of the reactions of **2** with phosphines indicate that a complicated mechanism, probably involving two phosphine-trappable intermediates in thermal equilibrium with **2**, is operative. Significantly, the reaction of **2** with phosphines is the first dimetallacycle transformation we have found in which the organometallic fragment is extruded in dinuclear form. This result provides a unique opportunity to employ crossover experiments to determine whether the two metal centers remain associated with each other during the reaction; i.e., whether the *o*-xylylene extrusion is truly a dinuclear elmination reaction. The outcome and interpretation of these experiments will be reported in a full paper.

Acknowledgment. We are grateful to Professor R. A. Andersen for helpful discussions and for disclosing research results prior to publication. Financial support for this work was provided by National Science Foundation Grant CHE79-26291. W.H.H. acknowledges an NIH National Research Service Award (F32-GM-07539) from the National Institute of General Medical Sciences.

ESR Detection of the Dimethyl Ether Radical Cation

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Received June 22, 1981

Despite their great importance as reaction intermediates, comparatively few oxygen-centered radicals have been characterized by ESR spectroscopy.[1,2] Here we report the radical cation of dimethyl ether, $(CH_3)_2O^+$, which is isoelectronic with the dimethyl aminyl radical $(CH_3)_2N$.[3-5] As far as we are aware, this is the first example of an oxygen-centered radical cation where the unpaired electron is not delocalized into an aromatic ring system as in the case of the anisole[6] and dimethoxybenzene[7] radical cations.

Bearing in mind the high reactivity of alkoxyl radicals in hydrogen atom abstraction reactions,[8] the dimethyl ether cation radical would be expected to react avidly with any potential hydrogen donor. This expectation is borne out by the very large rate constant of 1.9×10^{-9} cm^3 molecule^{-1} s^{-1} (1.1×10^{12} L mol^{-1} s^{-1}) measured for the gas-phase ion–molecule reaction of $(CH_3)_2O^+$ with $(CH_3)_2O$ to form the dimethyloxonium cation $(CH_3)_2OH^+$,[9] the reaction occurring essentially on every collision. Thus, $(CH_3)_2O^+$ would probably be difficult to detect if generated in a hydrogen-containing solvent or matrix. This problem has been avoided by using a γ-irradiation technique[10-12] which allows the radical cation to be generated through positive charge transfer from a Freon matrix to the dimethyl ether solute, the method satisfying the requirement that the $(CH_3)_2O^+$ species be trapped in a chemically inert environment.

