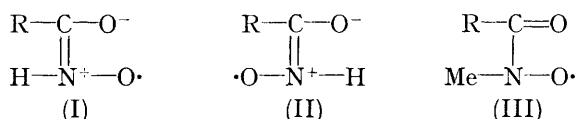


The Electron Spin Resonance Spectra of Some Hydroxylamine Free Radicals. Part IV.¹ Radicals from Alkylhydroxamic Acids and Amidoximes

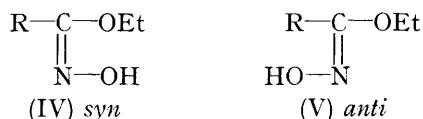
By (Miss) M. H. Millen and William A. Waters, The Dyson Perrins Laboratory, Oxford University

Electron spin resonance spectra have been obtained, by the flow method, by the oxidation of two alkylhydroxamic acids $\text{RC}(\text{:N}\cdot\text{OH})\cdot\text{OEt}$ in acid solution and from a number of amidoximes $\text{RC}(\text{:N}\cdot\text{OH})\cdot\text{NH}_2$ in alkaline solution. With the radical-anions from amidoximes, the hydroxyimino-group $^1\text{N}\cdot\text{OH}$ carries a larger electron spin density on nitrogen than does the imino-group $^2\text{N}\cdot\text{H}$. Geometrical isomers appear to be formed by the oxidation of ^2N -phenylbenzamidoxime, $\text{PhC}(\text{:}^1\text{N}\cdot\text{OH})\cdot^2\text{NHPh}$. The magnitudes of the splitting constants $a_{\text{N}-1}$ and $a_{\text{N}-2}$ on the nitrogen atoms of amidoxy-radical-anions, $\text{RC}(\text{:}^1\text{N}\cdot\text{O}\cdot)^{\cdot-}\text{NH}$, vary linearly, but in opposite directions, in accordance with the acid strength ($\text{p}K_a$) of the corresponding carboxylic acids RCO_2H .

E.s.r. studies in this laboratory^{1,2} have shown that geometrically isomeric free radicals (I) and (II) can be obtained by the one-electron oxidation of hydroxamic



acids in acidic solution, though only one isomer is formed in alkali, whilst *N*-methylhydroxamic acids yield the same radical (III) when oxidised either in acid or in alkali. We have extended this work to a study of the oxidations of two alkylhydroxamic acids (IV) or (V) and a series of amidoximes.



Radicals from Alkylhydroxamic Acids.—Ethylaceto-hydroxamic acid was obtained as a crystalline solid by the reaction between hydroxylamine and ethyl iminoacetate;³ its n.m.r. spectrum in carbon tetrachloride indicated that it was predominantly the *syn*-isomer (IV; $\text{R} = \text{Me}$). In aqueous acid it was rapidly hydrolysed to acetohydroxamic acid, but it could be oxidised even more rapidly. In alkali (0.1N sodium hydroxide) it was much more stable and resistant to ferricyanide oxidation. The oxidation, by the flow technique, of a neutral 10^{-2}M -solution of ethyl aceto-hydroxamic acid in 1% aqueous ethanol with 10^{-2}M -ceric sulphate in *m*-sulphuric acid gave a composite e.s.r. spectrum (Figure 1) of four main lines with relative intensities 1 : 2 : 2 : 1, corresponding to the NH group of a radical showing $a_{\text{N}} = a_{\text{H}} = 12.8$ OE and g 2.0055, together with 6 weaker lines corresponding to NH from another radical with a_{N} ca. 6.3 and a_{H} 10.7 OE. Magnification showed that the smaller main lines of Figure 1 had shoulders corresponding to some 1 : 3 : 3 : 1 splitting, indicative of the presence of a methyl group with $a_{\text{C-H}}$ ca. 2 OE [compare (II; $\text{R} = \text{Me}$) which has $a_{\text{C-H}}$ 1.85 OE].

¹ Part III, D. F. Minor, W. A. Waters, and J. V. Ramsbottom, *J. Chem. Soc. (B)*, 1967, 180.

² Part II, J. V. Ramsbottom and W. A. Waters, *J. Chem. Soc. (B)*, 1966, 132.

