**, *59* (Nov), 107.

(2) *Oxygen and Oxy-Radicals in Chemistry and Biology*; Rodgers, M. A. J., Powers, E. L., Eds.; Academic: New York, 1981.

(3) Simic, M. G. *J. Chem. Educ.* **1981**, *58*(2), 125.

(4) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic: New York, 1981; Chapters 2–4.

(5) Ingold, K. U. *Acc. Chem. Res.* **1969**, *2*, 1.

(6) (a) Van Sickle, D. E.; Mayo, F. R.; Arluck, R. M.; Syz, M. G. *J. Am. Chem. Soc.* **1967**, *89*, 967. (b) Van Sickle, D. E.; Mayo, F. R.; Gould, E. S.; Arluck, R. M. *J. Am. Chem. Soc.* **1987**, *89*, 977.

(7) (a) Pritzkow, W.; Rao, T. S. S. *J. Prakt. Chem.* **1985**, *327*(6), 887. (b) Dao, L. T. A.; Karla, B.; Pritzkow, W.; Schmidt-Renner, W.; Voerckel, V.; Willecke, L. *J. Prakt. Chem.* **1984**, *326*(1), 73.

(8) Howard, J. A.; Korcek, S. *Can. J. Chem.* **1971**, *49*, 2179.

(9) Bateman, L.; Cuneen, J. I. *J. Chem. Soc.* **1955**, 1596.

(10) Bateman, L.; Cuneen, J. I.; Ford, J. *J. Chem. Soc.* **1956**, 3056.

0022-3263/88/1953-1695$01.50/0

Table I. Oxidation of Tertiary Amines with Molecular Oxygen at High Pressures and Elevated Temperatures

amine (concn, M)	solvent	P_{O_2} (bars)	temp, °C	time, h	yield as of % conversion (% conversion)
trimethylamine (0.5)	H_2O	68[a]	100	14	98% Me_3NO (32)
trimethylamine (2.4)	H_2O	68	100	64	>95% Me_3NO (100)
trimethylamine (1.0)[b]	H_2O	68	100	64	0.4% Me_3NO (1)
trimethylamine (0.5)	CH_3CN	68	100	64	63% Me_3NO (30)
N,N-dimethyldodecylamine (0.22)	4:1 $MeOH/H_2O$	14	100	64	>95% *N,N*-dimethyldodecylamine oxide (100)
N-methylmorpholine (0.20)	H_2O	71	115	72	72% *N*–methylmorpholine oxide (88)
N,N-dimethylaniline (0.17)	4:1 $MeOH/H_2O$	71	105	23	<16% *N,N*-dimethylaniline oxide (>90)[c]
pyridine	H_2O	71	100	16	no rctn
N,N-dimethylbenzylamine (0.15)	2:1 $MeOH/H_2O$	71	115	7	66% *N,N*-dimethylbenzylamine oxide 15% benzaldehyde (84)

[a] O_2 concentration 0.11 M in water. [b] pH = 2.2. [c] *N*-Methylaniline is ~70% of converted amine.

($\geq$0.1 M). To attain such concentrations we have routinely carried out reactions at O_2 pressures of 70 bars or greater. At these oxygen pressures, oxygen concentrations in excess of 0.1 M are attained. In polar solvents and at moderately elevated temperatures (~100 °C), we have found that molecular oxygen will react with olefins, alkynes, thioethers,[12] and tertiary amines[13] in the absence of initiators or catalysts to yield products *uncharacteristic* of the above-described autoxidations carried out at ambient pressures. The oxygenation chemistry observed at high oxygen concentrations, as well as preliminary kinetic and mechanistic studies, is described in this report.

Experimental Section

Materials. All olefins and alkynes were purchased from either Wiley Organics or Aldrich Chemical Co., were checked for purity by capillary GC, and were purified by distillation or recrystallization when necessary. The acids used as standards were supplied by Aldrich or MCB. Benzil was purchased from the J. T. Baker Chemical Co. The *trans*-stilbene oxide used as a standard was purchased from Aldrich. The remaining epoxides were prepared by MCPBA (Aldrich) oxidation of the corresponding olefins in methylene chloride (MCB) and gave satisfactory analytical data (NMR, IR, mp, MS) in accord with literature values when available. Benzaldehyde was obtained from MCB. Benzophenone was obtained from Wiley Organics. The 1-phenyl-1,2-propanedione was supplied by Aldrich. Acetonitrile used as solvent was supplied by MCB (Omnisolv) or Fisher (HPLC grade) and was distilled from calcium hydride under argon prior to use. All the thioethers utilized were purchased from Aldrich, and the sulfoxides and sulfones were synthesized by standard methods. Dimethyl sulfone (Aldrich) and dodecane (Aldrich) were used as GC internal standards. Ultrahigh-purity oxygen (99.99%) was suppled by Matheson.

Procedures. Reaction mixtures containing 2% substrate by weight were placed in an all-*glass* liner (scrupulously cleaned, metal free) in a rocking autoclave (Autoclave Engineers) pressurized to pressures as high as 1000 psig of O_2 and heated rapidly to the reaction temperature. **Caution** must be exercised in performing such studies. Since these reactions are carried out above the flammable limits of acetonitrile, it is important that the pressure vessels be equipped with pressure release setups such as calibrated rupture disks (1200–1500 psi rated disks). Further it is recommended that such equipment be located in specially constructed pressure cells well-shielded from the experimentalist. Sampling with Teflon lines was accomplished by the use of HPLC valves in order to monitor reaction kinetics. Reactions at 200 psig of O_2 or less were run in a Griffen–Worden reactor described elsewhere.[14] Samples were analyzed directly by using a Hewlett-Packard 5880 gas chromatograph with a level IV terminal and a flame-ionization detector. Oxidation products were analyzed by using a 30 m × 0.25 mm DB-1 (J & W Scientific) capillary column with a 0.25-mm film thickness. Helium was used as the carrier and makeup gas. Most analyses were performed with the following temperature program: 115 °C for 5 min, 10 °C/min to 310 °C, 5-min hold. Other analyses include the following: 40 °C for 5 min, 10 °C/min to 180 °C, 10-min hold (3-dodecyne, 12m OV101 from Hewlett-Packard); 60 °C for 2 min, 4 °C/min to 220 °C, 10 min final (ester analyses, 30m DB-5 (J & W) or DB-1). Yields were determined by comparison with calibrated solutions of products and internal standard. More reproducible acid yields were obtained by esterification with 20% BF_3 in methanol followed by extraction with hexanes or ether and GC analysis.

