

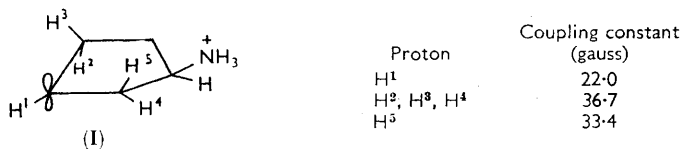
934. *Electron Spin Resonance Studies of Oxidation. Part III.¹ Some Alicyclic Compounds.*

By W. T. DIXON and R. O. C. NORMAN.

The electron spin resonance spectra of the radicals formed by the abstraction of a hydrogen atom from certain alicyclic compounds containing five- and six-membered rings are reported. Support is obtained for the view that the coupling between the unpaired electron and a C₂-proton* is dependent on the angle between the C₂-H bond and the singly occupied *p*-orbital. The results for the six-membered compounds which have been examined are satisfactorily interpreted on the basis that the radicals undergo chair-chair interconversion at a rate which is comparable with the difference in frequencies of the couplings of the axial and equatorial C₂-protons.

IN two previous Papers we described and discussed the electron spin resonance (e.s.r.) spectra of free radicals derived from the reaction of the hydroxyl radical with aliphatic compounds.^{1,2} We now first report the spectra of the radicals obtained in a similar manner from a number of five- and six-membered alicyclic compounds and then show that the results can be interpreted in terms of two premises. The first is that the coupling between C₂-protons and the unpaired electron is angular-dependent, and the second is that the six-membered cyclic radicals which we have studied undergo very rapid chair-chair interconversion.

Description of the Spectra.—(a) *Five-membered rings.* Cyclopentylamine gave a spectrum consisting of four quartets, each having lines of relative intensities 1 : 3 : 3 : 1. This indicates coupling between the unpaired electron and three equivalent protons ($a_{\text{H}} = 36.7$ gauss) and two non-equivalent protons ($a_{\text{H}} = 33.4$ and 22.0 gauss). Our assignments of this spectrum to the radical (I) and of the coupling constants as shown are made on the following grounds.



First, since the amine is essentially completely protonated in the strongly acid conditions used and the hydroxyl radical is known to have electrophilic character,¹ abstraction of hydrogen should occur with least difficulty from the carbon atom furthest from the amine group, to give (I) (cf. the lack of reactivity of methylamine towards $\cdot\text{OH}$, and the formation of $\cdot\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH}_3^+$ from *n*-propylamine¹). Secondly, the smaller of the doublet splittings is closely similar in magnitude to the values for C₁-protons in similar environments¹ and is therefore assigned to H¹. The triplet and the second doublet splitting remain to be assigned to the four C₂-protons. Of these four, H⁵ is in a slightly different environment from the remainder in that it is approximately in an eclipsed conformation with respect to the ammonio-ion on the adjacent carbon atom † and may reasonably be expected to couple to a different extent from the remaining three, possibly as the result of an electronic interaction with the nitrogen pole. Moreover, an analogy to this argument exists in the results for the radicals derived from cyclobutane-1,1-dicarboxylic acid: the

* *I.e.*, a proton on a carbon atom adjacent to the atom which bears the unpaired electron. For nomenclature, see Part I.²

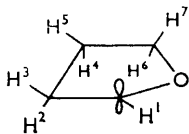
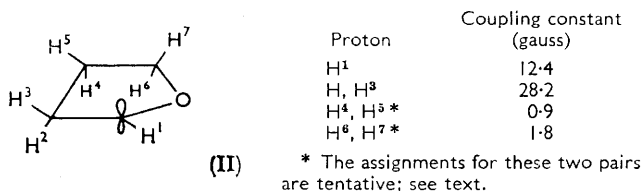
† The various eclipsing interactions in (I) will presumably result in the ring's being slightly buckled from the coplanar situation, as it is in cyclopentane. Nevertheless, this must remain a close approximation.

¹ Part II, Dixon, Norman, and Buley, *J.*, 1964,

² Dixon and Norman, *J.*, 1963, 3119.

C_2 -proton coupling constants are 1.5 gauss less in the radical in which these protons are eclipsed by carboxyl groups on the adjacent carbon than in the radical in which they are eclipsed by hydrogen atoms.¹

Tetrahydrofuran gave a spectrum consisting of two triplets, each of which was split further into seven lines (1 : 2 : 3 : 4 : 3 : 2 : 1), superimposed on some weak, ill-defined lines. This is attributed to the radical (II) on the following grounds.