Oxidation of ethylaceto-hydroxamic acid in methanol with a neutral methanolic solution of ceric ammonium nitrate gave a symmetrical 4-line spectrum ($a_{\text{N}} = a_{\text{H}} = 12.0$ OE), but each line was then too broad for any finer

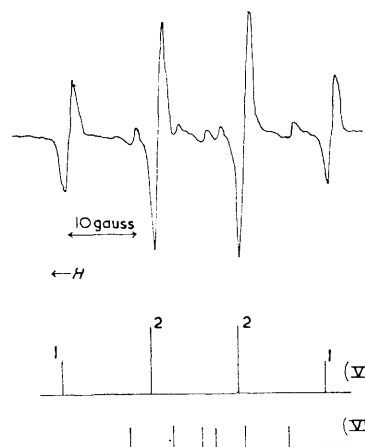
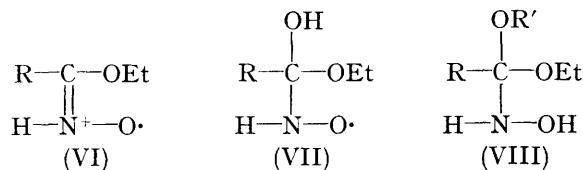


FIGURE 1 E.s.r. spectrum obtained by oxidising ethylaceto-hydroxamic acid with ceric sulphate in *m*-sulphuric acid

structure to be detected. The decreased splitting constants in methanol show the expected trend for solvation effects.⁴

Ethylbenzohydroxamic acid was obtained as a mixture of the stereoisomers (IV) and (V) ($\text{R} = \text{Ph}$), which were difficult to separate, and when the mixture was oxidised with acidic ceric sulphate only a weak, poorly resolved 4-line spectrum, corresponding to NH with $a_{\text{N}} = a_{\text{H}} = 12.7 \pm 1.0$ OE and g 2.0056, could be obtained. Evidently the ceric sulphate oxidation of the two ethyl



hydroxamic acids gives radicals with a_{N} splittings of over 12 OE and g -values comparable with those for

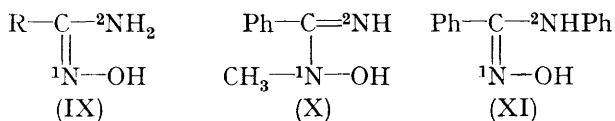
³ J. Houben and E. Schmidt, *Ber.*, 1913, **46**, 3616.

⁴ P. B. Ayscough and F. P. Sargent, *J. Chem. Soc. (B)*, 1966, 907.

Phys. Org.

C-alkylhydroxylamines, $\text{RNH}\cdot\text{O}$.^{1,5} Radicals (I) and (VI) would be expected to have very similar a_N splittings of 6–7 OE,² and so we suggest that the dominant radicals obtainable from ethylhydroxamic acids may have structure (VII) and be derived from solvated forms (VIII) of (IV) or (V), particularly since radicals such as (III), in which there is possible free rotation about C–N, have larger a_N values than those for the rigid radicals (I) and (II). However, the minor spectrum in Figure 1 might be that of (VI; R = Me) or of its geometrical isomer.

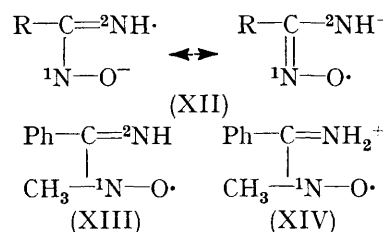
Radicals from Amidoximes.—Amidoximes, which could exhibit both geometrical isomerism and tautomerism, appear from physical measurements^{6–9} to exist in the *syn*-hydroxyimino-form (IX) which is stabilised by intramolecular hydrogen-bonding. For formamidoxime this has been confirmed by crystallographic X-ray analysis.¹⁰ However, analogues from *N*-alkylhydroxylamines must exist in the imino-form (X).