Electrochemical studies were performed by using a PAR 175 programmer, a PAR 173/174 potentiostat, PAR 4102 signal recorder, a Hewlett-Packard HP9825 computer, a Helwlett-Packard HP7225A plotter, and a PAR 9895A disk drive. Some cyclics were recorded on a Houston Instruments 2000-6-5 X-Y recorder. Tetrabutylammonium tetrafluoroborate (0.1 M) was used as the electrolyte and was crystallized and dried before use. A glassy carbon electrode was used for the cyclic voltammetry, and an Ag/AgCl reference electrode was employed. NMR spectra were recorded on Varian CFT20 (^{13}C) and JEOL 270 (^{1}H and ^{13}C) instruments.

Results

Tertiary Amine Autoxidation. The autoxidation of tertiary amines proceeds slowly under high oxygen pressures ($\geq$50 bars) at elevated temperatures (>90 °C) in polar solvent media to yield, in some instances, high yields of *N*-oxides (Table I).[15] The autoxidation when performed in aqueous media leads to the highest yields of *N*-oxide product, likely due to the fact that *N*-oxides undergo Cope elimination chemistry in anhydrous media.[16] To obtain homogeneous solutions with non-water-soluble amines, we used alcohol cosolvents. In such systems only very low levels of alcohol oxidation products resulted; therefore, peracids are not the *N*-oxide-producing oxidants in these systems. The yields of *N*-oxides in aqueous media are generally in excess of 50% for trialkyl amines, even though these autoxidations are very slow and require several days for high conversions. Aromatic tertiary amines such as pyridine are unreactive, and activated amines such as substituted anilines are subject to dealkylation with little *N*-oxide formation. Also ammonium cations of the tertiary amines are virtually unreactive under these conditions.

The autoxidation of trialkyl amines at high O_2 pressures is first-order in molecular oxygen and also first-order in the tertiary amine substrate. Selectivity to *N*-oxide is also dependent on O_2 pressure (see supplementary table), with selectivity increasing as O_2 pressure increases. The temperature dependence of the autoxidation of dimethyldodecylamine at 68 bars of O_2 in 4:1 $EtOH/H_2O$ over the temperature range 80–115 °C gives an activation energy of 19.8 kcal/mol (see supplementary Figure I). The effect of ring size on the rate of autoxidation has been investi-

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[11] Bateman, L.; Cuneen, J. I.; Ford, J. *J. Chem. Soc.* **1957**, 1539.

[12] Wallace, T. J.; Pobiner, H.; Baron, F. A.; Schriesheim, A. *Chem. Ind.* (*London*) **1965**, *27*, 945.

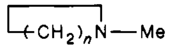
[13] Beckwith, A. L. J.; Eichinger, P. H.; Mooney, B. A.; Prager, R. H. *Aust. J. Chem.* **1983**, *36*, 719.

[14] Shumate, R. E.; Riley, D. P. *J. Chem. Educ.* **1984**, *16*(10), 923.

[15] Riley, D. P.; Correa, P. E. *J. Org. Chem.* **1985**, *50*, 1563.

[16] Laughlin, R. G. *J. Am. Chem. Soc.* **1973**, *95*, 3295.

Table II. Rate Constants for the Autoxidation of Cyclic *N*-Methyl Tertiary Amines at 90 °C under 68 Bars of Oxygen Pressure in Water

k_{obs}, h^{-1}	rel rate[a]	 n	rel rate for $Fe(CN)_6^{3-}$ oxidation[b]
0.38	7.6	4	53
≥0.05	1	5	1.0
1.	38	6	420

[a] Selectivity to *N*-oxide ≥75% in all cases. [b] Reference 14.

gated by using three cyclic *N*-methyl tertiary amines: *N*-methylpyrrolidine, *N*-methylpiperidine, and *N*-methylhexamethyleneimine (Table II). The ring size plays a very important role in the rate of autoxidation, with the slowest rate occurring on oxidation of the six membered ring amines. The ring-size effects noted in these autoxidations parallel those exhibited on the rate of oxidation of the same amines with hexacyanoferrate^{3-}.[17]

Thioether Autoxidations. In general the autoxidations of aliphatic thioethers proceed at elevated temperatures (~100 °C) and pressures (P_{O_2} ~70 bars) to yield sulfoxides in very high yield (see Table III).[18] These reactions are slow, but are first-order in the substrate thioether (see supplementary Figure II for data pertaining to decyl methyl sulfide). The observed reaction rates also were found to exhibit a first-order dependence in oxygen pressure over the pressure range studied (60–100 bars) (see supplementary Figure III for methionine in H_2O). In general, the selectivity to sulfoxide also increases as the oxygen pressure increases.

Solvent polarity also plays a key role in affecting the selectivity to sulfoxide in these high-pressure autoxidations. In Table IV are shown the results of a series of autoxidations of benzyl methyl sulfide. The selectivity for sulfoxide is very dependent on the solvent, i.e., the selectivity for sulfoxide increases as the solvent polarity increases.

The study of the effect of ring size (Table V) on the rate of the autoxidation of three thioethers, tetrahydrothiophene, pentamethylene sulfide, and hexamethylene sulfide, reveals that ring size again plays a role in the relative rate of autoxidation with a similar reactivity trend, but the magnitude of the effect is considerably diminished over that observed with the tertiary amines. The temperature dependence on the rate of autoxidation was studied for the benzyl methyl sulfide at 70 bars of O_2 over the temperature range 85–120 °C. Activation energies were found to be 22 kcal/mol in a 3:2 CH_3CN/H_2O solvent system and 25.8 kcal/mol in CH_3CN (see supplementary Figure IV).