(II)

Abstraction from the α -position is to be expected by analogy with the results for acyclic ethers.¹ Further, the doublet splitting is about the same as that of the C_1 -proton in $\cdot\text{CH}(\text{OEt})\text{CH}_3$, derived from diethyl ether, whereas the radical formed by abstraction from the β -position would be expected to give a C_1 -proton splitting of about 20 gauss.¹ The triplet is therefore assigned to the two equivalent C_2 -protons on the β -carbon atom. The narrowly spaced seven-line pattern is evidently the result of two further triplet splittings, one twice as great as the other. The coupling constants are of the usual order of magnitude for C_3 -protons,^{1,2} and the splittings are therefore ascribed to the two remaining pairs of protons, each of which is in a C_3 -position. It is not possible unambiguously to assign each splitting to a particular pair, but since there is evidence that an ethereal oxygen atom which is bonded to a carbon possessing an unpaired electron acquires a considerable spin density,¹ it is probable that the larger of the two splittings is due to the C_3 -protons next to oxygen, *i.e.*, to H⁶ and H⁷.

Three other five-membered cyclic compounds were examined. Cyclopentanol and cyclopentanone gave highly complex spectra, which could not be analysed, evidently because abstraction of hydrogen occurs from at least two carbon atoms in each molecule. Pyrrolidine caused only a small reduction in the amplitude of the singlet ascribed to the hydroxyl radical, evidently because of the deactivating effect of the protonated amino-group, and the resulting weak spectrum from the organic compound could not be analysed with certainty.

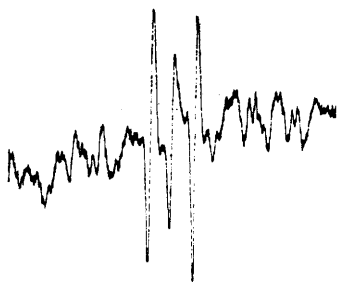


FIG. 1. Spectrum from cyclohexanol.

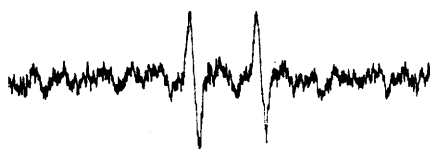


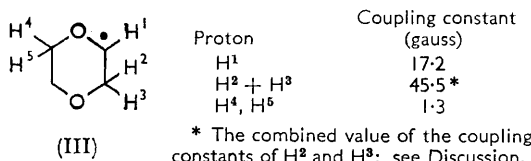
FIG. 2. Spectrum from cyclohexylamine.

(b) *Six-membered rings.* The spectrum from cyclohexanol (Fig. 1) contained three sharp central lines together with a number of other less intense lines. By analogy with the results for acyclic alcohols, the most reactive hydrogen in cyclohexanol (towards $\cdot\text{OH}$) should be that on the α -carbon, but there is also a number of hydrogens in only slightly less reactive positions (*e.g.*, four β -hydrogens) so that more than one radical would be expected (*cf.* the spectrum from isopropyl alcohol which consists of a strong spectrum

of the radical formed by abstraction of the one α -hydrogen superimposed on a weak spectrum of the radical formed by abstraction of one of the six β -hydrogens.²⁾ The nature of this complex spectrum is discussed further below.

The spectrum from cyclohexylamine (Fig. 2) was basically similar to that from cyclohexanol except that only two lines of much greater intensity than the remainder were present, equidistant from the centre. Again, abstraction from more than one C-H bond would be expected, for while the C-H furthest from the protonated amino-group should be the most reactive position for attack, the radical obtained by abstraction from one of the two γ -carbons should also be formed, by analogy with the result for cyclopentylamine.

Because of the difficulties in interpreting the spectra of mixtures of radicals, it was desirable to study the behaviour of a six-membered alicyclic compound which has only one type of C-H bond from which abstraction may occur and which is sufficiently water-soluble for application of the present experimental method. Dioxan was therefore chosen. It gave a spectrum (Fig. 3) consisting of four triplets together with two broad, unresolved lines each of which was at the centre of a pair of triplets. This is ascribed to the radical (III) in which coupling occurs with the C₁-proton (H¹), the two C₂-protons (H², H³), and the two C₃-protons (H⁴, H⁵). The origin of the broad central lines and the magnitude of the coupling with the C₂-protons are discussed below.