Compounds (IX)–(XI) are amphoteric, but in water or aqueous alcohol they behave as bases rather than as acids. Although the salts of aromatic amidoximes (IX) appear to be oxidised rapidly by acidic ceric sulphate, they did not yield free radicals suitable for detection by e.s.r. However, by the flow technique, strong e.s.r. signals were obtained by oxidising the free bases with potassium ferricyanide in 0.1*N*-sodium hydroxide. These spectra were symmetrical, and since they did not change on variation of the flow rate (compare Part III¹), they must correspond to the immediately formed radical-anions of the amidoximes themselves. The spectra were all of the type of Figure 2, in having 18 lines of approximately equal intensity, except when obvious overlapping occurred between four pairs of lines towards the centre of the spectrum. This pattern indicates interaction of the odd electron and two non-equivalent nitrogen atoms, and one hydrogen atom, as in (XII). Formulation as a *syn*-structure is supported by the fact that the radical from phenylacetamidoxime, $\text{PhCH}_2\cdot\text{C}(\text{NH}_2)\text{N}\cdot\text{OH}$ showed no sign of further splitting due to the methylene group.

The measured splitting constants for a number of these radicals are in the Table. Of the two nitrogen splittings we assign the larger value to the nitrogen atom (¹N) of the oxymino-group, partly because this nitrogen is nearer to the oxy-radical centre (¹N–O \cdot) but more particularly since the assignment $a_{N-1} > a_{N-2}$ accords with the spectrum obtained by oxidising (X) in alkaline solution; this corresponds to structure (XIII) with

a_{C-H} 9.66, a_{N-1} 9.66, a_{N-H} 5.0, and a_{N-2} 3.0 OE, and g 2.0060, though only 27 lines from a predicted 36 have been resolved clearly. Following methylation at ¹N, the



larger nitrogen splitting has increased considerably, but the smaller nitrogen splitting is very little altered. This is to be expected only if $a_{N-1} > a_{N-2}$, since in changing from (XII) to (XIII) only the environment of ¹N has been altered drastically.

Compound (X) forms with acids a salt which on ceric sulphate oxidation yields a radical (XIV), the spectrum of which has 42 resolvable lines out of the 84 expected but can be analysed to correspond to a_{C-H} (in CH_3) 8.15, a_{N-1} 5.74, a_{N-H} (in NH_2) 3.74, and a_{N-2} 2.87 OE, with g 2.0064. Evidently protonation of (XIII) has drawn away some of the electron spin density from ¹N, but, as shown by the well resolved ends of the spectrum, the added proton has formed an NH_2 group and so must be attached to ²N.

Splitting constants for amidoxy-radicals,
 $\text{RC}(\cdot\text{N}^{\cdot}\text{H})\text{N}-\text{O}^{\cdot}$

R	a_{N-1} (OE)	a_{N-1} (OE)	a_H (OE)	g	pK_a	σ
C_6H_5	7.95	3.24	5.53	2.0068	4.21	0.00
$\text{C}_6\text{H}_5\cdot\text{CH}_2$	8.00	3.20	5.13	2.0068	4.31	—
<i>p</i> - $\text{CH}_3\cdot\text{C}_6\text{H}_4$	8.05	3.10	5.19	2.0068	4.47	–0.27
<i>p</i> - $\text{CH}_3\cdot\text{C}_6\text{H}_4$...	8.04	3.15	5.29	2.0068	4.37	–0.17
<i>p</i> - $\text{Br}\cdot\text{C}_6\text{H}_4$	7.83	3.33	5.49	2.0069	3.97	+0.23
<i>p</i> - $\text{NO}_2\cdot\text{C}_6\text{H}_4$...	7.55	3.53	5.88	2.0069	3.43	+0.78

pK_a values are listed for RCO_2H , and σ -values for the aryl *para*-substituent.

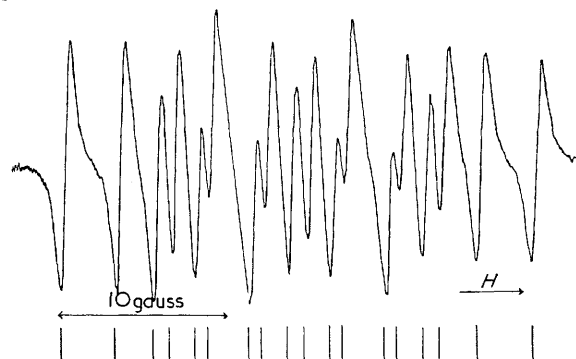


FIGURE 2 E.s.r. spectrum obtained by oxidising benzamidoxime with alkaline ferricyanide

²N-Phenylbenzamidoxime (XI) can be prepared by the action of hydroxylamine on thiobenzanilide.¹¹ On ferricyanide oxidation in alkali it gave an unsymmetrical

⁵ R. O. C. Norman and R. J. Pritchett, *Chem. and Ind.*, 1965, 2040.