Olefin and Diene Autoxidations. In Table VI are listed examples of high oxygen pressure autoxidations of olefins. The reactions were carried out at elevated temperatures (100–125 °C), and under these conditions, the reactions generally proceed slowly in the absence of any initiators or catalysts. These olefin autoxidations are first-order in olefin concentration (see supplementary Figure V for a *trans*-stilbene study), and the observed reaction rates are first-order in oxygen pressure over the ranges investigated (28–70 bars). The rates are also observed to parallel the ease of oxidation as reflected in the oxidation potential of each olefin within a series of similar olefins. An example of this trend is found in the relative ease of oxidation of a series of β-substituted styrenes. The irreversible oxidation potentials (E_p) were found to be +2.0 V for *trans*-β-methylstyrene, +1.6 V for *trans*-β-methoxystyrene, and ≥+2.4 V for *trans*-methylcinnamate. The olefin with the highest E_p value undergoes very little reaction, while the olefin with the lowest E_p in this series, *trans*-β-methoxystyrene, reacts very rapidly to yield cleavage products. The rate of reactivity difference between *trans*- and *cis*-β-methylstyrene is surprising, given that we observe identical oxidation potentials for these olefins. Similarly, *cis*-stilbene was found to be completely unreactive while *trans*-stilbene autoxidizes readily; again, E_p for *cis*- and *trans*-stilbene were identical. That *cis*-stilbene is completely unreactive to autoxidation while *trans*-stilbene is reactive and yields a high selectivity for cleavage is a striking result. When *cis*-stilbene is mixed with *trans*-stilbene and subjected to high O_2 pressure autoxidation, *cis*-stilbene reacts at the same rate as *trans*-stilbene and yields similar products in the same distribution (Table VI), although traces of cis epoxide were detected.

In general, the high O_2 pressure autoxidations yield products that are apparently derived from site-specific cleavage of the olefin. Even with those substrates containing allylic CH's, specific cleavage chemistry is occurring, as well as the "normal" α-hydrogen abstraction. For example, the symmetrical olefin *trans*-5-decene undergoes symmetrical cleavage; i.e., the C_5 acid is produced along with shorter chain acids in lesser yields, but no C_6 or longer chain length acids are observed (see Scheme II). These high oxygen pressure autoxidations also display steric inhibition. For example, both di-*tert*-butylethylene and triphenylethylene are unreactive. Also aromatic olefins, such as phenanthrene, are unreactive. These autoxidations also give better selectivity to site-specific cleavage as the O_2 pressure increases.

The reactivity of conjugated dienes was also studied, and two examples are shown in Table VI. In addition to the formation of epoxide products, cleavage chemistry yielding acids and aldehydes was a major pathway. The cleavage products that were observed appear to result from 1,2-oxygen addition or cleavage, while no 1,4-addition-derived products were observed.

That aldehydes are observed as the major products of several of these autoxidations and not their acid congeners is surprising, especially since the aldehydes autoxidize relatively rapidly under the reaction conditions to yield the same acids. This observation is especially striking with the *trans*-stilbene autoxidation. In this system, the major observed product by gas chromatography is benzaldehyde, but when benzaldehyde is injected into the reactor, it oxidizes rapidly to yield benzoic acid. That a relatively stable intermediate species forms in these autoxidations prompted an investigation into its possible nature. Autoxidations performed in CD_3CN made it possible to monitor aliquots of the reaction directly via ^1H NMR and ^{13}C NMR. No unique features were present that could make it possible to assign the spectra; e.g., in a typical analysis of an aliquot taken directly from the reactor, GC indicated 70% benzaldehyde while NMR indicated that less than 10% total of benzoic acid plus benzaldehyde was present. Unfortunately, there are no distinct resonances outside the aromatic region to aid in the identification of an intermediate. Mass spectra analyses indicate that only stilbene, benzaldehyde, and benzoic acid are present. Finally, an independent synthesis of the *trans*-stilbene dioxetane[19] was made, and the dioxetane was subjected to

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[17] Lindsay-Smith, J. R.; Mead, L. A. V. *J. Chem. Soc., Perkin Trans. 2* **1973**, 206.

[18] Correa, P. E.; Riley, D. P. *J. Org. Chem.* **1985**, *50*, 1787.

[19] Koo, J.-Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1977**, *99*, 5403.

Table III. Thioether Autoxidations at High Oxygen Pressures[a] and Elevated Temperatures

SR_2	$[SR_2]$, M	solvent	temp, °C	time, h	yield as of % conversion (% conversion)
decyl methyl sulfide	0.21	4:1 $EtOH/H_2O$	100	64	90% sulfoxide (95%)
decyl methyl sulfide	0.21	4:1 acetone/H_2O	100	64	85% sulfoxide 12% sulfone (97%)
decyl methyl sulfide	0.21	CH_3CN	100	64	80% sulfoxide 2% sulfone (88%)
decyl methyl sulfide	0.21	benzene	100	64	trace sulfoxide (19%)
tetrahydrothiophene	0.21	CH_3CN	100	30	88% sulfoxide (91%)
methyl phenyl sulfide	0.16	CH_3CN	120	64	trace sulfoxide (~10%)
diphenyl sulfide	0.16	CH_3CN	145	60	no rctn
methionine	0.13	H_2O	105	21	93% sulfoxide (94%)

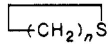
[a] P_{O_2} = 70 bars.