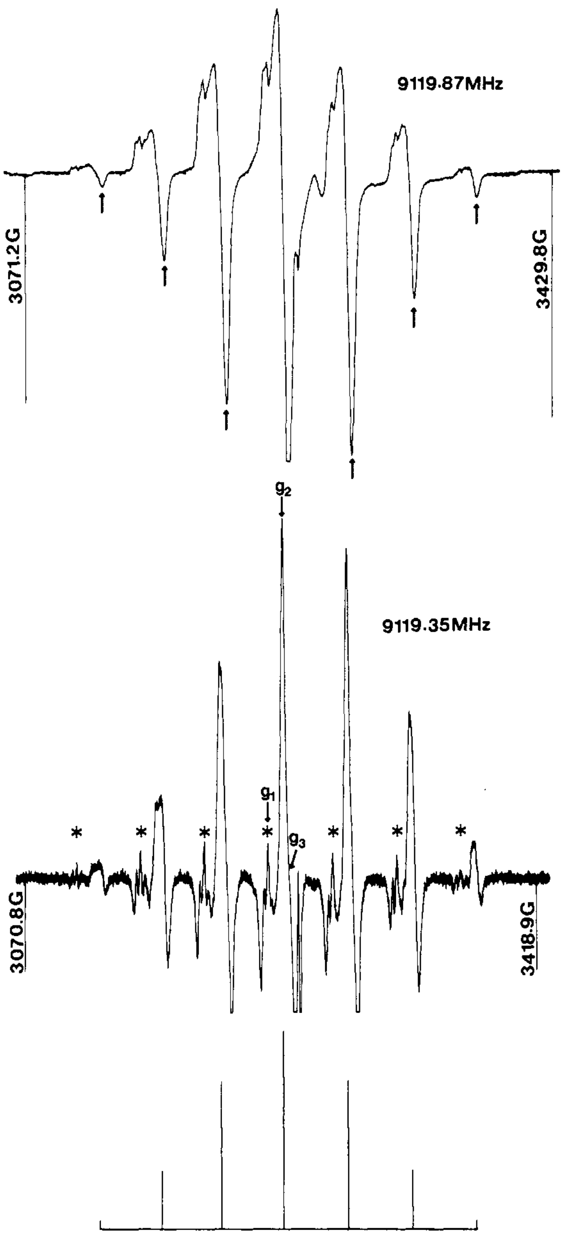

Figure 1. First-derivative (upper) and second-derivative (lower) ESR spectra of a γ-irradiated solid solution of 5 mol % dimethyl ether in trichlorofluoromethane recorded at 97 K after irradiation (dose, 1 M rad) at 77 K. The stick diagram shows the seven hyperfine components from the dimethyl ether radical cation, the anisotropy in the line positions extending between the two sets of features marked by asterisks (lower spectrum) and arrows (upper spectrum). The larger signal amplitudes for the high-field lines are due to a line-narrowing effect resulting from $g_1 > g_3$ and $A_1 > A_3$ (see text).

Table I. ESR Parameters for the Dimethyl Ether Radical Cation in a Freon 11 Matrix at 97 K

components of g tensor and g_{iso}	^{1}H hyperfine couplings, G
$g_1 = 2.0138$	$A_1 = 43.6$
$g_2 = 2.0072$	$A_2 = 42.8$
$g_3 = 2.0045$	$A_3 = 42.5$
$g_{iso} = 2.0085$	$a_\beta(6H)^a = 43.0$

[a] Isotropic coupling = (1/3) $(A_1 + A_2 + A_3)$.

Figure 1 shows the first-derivative and second-derivative ESR spectra obtained from a γ-irradiated solid solution of dimethyl ether in trichlorofluoromethane (Freon 11) at 97 K. The first-derivative spectrum consists of seven lines with approximately binomial intensity ratios (1:6:15:20:15:6:1) as expected for hyperfine interaction with six equivalent ^{1}H ($I = {}^1/_2$) nuclei. Each line in the binomial pattern is asymmetrically broadened, and this

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Table II. Spin Densities and ^{1}H Hyperfine Couplings Calculated for the Dimethyl Ether Radical Cation by the INDO Method[a]

atom	coordinates,[a] Å			atomic orbital	spin density	^{1}H hyperfine coupling,[b] G
	x	y	z			
C	0.983	0	0.688	$2p_y$	−0.033	
H_{1y}	0.983	0.901	1.319	1s	0.107	57.8
H_{2y}	0.983	−0.901	1.319	1s	0.107	57.8
H_3	1.884	0	0.057	1s	−0.002	−1.3
O	0	0	0	$2p_y$	0.712	

[a] To satisfy the C_{2v} point group, each of the two methyl group conformations is chosen so that one hydrogen (H_3) is in the nodal plane of the oxygen $2p_y$ orbital, as shown in Figure 2b. [b] The average ^{1}H coupling is 38.1 G.

broadening can be attributed mainly to **g** anisotropy since the line shapes for each pair of $\pm M_I$ components are not inverted with respect to each other. Together with the presence of characteristic line shapes, this absence of an inversion center for the spectrum supports a spectral analysis in terms of different **g**-tensor components, the anisotropy from the ^{1}H hyperfine coupling contributing much less to the overall line width.

Analysis of the line shape structure in the first-derivative spectrum reveals that for each line of the septet, there is a clearly defined feature on the low-field side of the main component. This set of features is marked by asterisks in the second-derivative spectrum (Figure 1) and can be assigned to the seven hyperfine components associated with the maximum **g**-tensor component (g_1). Similarly, the high-field extrema of the main components, identified by the arrows marking the negative excursions in the first-derivative spectrum, are assigned to the pattern originating from the minimum **g**-tensor component (g_3). The spectral analysis is completed by assigning the major septet peaks in the second-derivative spectrum to the set of hyperfine lines belonging to the intermediate **g**-tensor component (g_2). As the sample temperature was raised above 100 K, the spectral features associated with the g_1 component gradually diminished in intensity until they had almost disappeared at 155 K (see supplementary material). The asymmetric line shape of the main absorption envelope remained, however, indicating that the motion of the radical at this temperature suffices only to bring about a partial averaging of the **g**-tensor components. The ESR parameters derived from the analysis of the low-temperature spectrum (Figure 1) are given in Table I.