Finally, piperidine gave a spectrum (Fig. 4) consisting of two triplets, each of approximate relative intensities 1 : 3 : 5 : 1. By analogy with the behaviour of other amines, the most probable radical to which this signal may be assigned is that which results from abstraction of hydrogen from the γ -position. The doublet splitting, 21.9 gauss, is of the usual order of magnitude for C₁-protons in similar environments and is assigned as such, but the two triplets (splitting: 48.9 gauss) are not due to coupling with two equivalent protons, for the relative intensities of the lines would then be 1 : 2 : 1. The nature of the spectral pattern is discussed below.

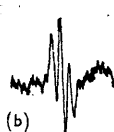
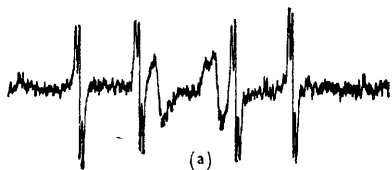


FIG. 3. Spectrum from dioxan: (a) complete spectrum; (b) triplet (1 : 2 : 1) structure of each of the sharp resonances revealed by slower scan.

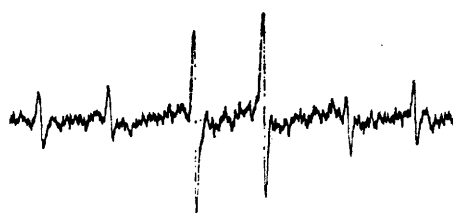


FIG. 4. Spectrum from piperidine.

The Angular Dependence of C₂-Proton Coupling Constants.—It has been argued that, if the hyperfine coupling of C₂-protons occurs solely by a hyperconjugative mechanism, it should be zero when the C₂-H bond lies in the nodal plane of the unpaired electron and maximal when it is in a plane perpendicular to the nodal plane, and in general it should be proportional to cos² θ , where θ is the angle between projections of the 2p_z-orbital of C₁ and the C₂-H bond on a plane perpendicular to the C₁-C₂ bond.³ Evidence for an angular dependence has recently accumulated from studies of acyclic systems at temper-

³ Symons, *Tetrahedron*, 1962, 18, 333.

atures low enough effectively to prevent rotation about carbon-carbon single bonds.^{3,4} For example, above 200°K the three C₂-protons in MeĊH·CO₂H couple equivalently, whereas below 100°K the complex spectra could be interpreted in terms of the non-equivalence of C₂-protons, this arising from differences in the value of θ for each proton.⁵ It is found that, although the simple relationship between C₂-coupling and θ suggested above ($a_{\text{H}} \propto \cos^2\theta$) is fitted reasonably satisfactorily by the experimental data, closer agreement is obtained by elaboration of this relationship to the form of equation (1),

$$a_{\text{H}} = B_0 + B \cos^2\theta \quad (1)$$

where B_0 is between 3 and 4 gauss.^{6,7}

The magnitude of the C₂-coupling in the radicals derived from five-membered rings can be understood in these terms. The value of θ for each C₂-proton is defined by the geometry of the ring, and although this is likely to be slightly distorted from coplanarity owing to eclipsing interactions, θ should be close to 30° and $\cos^2\theta$ close to $\frac{3}{4}$. This is larger than the *average* value of $\cos^2\theta$ ($\frac{1}{2}$) in acyclic systems, and it follows that the coupling constants should be correspondingly greater for the five-membered radicals, as observed. We have previously interpreted the values for the radicals obtained from cyclobutane-1,1-dicarboxylic acid in this way.¹

Further, quantitative comparison of the data for five-membered cyclic radicals with those for acyclic radicals of otherwise similar structure enables equation (1) to be tested. The procedure may be illustrated for the radical (I) obtained from cyclopentylamine which may suitably be compared with $\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\overset{+}{\text{N}}\text{H}_3$ (IV), derived from n-propylamine.¹ First, account is taken of the fact that the spin densities at C₁ in (I) and (IV), as measured by the C₁-proton splittings (22.0 and 22.5 gauss, respectively) are slightly different, and the C₂-coupling in (IV) (26.9 gauss) is therefore multiplied by the factor (22.0/22.5). Application of equation (1), with insertion of a value for B_0 of 3.5 gauss, gives a value for B of $2(26.9 \times 22.0/22.5 - 3.5) = 45.6$ gauss, from which the *predicted* value for the C₂-coupling in (I), assuming a value for θ of 30°, is given by:

$$a_{\text{H}} = 3.5 + 45.6 (0.75) = 37.7 \text{ gauss} \quad (2)$$

This value is reasonably close to that (36.7 gauss) observed for the three C₂-protons in (I) which are thought not to be eclipsed by the protonated amino-group. Insertion of $B_0 = 0$ leads to $B = 52.6$, and to a predicted value of 39.1 gauss, which is in less satisfactory agreement with experiment.