Table IV. Solvent Dependence on the Rate and Specificity of the Benzyl Methyl Sulfide Autoxidation at 115 °C under 70 Bars of Oxygen Pressure

solvent[a]	sulfoxide/thioether converted[b]	k_{obs}, h^{-1}
benzene	0	≤0.01
acetone	0.28[c]	0.92
CH_3CN	0.41	0.10
60% CH_3CN/40% H_2O	0.68	0.09
40% CH_3CN/60% H_2O	0.82[d]	0.07

[a] Substrate concentration is 0.20 M initially. [b] Yields from samples at time = 6 h. [c] Major side product benzoic acid. [d] Traces of benzaldehyde and benzoic acid.

Table V. Rate Constants for the Autoxidation of Cyclic Thioethers in 60% Acetonitrile/40% Water at 115 °C under 70 Bars of Oxygen Pressure[a]

 *n*	k_{obs}, h^{-1}
4	0.27
5	0.11
6	0.18

[a] Yield of sulfoxide exceeds 85% in all cases.

the reaction conditions. It virtually instantaneously converts to ~80% benzaldehyde, but the remainder converts very slowly to benzaldehyde, suggesting that a stable aldehyde precursor is formed in these systems.

Alkyne Autoxidations. Autoxidations of aliphatic alkynes were found to proceed at high temperatures (110 °C) and oxygen pressures (15–70 bars) to products that are again apparently derived from site-specific cleavage chemistry (Table VII). This is similar to the observed chemistry of olefins under the same conditions, and in analogy to the olefin oxidation, no longer chain acids are produced in the aliphatic alkyne system. In contrast to the olefin case, the autoxidation of aromatic substituted alkynes proceeds with lesser reactivity. For example, diphenylacetylene is completely unreactive, while *trans*-stilbene is very reactive; and phenylacetylene is virtually unreactive, whereas styrene is very reactive. The oxidation potential (Table VIII) of stilbene is lower (E_p ~1.6 V) than the corresponding internal aliphatic olefins (E_p >2.1 V), but so also is the oxidation potential of diphenylacetylene (E_p ~2.0 V) lower than that of internal aliphatic alkynes (E_p ~2.4 V). Interestingly, the sole observed product from phenylmethylacetylene is the α-diketone, 1-phenyl-1,2-propanedione.

Electrochemical Studies. The anodic peak potentials for the oxidation of a number of substrates are given in Table VIII. None of the cyclic voltammagrams show reversible behavior. We also carried out electrochemical studies on these organic substrates under high oxygen pressures (up to 1000 psi). To our knowledge, this is the first reported example of such studies. The high-pressure cyclic voltammetry (HPCV) shows for most systems no change in the E_p values under 1000 psi of oxygen in acetonitrile solutions in a standard glass three-electrode cell placed inside a standard Autoclave Engineers rocking autoclave with the appropriate leads.

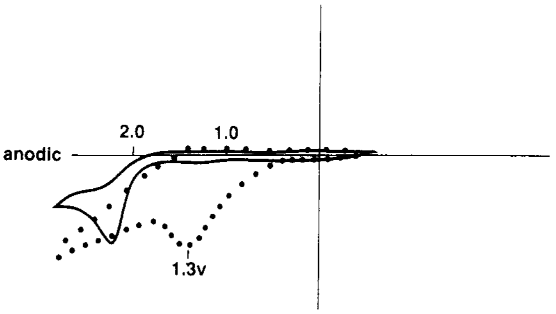


Figure 1. Cyclic voltammogram (see Experimental Section) for 6-dodecyne under N_2 (—) and under 1000 psig of O_2 pressure (···) in acetonitrile.

The results of the HPCV studies are shown in Table VIII. While for most of the systems there is no change in the E_p from atmospheric pressure to 1000 psi of O_2 for some of the olefins, a new wave begins to appear near +1.5 V at 200 psi of O_2 (Figure 1). At 1000 psi, this wave dominates the CV (Figure 1). The new wave is observed in the HPCV of oleic acid, 6-dodecyne, methyl oleate, *cis*-β-methylstyrene, and *trans*-β-methylstyrene at potentials ranging from +1.3 to +1.6 V. Two experiments verify that this is a real solution species and not an experimental artifact. First, the plot of peak current of this new wave is linear with respect to the concentration of oxygen over a range of 100–600 psi of O_2 with a limiting (saturation) effect from 700–1000 psi of O_2 (see supplementary Figure VI). Second, the peak current I_p is linear (supplementary Figure VII) with the root of the sweep rate over a range of 5 mV/s to 20 V/s and intercepts the current axis at the origin.[20] The wave also appears in methylene chloride solvent and has a linear relationship with the pressure of O_2. This wave does not appear in *trans*-stilbene or di-*tert*-butylethylene. In addition, the wave does not appear on addition of water or Ag^+ ions to the atmospheric CV and does not appear in a Pt electrode system or under high pressure of N_2.

We have attempted to correlate this wave with the known effect of molecular oxygen association with organic substrates on the UV/vis absorption spectra.[21] While we have been able to verify the effects of O_2 on the high-pressure UV/vis (HPUV) spectrum of phenanthrene, the

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(20) Nicholson, R. J.; Shain, I. *Anal. Chem.* **1964**, *36*, 706.
(21) Evans, D. F. *J. Chem. Soc.* **1953**, 345.

Table VI. Examples of Olefin Autoxidation at High Oxygen Pressures and Elevated Temperatures in Dry Acetonitrile Solvent