The assignment of the spectrum to the oxygen-centered π radical cation of dimethyl ether is unambiguous. First, the interaction with six equivalent ^{1}H nuclei is expected for the two methyl groups undergoing free rotation, and the relatively small ^{1}H hyperfine anisotropy (Table I) is characteristic of β-hydrogen couplings.[13] Second, the fact that the isotropic coupling, a_β(6H) = 43.0 G, greatly exceeds the corresponding value of 24.7 G for the six β hydrogens in the isoelectronic $(CH_3)_2CH$ radical[14] is consistent with recent studies on alkoxyl radicals[15-17] which show that β-hydrogen couplings are significantly larger in oxygen-centered than in carbon-centered π radicals.[18] Third, the appreciable positive g shift (Table I) for one of the **g**-tensor components (g_1) is typical of oxygen-centered radicals.[15-17] Lastly, INDO calculations[19] (Table II) confirm the structure of the radical (Figure 2) and yield an average value for a_β(6H) of 38.1 G, in reasonable agreement with the experimental result (43.0 G).

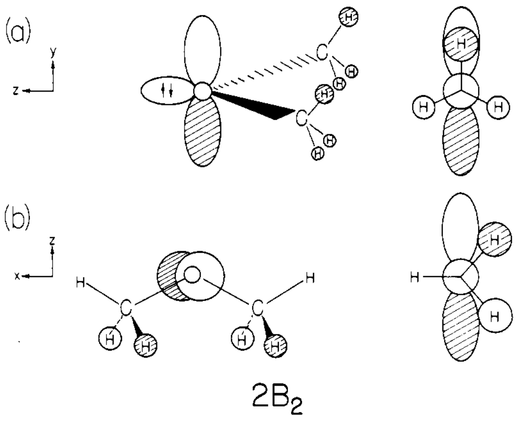

Figure 2. (a) Eclipsed and (b) bisected conformations of the methyl groups in the dimethyl ether radical cation, the CH_3 group orbitals possessing pseudo-π and π symmetry, respectively, with respect to the COC plane of the molecule. The oxygen p_y and the hydrogen π_y orbitals containing most of the spin population (Table II) are shown. Note that only conformation b possesses C_{2v} symmetry and that the calculated hydrogen 1s spin population for a rotating methyl group is obtained by averaging the results for the three hydrogens (Table II) in structure b.

As depicted in Figure 2, the unpaired electron resides mainly in the p_y orbital on oxygen, the only other significant spin populations being in the hydrogen 1s orbitals (Table II) which constitute the methyl group orbitals. This $2B_2$ molecular orbital in the C_{2v} point group (Figure 2b) is usually described as a nonbonding orbital[20] since there is very little contribution from the p_y basis orbitals on the adjacent carbons. This situation arises because the p_y orbital on oxygen interacts with both the $\pi_y(CH_3)$ and $\pi_y^*(CH_3)$ group orbitals, resulting in the effective cancellation of the contributions from the methyl carbons.[21] The **g**-tensor components can also be interpreted in terms of this structure for the radical. Thus, the large positive shift represented by g_1 is identified with the g_{xx} component since the magnetic field along this direction brings about the mixing of the singly occupied p_y orbital on oxygen with the $6A_1$ lone-pair orbital pointing along the z axis (Figure 2a), the energy separation between these orbitals being relatively small.[20,22] A similar argument can be used to assign the intermediate g_2 component to g_{zz}, the p_y SOMO mixing in this case with the filled 4 $B_1(\sigma_{CO})$ MO immediately beneath the $6A_1$ level.[20] Finally, just as for the alkoxyl radicals,[16] the minimum g_3 (g_{yy}) component lies along the direction which is parallel to the symmetry axis of the singly occupied p orbital on oxygen.

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(21) A similar explanation is given in ref 20 (p 31) for the construction of the 2A″ orbital in the eclipsed ethyl cation.

(22) The g_{max} component for alkoxyl radicals is generally in the range 2.054–2.093[16] and therefore is much larger than the value of 2.0138 obtained here for $(CH_3)_2O^+$. This difference is attributable to the likelihood of a much smaller energy separation between the two nonbonding oxygen orbitals in alkoxyl radicals. These oxygen p orbitals are, of course, degenerate in isolated RO radicals and the degeneracy is lifted only by the asymmetric influence of hydrogen bonding in the solid state, a far smaller perturbation on the orbital energies than that produced in going from RO to R_2O^+.

Acknowledgment. This research has been supported by the Division of Chemical Sciences, Office of Basic Energy Sciences, U.S. Department of Energy (Report DOE/ER/02968-137). We thank Dr. S. Steenken for stimulating our interest in aliphatic ether radical cations.

Supplementary Material Available: The solid-state ESR spectrum of $(CH_3)_2O^+$ at 155 K (1 page). Ordering information is given on any current masthead page.