Application of the same procedure to the radicals formed from tetrahydrofuran, (II), and diethyl ether (for which the C₁- and C₂-couplings are 14.3 and 22.6 gauss, respectively¹) leads to predicted values for the C₂-coupling in (II) of 27.7 and 29.4 gauss for $B_0 = 3.5$ and 0, respectively. Agreement with the experimental value (28.2 gauss) is good, and again slightly better for $B_0 = 3.5$.

The results for the five-membered cyclic radicals are therefore consistent with the thesis that the magnitude of the coupling of C₂-protons is angular-dependent, and moreover acceptable agreement is obtained with the results predicted by equation (1). It appears that the value for B_0 of 3.5 gauss is more satisfactory in this respect than $B_0 = 0$, but in view of the approximation that had necessarily to be made in the application of this equation to the five-membered radicals (that $\theta = 30^\circ$), we do not suggest that the present results provide a wholly satisfactory test for finding the most appropriate value for B_0 .

Chair-Chair Interconversions of Six-membered Cyclic Radicals.—Cyclohexane and many

⁴ Symons, *Ann. Reports*, 1962, **59**, 57.

⁵ Horsfield, Morton, and Whiffen, *Mol. Phys.*, 1962, **5**, 115.

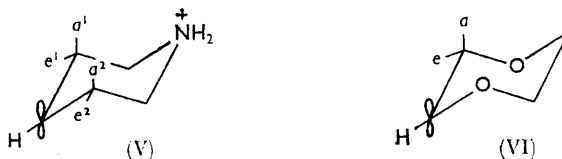
⁶ Horsfield, Morton, and Whiffen, *Mol. Phys.*, 1961, **4**, 425.

⁷ Symons in "Advances in Physical Organic Chemistry," Volume 1, ed. V. Gold, Academic Press, London and New York, 1963, p. 284.

of its derivatives exist predominantly in two chair conformations which are interconvertible. The rate of interconversion is reduced by lowering the temperature, and this gives rise to changes in the nuclear magnetic resonance spectrum. At temperatures down to -50° a single peak is observed which represents the average effect of the axial and equatorial protons, and on further cooling this peak shows progressive broadening until, at -70° , two distinct peaks, incompletely resolved, are observed, corresponding to the individual effects of the axial and equatorial protons.⁸ The broad absorption is a result of the lifetime uncertainty of a particular chair conformation and occurs when the rate of interconversion is comparable in magnitude with the difference in absorption frequencies due to the axial and equatorial protons.

The same principles apply to electron spin resonances. For example, the alternation in line-widths in the spectrum from a durensemiquinone radical has been shown to be due to a rapid isomerisation between *cis*- and *trans*-forms of the radical, and the theory has been described.⁹ The nature of the electron spin resonance spectra derived from piperidine and dioxan can be understood in similar terms. The values of θ for axial and equatorial C_2 -protons differ, and from the discussion in the previous section these protons would be expected to couple to different extents with the unpaired electron. If, then, the six-membered cyclic radical interconverts from one chair into the other chair conformation at a rate comparable with the difference in couplings of the axial and equatorial protons, certain sharp and certain broad resonances should be observed in the spectrum.

Consider the radical (V) formed from piperidine. As a result of the interconversion of the chair conformation shown into the alternative chair conformation, the axial and equa-



torial protons change places. If, in a given case, an axial proton changes places with an equatorial proton of the same spin, there is no change in the total spin interaction so far as this pair of protons is concerned, but if the exchanging protons are of different spin a change in the total spin interaction results. In general, for one spin orientation of the C_1 -proton, the situations shown in Table I can occur on interconversion.

TABLE I.