substrate (concn, M)	time, h	temp, °C	P_{O_2}, bars	% conversion	yield as % of converted substrate
trans-stilbene (0.11)	16	100	70	73	benzoic acid (2) benzaldehyde (66)[a] trans epoxide (22) 1,1-diphenylethylene epoxide (4) benzophenone (3)
cis-stilbene (0.11)	16	100	70	no rctn	
styrene (0.11)	10	100	28	78	benzaldehyde (67)[a] benzoic acid (17) styrene epoxide (11)
trans-β-methoxystyrene (0.15)	1	110	28	100	benzaldehyde (63)[a] benzoic acid (20)
trans-methylcinnamate (0.15)	70	110	28	1	benzaldehyde (100)[a]
trans-β-methylstyrene (0.15)	6	110	28	72	benzaldehyde (37)[a] benzoic acid (19) trans epoxide (14) 1-phenyl-1,2-propanedione (7) 2-hydroxypropiophenone (4) 1-hydroxy-1-phenylacetone (1)
cis-β-methylstyrene (0.15)		110	28	10	rate of conversion $^1/_7$ that of trans, but same products and yields
1,1-diphenylethylene (0.11)	6	115	28	100	benzophenone (75) 1,1-diphenylethylene oxide (9)
trans-5-decene (0.14)	7.5	120	70	>95	trans epoxide (35); no cis C_5 acid (21) C_4 acid (6) C_{10} alcohols (31)
triphenylethylene	24	110	70	no rctn	
phenanthrene	64	110	70	no rctn	
di-*tert*-butylethylene	64	110	70	no rctn	
trans,trans-1,4-diphenylbutadiene	7	115	70	>95	benzaldehyde (38) benzoic acid (30) *trans*-cinnamaldehyde (34) *trans*-cinnamic acid (16)
2,4-octadiene	1.5	100	28	100	2-butenal (15) 2-hexenal (15) butanal (5) butanoic acid (18) 2-butenoic acid (13) 2-hexanoic acid (20) 2,3:4,5-diepoxyoctene (1.1) 3,4-epoxy-2-octene (9) 2,3-epoxy-4-octene (1.5)
trans-cyclododecene	9	110	70	90	*trans*-1,2-epoxycyclododecane (21) 1,12-dodecanedioic acid (39) 1,11-undecanedioic acid (18) 1,10-decanedioic acid (7) 1,9-nonanedioic acid (2.5)
cis-cyclododecene	9	110	70	no rctn	

[a] Benzaldehyde forms via the breakdown in the GC injector (250 °C) of an unstable unknown produced in the reaction (see text).

Table VII. Examples of Alkyne Autoxidations at Elevated Oxygen Pressures and Temperatures in Dry Acetonitrile Solvent

alkyne	time, h	P_{O_2}, bars	temp, °C	% conversion	yield as % of conversion
1-octyne	16	15	110	67	heptanoic acid (31) hexanoic acid (7)
6-dodecyne	6	15	110	66	hexanoic acid (18) pentanoic acid (7.5)
6-dodecyne	6	70	110	90	hexanoic acid (35) pentanoic acid (19)
$PhC\equiv CH$	70	15	115	~1	
$PhC\equiv CCH_3$	45	70	115	10	1-phenyl-1,2-propanedione (80%)
$PhC\equiv CPh$	45	70	115	0	no rctn

HPUV spectra of 6-dodecyne and methyl oleate show no change (250–700 mm) from atmosphere to 1000 psi of O_2. Conversely, the HPCV of several known molecular association systems have been determined. Of these systems, *N,N*-dimethylaniline showed no change in the HPCV, and styrene and naphthalene showed a small increase in current which could not be reproducibly correlated with O_2 pressure due to severe film formation on the electrode surface.

High pressure controlled potential coulometry (HPCPC) measurements were carried out by using the same apparatus as the HPCV. The working electrode is a larger glassy carbon electrode which is sand blasted to produce a higher surface area. Some experiments were carried out by using a carbon felt electrode giving an even larger surface area. In these studies, the solvent–electrolyte system is preelectrolyzed for 1×10^3 s, the substrate is added, and the coulometry is run for $1–5 \times 10^3$ s. The HPCPC experiments on the olefin systems are limited by severe film formation on the electrode surface. Studies of methyl oleate, 6-dodecyne, and *trans*-stilbene showed a rapid decrease of current with time, and GC analyses of the resulting solutions (or the esterified solutions) indicate that no oxidation products are formed. The best results of HPCPC are obtained on decyl methyl sulfide.[22] These experiments not only yield oxidation products but are highly selective toward the sulfoxide and have reasonable Coulombic efficiencies and, under certain conditions, good mass balance. The results of these studies are summarized in Table IX. Several reaction parameters are summarized in the table. The remaining sulfide and sulfoxide are reported as a percent of the starting sulfide concentration (6.0×10^{-3} M). The Coulombic efficiency (E) is reported as $E = 100\% \times$ (moles of sulfide consumed)/(equivalents of charge passed). As expressed, this value is dependent on the mechanism. We assume here a one-electron oxidation followed by a chemical reaction. If a one-electron oxidation followed by a chain reaction occurred, efficiencies greater than 100% would result. There are several points of interest in these results: (1) At 100 °C, higher conversions and higher efficiencies are observed. (2) Undivided cells (no diffusion barrier between the working and auxiliary electrode) produce higher conversions but lower efficiencies. This is attributed to diffusion of superoxide ($O_2^{\bullet-}$) (produced at the auxiliary electrode) to bulk solution where it can react with the sulfide oxidation product (radical cation) to yield sulfoxide[23] (increasing conversion) or be reoxidized at the anode (decreasing efficiency). (3) Experiments on a carbon felt electrode (CFE) show higher conversions at shorter times, lower efficiencies, and better mass balance. These effects are all attributed to the structure of the CFE.[24]

Attempts to electrochemically initiate a chain reaction were made. These experiments, carried out at 100 °C, 1000 psi of O_2, on a glassy carbon electrode, and at room temperature, 1000 psi of O_2, on a CFE, yielded *stoichiometric* amounts of sulfoxide. Pulses ranged from 0.29 coulomb (~20 s or 1% of a 6×10^{-3} M sulfide solution) to 60 coulombs. The solution was monitored by CV for periods of 0.5–2.0 h and subsequently analyzed by GC. There is no indication of electroinitiation (chain reaction) in these systems.