On the Nature of the Intermediate between 4a-Hydroperoxyflavin and 4a-Hydroxyflavin in the Hydroxylation Reaction of *p*-Hydroxybenzoate Hydroxylase. Synthesis of 6-Aminopyrimidine-2,4,5(3*H*)-triones and the Mechanism of Aromatic Hydroxylation by Flavin Monooxygenases

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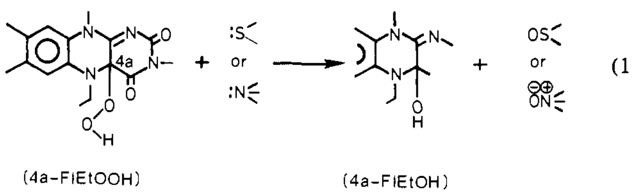
There appears to be a consensus that the reactions of reduced flavoenzyme monooxygenases with molecular oxygen provide enzyme-bound 4a-hydroxyperoxyflavin (4a-FlHOOH).[1-4a] In the N- and S-oxidation of amines by hepatic microsomal flavomonooxygenase,[5,6] substrate oxidation is accompanied by the conversion 4a-FlHOOH → 4a-FlHOH. The mechanism of the enzymatic reaction[7] appears to be identical in essential features with the bimolecular N- and S-oxidations with authentic 4a-hydroperoxyflavins (reaction 1).[2b,f,j] No evidence for intermediates could be obtained, and the reactions are quantitative.[2i,7] In contrast, the mechanisms for bacterial hydroxylases responsible for hydroxylation of electron-rich aromatic compounds are poorly understood. The enzyme *p*-hydroxybenzoate hydroxylase serves as the most useful example for this class of enzymes.[8]

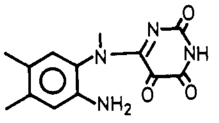


(1)

A strongly absorbing species (X) is formed from 4a-FlHOOH during the hydroxylation of a number of alternate substrates by *p*-hydroxybenzoate hydroxylase.[8] The disappearance of X is accompanied by the appearance of a species to which a 4a-hydroxyflavin structure (4a-FlHOH) was assigned (reaction 2).

$$\underset{\substack{\lambda_{max}\ 380\text{-}390\ \text{nm} \\ e \sim 9000\ M^{-1}\ cm^{-1}}}{\text{4a-FlHOOH}} \longrightarrow \underset{\substack{\lambda_{max}\ 390\text{-}420\ \text{nm} \\ e \sim 15\,000\ M^{-1}\ cm^{-1}}}{X} \longrightarrow \underset{\substack{\lambda_{max}\ 380\text{-}385\ \text{nm} \\ e \sim 9000\ M^{-1}\ cm^{-1}}}{\text{4a-FlHOH}} \qquad (2)$$

The aromatic hydroxylation reaction differs, therefore, from the N< and S< oxidation reactions in which an intermediate (X) is not seen. The spectral observation of a well-defined intermediate occurring in time between 4a-FlHOOH and 4a-FlHOH is most important. Structure I has been assigned to X.[8] Massey and co-workers have proposed that I arises in concert with oxygen-atom transfer from 4a-FlHOOH to substrate (reaction 3).[8] Species I was predicted by Hamilton[9] in 1971 as the immediate product of monooxygen transfer from his hypothetic carbonyl oxide II. Structures I and II have not only received a great deal of attention with respect to mechanism in flavomonooxygenase reactions, but structures completely analogous to I and II have been considered by Bailey and Ayling[10] to arise along the reaction paths for pteridine monooxygenases (responsible for initiation of the biosynthesis of neuroactive amines through hydroxylation of phenylalanine, tyrosine, and tryptophan). An assessment of the plausibility that X (reaction 3) ≡ I, which has been disputed,[11] is most easily accomplished by independent synthesis of I and comparison of the spectral properties of X and I. The objective of this study has been to synthesize *N*,*N*-dimethyl-I (i.e., IX) and compare its spectral properties to those of X (reaction 2). 6-Amino-5-oxouracils (or 6-aminopyrimidine-2,4,5-triones) have not been isolated.[12,13] We describe herein our efforts to synthesize substituted 6-aminopyrimidine-2,4,5(3*H*)-triones from 5,6-diaminouracils and the first successful synthesis via 4a-5 ring opening of a suitably substituted flavin.



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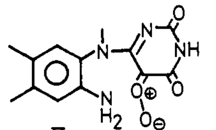

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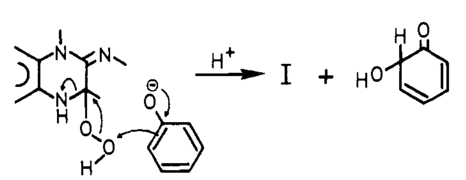

(3)

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