	Spin orientations in Chair I				Total spin interaction in		Difference in interaction on interconversion	Average
	a_1	e_1	a_2	e_2	Chair I	Chair II		
(1)	+	+	+	+	$2a + 2e$	$2a + 2e$	0	$2a + 2e$
(2)	+	+	+	-	$2a$	$2e$	$2a - 2e$	$a + e$
(3)	+	+	-	+	$2e$	$2a$	$-2a + 2e$	$a + e$
(4)	+	-	+	+	$2a$	$2e$	$2a - 2e$	$a + e$
(5)	-	+	+	+	$2e$	$2a$	$-2a + 2e$	$a + e$
(6)	+	+	-	-	0	0	0	0
(7)	+	-	+	-	$2a - 2e$	$-2a + 2e$	$4a - 4e$	0
(8)	+	-	-	+	0	0	0	0
(9)	-	+	+	-	0	0	0	0
(10)	-	+	-	+	$-2a + 2e$	$2a - 2e$	$-4a + 4e$	0
(11)	-	-	+	+	0	0	0	0
(12)	+	-	-	-	$-2e$	$-2a$	$2a - 2e$	$-a - e$
(13)	-	+	-	-	$-2a$	$-2e$	$-2a + 2e$	$-a - e$
(14)	-	-	+	-	$-2e$	$-2a$	$2a - 2e$	$-a - e$
(15)	-	-	-	+	$-2a$	$-2e$	$-2a + 2e$	$-a - e$
(16)	-	-	-	-	$-2a - 2e$	$-2a - 2e$	0	$-4a - 4e$

⁸ Jensen, Noyce, Sederholm, and Berlin, *J. Amer. Chem. Soc.*, 1960, **82**, 1256.

⁹ Carrington, *Mol. Phys.*, 1962, **5**, 425.

Of these, (1), (6), (8), (9), (11), and (16) result in no change in the total nuclear spin interaction on interconversion. Thus, in (1), the unpaired electron is always in the environment of two (+) axial and two (+) equatorial protons, and similarly in (16) it is always in the environment of two (-) axial and two (-) equatorial protons. Sharp resonances therefore occur at low and high field. The situations represented by (6), (8), (9), and (11), in which the effects of the nuclear spins nullify each other, lead to a sharp line at the centre of the field, and since there are four times as many ways in which this situation can occur as either (1) or (16), the centre line is four times as intense as the extreme lines. The remaining situations all lead to a change in nuclear spin interaction on interconversion, and this should result in there being broadened lines of intensity four at the two positions intermediate between the centre and extreme lines, and some broadening, of intensity two, about the central line. Since the intensity of an absorption in the derivative spectrum is proportional to the height of the peak and to the square of its width at half-height, the broad absorptions may be expected to be of very small amplitude with respect to the sharp ones and therefore difficult to discern.

When account is taken of the second possible orientation of the C_1 -proton, this theory leads to the prediction that the radical (V) should consist of two groups of three sharp lines of intensities 1 : 4 : 1 together with weaker broad lines. Insofar as the sharp lines are concerned, the observed spectrum is close to this.

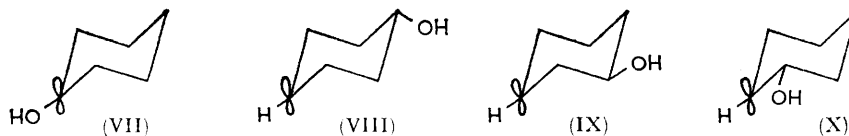
The radical (VI) derived from dioxan presents a simpler case since there is only one pair of C_2 -protons. Interconversion of the two chair conformations gives rise to the possibilities in Table 2, for one orientation of the C_1 -proton.

TABLE 2.

Spin orientations in Chair I		Total spin interaction in Chair I		Difference in interaction on interconversion		Average
a	e	Chair I	Chair II			
+	+	a + e	a + e	0		a + e
+	-	a - e	-a + e	2a - 2e		0
-	+	-a + e	a - e	-2a + 2e		0
-	-	-a - e	-a - e	0		-a - e

The spectrum should consist of two sharp lines of unit intensity at low and high field with a broad line of intensity two at their centre. When account is taken of the second possible orientation of the C_1 -proton and of the triplet splitting from the C_3 -protons, the observed spectrum is seen to have these characteristics.