Table VIII. Irreversible One-Electron Oxidation Potentials Measured in Acetonitrile at Ambient Pressure and at 70 Bars of Oxygen Pressure[a]

substrate	E_p, V (CV)	E_p, V (HPCV)
decyl methyl sulfide	+1.85	no change
thioanisole	+1.50	no change
diphenyl sulfide	+1.75	no change
tetrahydrothiophene	+1.68	no change
pentamethylene sulfide	+1.76	no change
hexamethylene sulfide	+1.80	no change
N-methylmorpholine	+1.1	no change
dimethyldodecylamine	+1.2	no change
5-decene	+2.1	+1.60
6-dodecyne	+2.4	+1.3
diphenylacetylene	+2.00	no change
oleic acid	+2.25	+1.6
methyl oleate	+2.3	+1.3
trans-stilbene	+1.6	no change
cis-β-methylstyrene	+2.4	+1.4
trans-β-methylstyrene	+2.0	+1.4
di-*tert*-butylethylene	+1.6	no change

[a] All systems are measured on a glassy carbon electrode in a 0.1 M tetra-*n*-butylammonium tetrafluoroborate acetonitrile solution vs Ag/AgCl.

Discussion

The autoxidation of electron-rich substrates under ambient conditions can, in general terms, be characterized by α-oxidation (or allylic) oxidation products. The high oxygen concentration autoxidation reactions described here are unoptimized but in general produce products that are unusual for autoxidation under ambient conditions. The types of products observed at higher oxygen pressures and at elevated temperatures are not derived from the typical α-oxidation chemistry observed under ambient conditions. But the reaction of oxygen with tertiary amine, thioether, olefin, or alkyne at high pressures share several common features. First, these reactions are all first-order with respect to both oxygen and substrate. Further, the products are inconsistent with neutral free radical chain chemistry, and a polar medium is required to promote the chemistry. These features (especially the polar solvent effect and the first-order dependencies in substrate and oxygen) suggest a common mechanism involving an initial electron transfer from the substrate to oxygen. Further, since the rate of the alkene autoxidations correlates with the ease of oxidation within the class of β-substituted styrenes and since ring-size effects on the rate of tertiary amine and thioether autoxidations also correlate with the ease of formation of planar radical cation intermediates, electron transfer from substrate to oxygen is the most logical initial step in the mechanism of these autoxidations. The observation that cis olefins react much more slowly than trans olefins requires comment in the context of this discussion. While the origin of this effect is unknown, it is possible that the cis olefins present an increased steric inhibition to the approach of oxygen, thus diminishing the rate of electron transfer.

The high-oxygen-concentration and high-temperature autoxidation of the various electron-rich substrates can be accommodated by a radical cation mechanism identified by several researchers for the oxidation of olefins such as biadamantylidene[25–27] and other Bredt's rule protected monolefins.[28,29] In such systems the olefin can be oxidized to produce a relatively stable radical cation which under ambient conditions can be trapped by the triplet ground state oxygen molecule to yield an oxygenated radical cation, a potent oxidant.[25] The subsequent chemistry is

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[22] Cottrell, P. T.; Mann, C. K. *J. Electrochem. Soc.* **1969**, 1499.

[23] Akasaka, T.; Ando, W. *Tetrahedron Lett.* **1985**, *26*, 5049.

[24] The web-like structure of a CFE has varied effects on the electrochemistry. The most important effect is that it approximates homogeneous charge transfer in bulk solution. The geometry of the electrode precludes the formation of the outer Helmholtz layer such that the radical cations are formed in an environment similar to bulk solution. This increases the probability of reaction with solution species such as O_2 (raising the conversion) and decreases the probability of reaction between two radicals or radical byproducts (improving mass balance). We are assuming that mass balance suffers from such reactions as have been previously reported for the electrolysis of dimethyl sulfide under anhydrous, oxygen-free conditions.[20] In addition, the geometry of the CFE produces distorted electric field gradients with high gradients at some points and low gradients at others. This effect lowers the Coulombic efficiency.

[25] Nelson, S. F.; Kapp, D. L.; Gerson, F.; Lopez, J. *J. Am. Chem. Soc.* **1986**, *108*, 1027.

[26] Clennan, E. L.; Simmons, W.; Almgren, C. W. *J. Am. Chem. Soc.* **1981**, *103*, 2098.

[27] Nelsen, S. F.; Akaba, R. *J. Am. Chem. Soc.* **1981**, *103*, 2096.

[28] Nelsen, S. F.; Teasley, M. F.; Kapp, D. L. *J. Am. Chem. Soc.* **1986**, *108*, 5503.

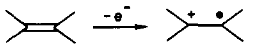
[29] Nelsen, S. F.; Teasley, M. F. *J. Org. Chem.* **1986**, *51*, 3221.

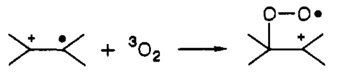
Table IX. HPCPC Results for Decyl Methyl Sulfide in Acetonitrile (0.1 M n-Bu_4NBF_4) under 70 Bars of Oxygen Pressure

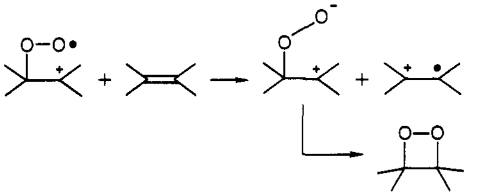
electrode	temp, °C	cell	time, s	% sulfide	% sulfoxide	E
GCE	RT[a]	divided	5×10^3	40	4	71%
GCE	100	divided	5×10^3	21	10	91%
GCE	RT	undivided	5×10^3	66	25	37%
GCE	100	undivided	5×10^3	42	34	80%
CFE	RT	divided	1×10^3	59	32	47%
CFE	RT	divided	2×10^3	9	83	41%

[a] RT = room temperature.

a radical cation chain sequence yielding ultimately a stable dioxetane (eq 1–3). With both cyclic tertiary amines and cyclic thioethers we observe a ring-size effect on the rate of reactivity. The trends are consistent with an electron-abstraction mechanism producing a transition state resembling the planar intermediate radical cation. Thus, the geometry on the nitrogen or sulfur in the transition state for electron abstraction resembles a planar radical cation rather than the tetrahedral arrangement of the substrate. Such reactivity trends have been observed in other studies of N-methyl cyclic tertiary amines with $Fe(CN)_6{}^{3-}$ as the oxidant, and the same relative rate effects were noted as in our studies, k_{rel} following the trend six-membered ring ≪ five- or seven-membered ring.[17]