⁶ J. Barrans, R. Mathis-Noel, and F. Mathis, *Compt. rend.*, 1957, **245**, 419.

⁷ W. J. Orville-Thomas and A. E. Parsons, *Trans. Faraday Soc.*, 1958, **54**, 460.

⁸ D. Prevoršek, *Compt. rend.*, 1958, **247**, 1333.

⁹ O. Exner, *Coll. Czech. Chem. Comm.*, 1965, **30**, 652.

¹⁰ D. Hall and F. J. Llewellyn, *Acta Cryst.*, 1956, **9**, 108.

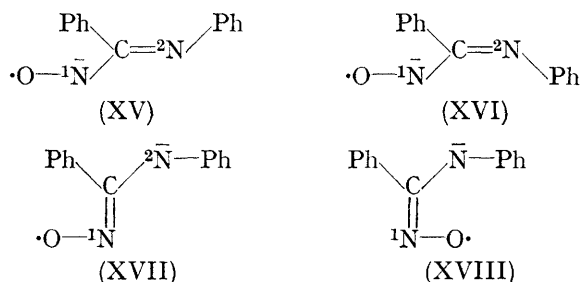
¹¹ H. Müller, *Ber.*, 1886, **19**, 1669.

e.s.r. spectrum (Figure 3) which can be analysed to correspond to two overlapping 9-line spectra with slightly different g values:

Spectrum (a) a_{N-1} 10.83; a_{N-2} 2.67 OE; g 2.0066

Spectrum (b) a_{N-1} 10.00; a_{N-2} 3.33 OE; g 2.0058

Clearly, the radicals giving Figure 3 contain no NH group since paired lines are absent, and so they must be the geometrical isomers (XV) and (XVI), since structures of types (XVII) and (XVIII) would be expected to give smaller a_{N-1} values and larger g -values. On steric grounds we suggest that the predominant radical [spectrum (b)] has structure (XVI) in which the two phenyl groups are the further apart.



Effects of Polarity on Structures of Amidoxy-radicals.—In figure 4 the splitting constants a_{N-1} and a_{N-2} for the amidoxy-radicals (XII) listed in the Table have been

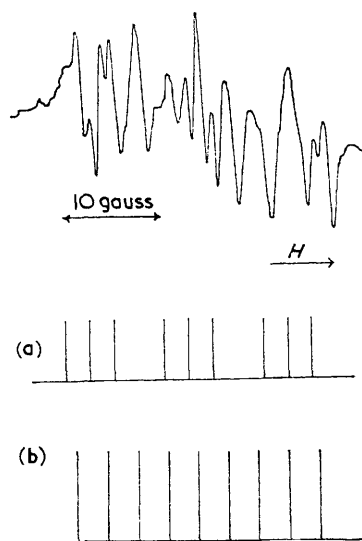


FIGURE 3 E.s.r. spectra of the geometrically isomeric radicals (XV) and (XVI)

plotted against the pK_a values of the corresponding carboxylic acids RCO_2H . Since Hammett's σ -constants can be computed from the pK_a values of aromatic acids, it is unnecessary to demonstrate that similar linear plots can be constructed from σ -values. Remembering that

¹² W. D. Phillips, *Ann. New York Acad. Sci.*, 1957–1958, **70**, 817.

¹³ O. Exner, V. Jehlička, and A. Reiser, *Coll. Czech. Chem. Comm.*, 1959, **24**, 3207.

the amidoxy-radicals (XII) are also anions, these changes in splitting constants must be due to the redistribution of the overall negative charge. It is interesting that this affects the unpaired electron spin densities a_{N-1} and a_{N-2} in opposite ways.