It is now possible to discuss the nature of the spectra derived from cyclohexylamine and cyclohexanol. That from cyclohexylamine resembles that from piperidine in having two lines of much greater intensity than the remainder near the centre, together with a number of lines of about one-quarter of this intensity towards the extremities of the spectrum. Although the exact spectral pattern cannot be discerned with certainty, it is probable that the main radical formed from cyclohexylamine has basically the same spectrum as that derived from piperidine. The spectrum from cyclohexanol also contains two intense lines around the centre, together with a third, slightly less intense line at the centre of the first two. On the basis of the above discussion it is likely that this spectrum is due to a mixture of the radicals (VII), (VIII), (IX), and (X), and that the central line



and the two intense lines surrounding it are, respectively, the centres of a quintet due to (VII) and of two quintets due to (VIII) and (IX) (whose spectra should be the same within the limits of resolution of the spectrometer). The second and fourth lines of each quintet

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are, then, not discernible because they are subject to uncertainty broadening, while the extreme lines, which should be one-quarter of the intensity of the central ones, cannot be discerned with certainty from the background. It is noteworthy that (X) should give a spectrum in which *all* the lines are subject to uncertainty broadening and which would therefore be difficult to diagnose.

The individual coupling constants for the axial and equatorial protons in the radicals derived from piperidine and dioxan could in principle be measured by lowering the temperature at which their spectra are observed to the point at which the chair-chair interconversion rate is slow enough to give sharp resonances for each type of proton, but such experiments cannot be conducted with the aqueous solution technique which we have used. We know, however, the *combined* values of the coupling constants for these protons. If the value of θ for the axial C_2 -proton is ω , that for the equatorial C_2 -proton is $(120 + \omega)$. It follows that:

$$\begin{aligned} a_{ax} &= B_0 + B \cos^2 \omega \\ a_{eq} &= B_0 + B \cos^2(120 + \omega) \\ a_{ax} + a_{eq} &= 2B_0 + B[\cos^2 \omega + \cos^2(120 + \omega)] \end{aligned}$$

This leads to:

$$a_{eq} = \frac{1}{2}[a_{ax} + a_{eq} \pm \sqrt{3}(c - \frac{1}{2}B)(\frac{3}{2}B - c)],$$

where

$$c = a_{ax} + a_{eq} - 2B_0.$$

For the radical from piperidine, $(a_{ax} + a_{eq}) = 48.9$ gauss. A value for B can again be estimated from the data for $\cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot \dot{N}H_3$, allowance being made for the difference in spin densities at C_1 in the two radicals. Solution of the above equations ($B_0 = 3.5$) then gives values for a_{ax} and a_{eq} of 43.9 and 5.0 gauss, with corresponding values for θ of approximately 19 and 79°. A similar treatment for the radical from dioxan, calculations being based on the data for $\cdot CH(OEt) \cdot CH_3$, gives $a_{ax} = 41.8$ gauss ($\theta = 26^\circ$) and $a_{eq} = 3.7$ gauss ($\theta = 86^\circ$).

If each of the radicals obtained from piperidine and dioxan had a perfect chair conformation, the axial and equatorial C_2 -protons would have values of θ of 30 and 90°, respectively, but slight distortion from this situation should occur in order that the CCC or CCO angle at the carbon from which hydrogen has been abstracted may enlarge from the tetrahedral value to one close to 120°. Although the precise geometry of the radicals is unknown, the values of θ derived above appear reasonable.

On the basis of our interpretation of the spectral patterns of the six-membered radicals, an approximate value for the rate of interconversion of the chair conformations can be deduced from the difference, $\Delta\nu$, in the couplings of the axial and equatorial protons.¹⁰ In each case $\Delta\nu \sim 38$ gauss, so that the calculated rate of interconversion is of the order of 5×10^8 sec.⁻¹.

EXPERIMENTAL

The flow system and the procedure for the generation and observation of the radicals have been described.² The concentration of the organic compound necessary for the complete elimination of the signal ascribed to the hydroxyl radical and the consequent appearance of a spectrum from the organic radical was lower for the cyclic alcohols and ethers ($< M/10$) than for the amines (between $M/5$ and M) as expected from previous studies.¹

The spectrometer was calibrated by examining the spectrum of $\cdot CH_2OH$ at frequent intervals,² and coupling constants were reproducible to within ± 0.3 gauss.

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¹⁰ Pople, Schneider, and Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill New York, 1959, p. 223.