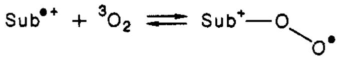

(1)


(2)


(3)

In these high-pressure oxidations, the data support an initial unfavorable rate-determining step involving electron transfer from the substrate to oxygen yielding a radical cation plus superoxide (eq 4). The more logical subsequent steps include oxygenation of the radical cation (eq 5) or direct combination of superoxide and radical cation (eq 6). The oxygenated radical cation intermediate **1** could then either react with substrate (radical cation chain chemistry analogous to eq 1–3) (eq 7) or react with superoxide (eq 8). Any of these pathways are possible, but at least for olefins and thioethers, sufficient experimental results exist so that we can suggest a most probable pathway for autoxidation. Further, in each of these systems, the reactions depend on high oxygen concentration not only for reasonable reaction rates but also for good selectivities. In general, the selective chemistry, whether cleavage of olefin or alkyne, or N-oxide or sulfoxide formation, is favored at higher O_2 pressures. This result implies that O_2 itself is involved in the step generating the selectivity. This is consistent with oxygen trapping of the radical cation (eq 5), as opposed to α-radical formation upon deprotonation.

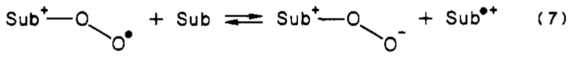
$$\mathrm{Sub} + \mathrm{O_2} \rightleftharpoons \mathrm{Sub}^{\bullet+} + \mathrm{O_2}^{\bullet-} \qquad (4)$$


$$\mathrm{Sub}^{\bullet+} + {}^3\mathrm{O_2} \rightleftharpoons \mathrm{Sub}^{+}\text{—O—O}^{\bullet} \qquad (5)$$

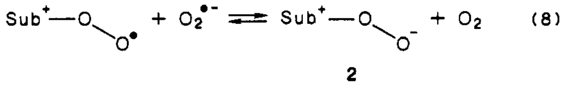
1


$$\mathrm{Sub}^{\bullet+} + \mathrm{O_2}^{\bullet-} \rightleftharpoons \mathrm{Sub}^{+}\text{—O—O}^{-} \qquad (6)$$

2


$$\mathrm{Sub}^{+}\text{—O—O}^{\bullet} + \mathrm{Sub} \rightleftharpoons \mathrm{Sub}^{+}\text{—O—O}^{-} + \mathrm{Sub}^{\bullet+} \qquad (7)$$

2

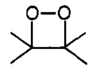

$$\mathrm{Sub}^{+}\text{—O—O}^{\bullet} + \mathrm{O_2}^{\bullet-} \rightleftharpoons \mathrm{Sub}^{+}\text{—O—O}^{-} + \mathrm{O_2} \qquad (8)$$

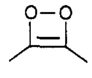
2

In these systems the structure of the zwitterionic intermediate **2** is worth comment. For thioethers, such a zwitterionic intermediate as the known **3**, $R_2S^+OO^-$, is proposed, and the bimolecular reaction of this with thioether is known to generate two molecules of sulfoxide (eq 9).[30] Tertiary amines could be expected to possess a

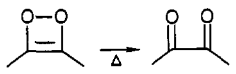
$$R_2S^+OO^- + R_2S \rightarrow 2\,R_2SO \qquad (9)$$

similar peroxide intermediate such as **4**, $R_3N^+OO^-$,[15] but for olefins and alkynes, precedent exists for a cyclic dioxetane or dioxetene intermediate structure (**5** and **6**).


5


6

The thermal cleavage of a dioxetane would yield aldehyde (site-specific cleavage), which under the reaction conditions would autoxidize to acid. This was confirmed in separate runs in which benzaldehyde was oxidized with O_2 under the olefin reaction conditions. In the case of stilbene oxidations, the results seem inconsistent with this mechanistic view. Since benzoic acid does not build up under the reaction conditions, an intermediate other than the unstable dioxetane must form, although NMR, IR, and other studies are not conclusive as to the nature of such a species. The alkyne autoxidation could be expected to produce a dioxetene **6**, or its equivalent, which would be expected to thermally rearrange to the α-diketone structure **7**:


7

Indeed the α-diketone product is observed in these autoxidations and has been observed previously in alkyne–O_2 oxidations.[31] Further, control reactions utilizing 6,7-dodecanedione were carried out at 120 °C under 200 psig and found to yield a first-order decay of α-diketone to pentanoic acid with a rate constant of 1.16 h^{-1}. This is very similar to the rate constant for 6-dodecyne autoxidation under the same conditions; e.g., the first-order rate constant equals 1.25 h^{-1}. Thus the α-diketone will undergo oxidative site-specific cleavage yielding 2 mol of acid at rates comparable to the overall observed alkyne autoxidation rates, demonstrating the chemical competence of the diketone intermediate.

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[30] Foote, C. S.; Peters, J. W. *J. Am. Chem. Soc.* **1971**, *93*, 3795.

[31] Turro, N. J.; Ramamurthy, V.; Liu, K.-C.; Krebs, A.; Kemper, R. *J. Am. Chem. Soc.* **1976**, *98*, 6758.