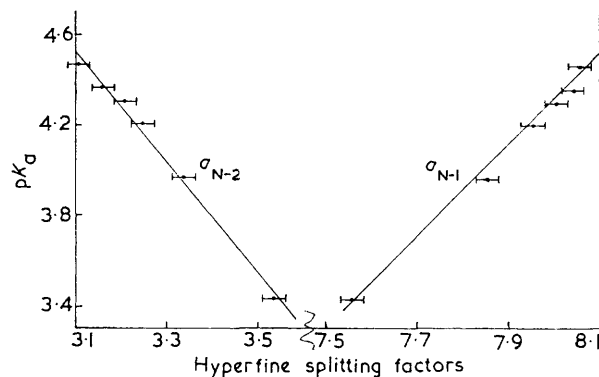


FIGURE 4 Splitting constants of amidoxy-radical-ions, and pK_a values of the corresponding carboxylic acids

EXPERIMENTAL

The e.s.r. measurements were made as described in Part III¹ using $1-3 \times 10^{-2}M$ solutions of the reactants.

Ethylacetohydroxamic Acids (IV and V; R = Me).—Ethyl iminoacetate hydrochloride (10 g.), prepared by the action of hydrogen chloride on methyl cyanide in dry ethanol, was slowly added with shaking to a solution of potassium carbonate (23 g.) in water (50 ml.) thoroughly cooled in ice-salt. The precipitated imino-ester was extracted into ether and added with shaking to a well cooled solution of hydroxylamine hydrochloride (7.1 g.) in water (25 ml.). The ether layer was separated, the aqueous layer further extracted with ether, and the combined ether solutions were dried and evaporated at room temperature, leaving an oil which, when cool, crystallised, m.p. 22–23° (4.5 g.) (lit.,³ 25–26°). The n.m.r. spectrum showed the presence of two isomers in the approximate ratio 8:1. The methylene proton splitting (1:3:3:1) of the more abundant isomer had the lower τ -value (5.88 compared with 6.18), and so, by comparison with aldoximes,¹² it was probably the *syn*-compound (IV) in which stabilisation by hydrogen-bonding is possible. After storage for some weeks the n.m.r. spectrum had changed in such a way as to indicate that isomerisation of (V) to (IV) (R = Me) had occurred.

Ethylbenzohydroxamic acid was prepared similarly, m.p. 23–26°. Its n.m.r. spectrum indicated that it was a ca. 2:1 mixture of isomers, but known methods for the separation of the two pure isomers¹³ were ineffective on a scale large enough for the requisite oxidation studies, and only the mixture was further examined.

Amidoximes.—These were prepared from nitriles and hydroxylamine by Tiemann's reaction¹⁴ as described more recently.¹⁵ Most products crystallised from the reaction mixture but it was necessary to purify benzamidoxime through the hydrobromide¹⁶ and phenylacetamidoxime by repeated precipitation from benzene solution with light petroleum. The identities and purities of the products

¹⁴ F. Tiemann, *Ber.*, 1884, **17**, 126.

¹⁵ G. Palazzo, M. Tavella, G. Strani, and B. Silvestrini, *J. Medicin. Pharmaceut. Chem.*, 1961, **4**, 351.

¹⁶ A. T. Fuller and H. King, *J. Chem. Soc.*, 1947, 963.

were checked by both infrared and n.m.r. spectroscopy and the accord of m.p.s with literature values.

N-Hydroxy-N-methylbenzamidine (X).—This was prepared by refluxing together in ethanol equivalent amounts of benzonitrile, *N*-methylhydroxylamine hydrochloride, and sodium carbonate. After 4 hr. the ethanol was removed at 40° and the residue fractionated under reduced pressure. The fraction with b.p. 62—64°/26 mm., on cooling, deposited crystals (30%), m.p. 130°, with satisfactory i.r. and n.m.r. spectra and, as required for $C_8H_{10}N_2O$, a molecular ion m/e 150.

²N-Phenylbenzamidoxime (XI), prepared from thio-benzanilide and hydroxylamine by Müller's method,¹¹ the thiobenzanilide having been made as described by Sachs and Loevy,¹⁷ had m.p. 133—136° (lit.,¹¹ 136°) and satisfactory i.r. and n.m.r. spectra.

We thank Mr. C. J. W. Gutch for help in the interpretation of the spectra.

[7/1557 Received, November 28th, 1967]

¹⁷ F. Sachs and H. Loevy, *Ber.*, 1903, **32**, 585.