In the thioether system we have demonstrated via HPCPC that oxidation of thioether in the presence of a high concentration of O_2 does not yield any evidence of chain chemistry, only stoichiometric oxidation. Thus, it is unlikely that the thioether autoxidation proceeds via a chain mechanism (eq 7). It is possible that back electron transfer from superoxide, generated in the initial electron transfer, to the oxygenated radical cation (eq 8) is the source of the zwitterionic intermediate **3**, or that self-termination of $2\ R_2SOO^{\bullet+} \rightarrow 2\ R_2SO + O_2$ occurs. Unfortunately, electrochemical initiation studies with olefins, alkynes, and tertiary amines were inconclusive with regard to chain chemistry versus direct back electron transfer from superoxide (eq 8) due to the severe problems with filming of the electrodes in these systems. Our best indication that chain chemistry plays a possible role in the olefin oxidations analogous to the system of ref 25–27 (eq 1–3) comes from our studies of mixed olefin reactions. For example, *cis*-stilbene is unreactive, while *trans*-stilbene reacts readily; also *cis*-β-methylstyrene is much less reactive than the trans isomer; and *cis*-cyclododecene is much less reactive than its trans isomer. Reactions were run for these systems in which 50:50 cis/trans isomers were present. In these three examples, the reactions proceeded at the same rate as the control reaction (no cis isomer present) and the cis isomer was consumed at the same rate as the trans isomer. These facts suggest that another more competent oxidant, in addition to O_2, is available to oxidize the cis olefin, e.g., the oxygenated radical cation of the trans isomer. Thus, oxidation of olefin (cis or trans) can occur via a chain mechanism analogous to eq 1–3. The diene olefin substrates autoxidize under these conditions to yield products derived almost exclusively from 1,2 not 1,4 chemistry. Thus, neither cyclic endoperoxides nor their derivatives appear. This is somewhat unexpected in view of previous reports.[32]

An important discovery, especially in view of the endoenergic nature of the initial electron-transfer step (eq 4), is that certain olefinic and alkynic substrates exhibit unusual electrochemical behavior at higher oxygen pressures. We observe an oxygen concentration dependence on the formation of a new easier-to-oxidize species in the HPCV (Figure 1). That this is a species and not due to surface absorption phenomena was supported by the linear nature of the plots of P_{O_2} versus peak current and the peak current versus (scan rate)$^{1/2}$, which intercepts the current axis at the origin. These results suggest that we are observing the oxidation of a new species, possibly the O_2 adduct, the nature of which has been the subject of much discussion.[21,33-35] If we are indeed observing the direct oxidation of an oxygen adduct, the implications for oxidation catalysis are significant. The apparent reduction in the olefin and alkyne oxidation potential when these substrates are complexed to O_2 is striking and may account for the type of chemistry we observe; i.e., initial electron transfer to O_2 is more favorable because the oxidation potential is nearly 1 V lower at high O_2 pressure. A number of electron-rich compounds are known to form such O_2 adducts, including olefins and alkynes, with measured equilibrium formation constants on the order 5–15 M^{-1}. In our system the *linear* O_2 dependence on the increase in current in the O_2-dependent oxidation wave or the *linear* decrease in current with the O_2 (free) substrate oxidation wave makes it possible to calculate equilibrium constants in the range 5–15 M^{-1}. These correlations support the view that an olefin or alkyne oxygen adduct is being oxidized under O_2 pressure.

Conclusions

The high oxygen concentration (pressure) oxidation of electron-rich substrates has been demonstrated to yield products that are not derived from normal autoxidation chemistry; i.e., such oxidations do not lead to products derived from α-oxidation processes. The autoxidation of olefins and alkynes at high oxygen pressure leads to cleavage products, thioethers yield sulfoxides, and tertiary amines yield *N*-oxides in excess of 50% yield. The origin of this unique chemistry appears to involve an unfavorable electron transfer from the substrate to oxygen followed by trapping of the resultant radical cation with molecular oxygen. This process apparently occurs at a faster rate than α-deprotonation to the neutral α-radical species, the precursor of the observed low O_2 pressure autoxidation products (eq 10). We propose that the relatively high O_2 concentration (≥0.5 M at 1000 psig in H_2O) makes it possible to efficiently trap a radical cation intermediate and leads to the types of products observed. These results also suggest that in the presence of better one-electron oxidants than O_2 we should be able to initiate or perhaps even catalyze selective oxygen oxidations of the type described here by efficiently trapping the radical cation with oxygen present in high concentrations. In fact, we have found that we can indeed achieve such catalysis for thioethers,[36] tertiary amines,[37] olefins,[38] and alkynes.[38] The efficient promotion or catalysis of this radical cation pathway is now the focus of our attention and will be the subject of additional reports.

$$\mathrm{Sub}^{\bullet+} \xrightarrow{-\mathrm{H}^+} \mathrm{X-\dot{C}HR} + \mathrm{H}^+ \qquad (10)$$

Acknowledgment. We acknowledge the many helpful discussions and suggestions of our colleagues Drs. E. Mihelich, W. F. Erman, and D. O'Connor, as well as the skilled experimental assistance of R. E. Shumate.

Supplementary Material Available: Seven figures (including two ln k_{obs} vs $1/T$ (Arrhenius) plots for dimethyldodecylamine and decyl methyl sulfide; a ln [decyl methyl sulfide] vs time plot and a ln [*trans*-stilbene] vs time plot for autoxidation reactions at high P_{O_2}; a plot of initial rate of DL-methionine disappearance vs P_{O_2}; a plot of peak current intensity vs P_{O_2} for methyl oleate; and a plot of peak current intensity of the 1.5-V anodic wave vs the (scan rate)$^{1/2}$) and a table showing the effect of P_{O_2} on the selectivity of an *N*-methylmorpholine autoxidation (8 pages). Ordering information is given on any current masthead page.

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[32] Tang, R.; Yue, H. J.; Wolf, J. F.; Mares, F. *J. Am. Chem. Soc.* **1978**, *100*, 5248.

[33] Buchachenko, A. L. *Russ. Chem. Rev.* (*Engl. Transl.*) **1985**, *54*(2), 117.

[34] Tsubomura, H.; Mulliken, R. S. *J. Am. Chem. Soc.* **1960**, *82*, 5966.

[35] Evans, D. F. *J. Chem. Soc.* **1961**, 1987.

[36] Riley, D. P.; Correa, P. E. *J. Chem. Soc., Chem. Commun.* **1986**, 1097.

[37] Correa, P. E.; Riley, D. P. U.S. Patent 4 565 891.

[38] Work in progress.