Electron Spin Resonance Studies. Part XXIX.¹ Alkylamino and a-Aminoalkyl Radicals

By N. H. Anderson and R. O. C. Norman,* Department of Chemistry, The University of York, Heslington, York Y01 5DD

Reactions initiated by the interaction between titanium(III) ions and some N-alkylhydroxylamines have been studied by e.s.r. spectroscopy and in one case by the isolation of products and determination of the stoicheiometry. Evidence is adduced that alkylamino-radicals are formed first but react so fast that they do not reach detectable concentrations; however, the spectra of the adducts which they form with the aci-anion from nitromethane in basic solution can be observed. One of the important modes of destruction of the alkylamino-radicals involves their rearrangement to α-aminoalkyl radicals; the spectra of the latter, as their conjugate acids, can be observed in acid solution, and they can also be efficiently scavenged by radical trapping agents in both acidic and basic media. The α-aminoalkyl radicals are effective one-electron reducing agents. The cations derived from them in this process undergo solvolysis to carbonyl compounds; in one case the carbonyl compound was obtained in over 50% yield, and in another there was evidence for its reaction with more of the hydroxylamine to form an adduct which gave a further radical by oxidation. The hyperfine splitting constants of several of the radicals are discussed; of especial note is the evidence from these data that the ammonio-group in protonated a-aminoalkyl radicals is ineffective in delocalising the spin and does not induce bending of the radicals from coplanarity at the tervalent carbon atom.

THE ONE-ELECTRON reduction of hydroxylamine by titanium(III) ion gives the amino-radical, and reactions of this species with unsaturated compounds have been studied both by product analysis² and by e.s.r. spectroscopy.^{1,3-6} We have now employed the e.s.r. method, in conjunction with flow-system techniques,⁶⁻⁹ to study the reduction of N-mono- or N-di-alkylated hydroxylamines by titanium(III) ion and some subsequent reactions of the resulting alkylamino-radicals.

E.s.r. Spectra and their Assignments.—(a) Reactions in acidic solution. Initial experiments in which acidified solutions of titanium(III) ion and an N-alkylhydroxylamine were mixed immediately before passage of the combined solution through the spectrometer cavity⁸ resulted in the appearance of weak, complex e.s.r. spectra which are discussed later. These results prompted us to include a radical-trapping agent¹⁰ as a third reactant stream⁶ in the hope of generating longer lived radicals which would reach higher concentrations and so facilitate spectral analysis. The following results were obtained.

¹ Part XXVIII, D. J. Edge, B. C. Gilbert, R. O. C. Norman,

and P. R. West, J. Chem. Soc. (B), 1971, 189.
 ² C. J. Albisetti, D. D. Coffman, F. W. Hoover, E. L. Jenner, and W. E. Mochel, J. Amer. Chem. Soc., 1959, 81, 1489.
 ³ C. Corvaja, H. Fischer, and G. Giacometti, Z. Phys. Chem.

(Frankfurt), 1965, 45, 1.

⁴ J. Dewing, G. F. Longster, J. Myatt, and P. F. Todd, Chem. Comm., 1965, 391. ⁵ W. E. Griffiths, G. F. Longster, J. Myatt, and P. F. Todd,

J. Chem. Soc. (B), 1967, 530. ⁶ D. J. Edge and R. O. C. Norman, J. Chem. Soc. (B), 1969,

182.

(i) *t-Nitrosobutane as trap*. Strong spectra were observed during the reactions of N-methyl-, N-ethyl-, and *N*-isopropyl-hydroxylamine in the presence of the nitroso-compound (3). The hyperfine splitting constants (Table 1) are incompatible with species formed by addi-

Table	1
-------	---

Hyperfine splitting constants (mT) of the radicals (4)

R1	\mathbb{R}^2	$a_{\rm N}(1)$	$a_{\rm N}(1)$	a _{β-н}	a_{Me}
н	H	1.51	0.22	1·15 (2H)	
н	Me	1.47	0.21	0·21 (1H)	0.04
Me	Me	1.57			

tion of radicals of the type (1) [the generation of which is to be expected according to reaction (1)] to the nitrosocompound, but are consistent with radicals of the type (4) formed by reaction (2). This assignment was supported by our finding that the spectrum observed during reaction of the amino-radical [from the titanium(III)hydroxylamine system] with t-butyl methylene nitrone¹¹ (5), which is attributable to the radical (6), was identical with that observed during reaction of titanium(III) ion

7 R. O. C. Norman, in 'Essays on Free-radical Chemistry,' Chem. Soc. Special Publ. 24, 1970, ch. 6.

⁸ W. T. Dixon and R. O. C. Norman, J. Chem. Soc., 1963,

 3119.
 ⁹ R. O. C. Norman and P. R. West, J. Chem. Soc. (B), 1969, 389.

¹⁰ M. J. Perkins, in 'Essays on Free-radical Chemistry,' Chem. Soc. Special Publ. 24, 1970, ch. 5.

¹¹ G. R. Chalfont, M. J. Perkins, and A. Horsfield, J. Chem. Soc. (B), 1970, 401.

with N-methylhydroxylamine in the presence of the nitroso-compound (3).

$$R^{1}R^{2}CH \cdot \dot{N}H_{2} \cdot OH + Ti^{III} \xrightarrow{H^{+}} R^{1}R^{2}CH \cdot \dot{N}H_{2} + H_{2}O + Ti^{1V} \quad (I)$$
(I)

$$R^{1}R^{2}\dot{\mathbf{C}}\cdot\overset{\uparrow}{\mathbf{N}}H_{3} + Me_{3}C\cdot\mathbf{NO} \longrightarrow R^{1}R^{2}C-\mathbf{N}-CMe_{3} \qquad (2)$$

(2) (3)
$$\stackrel{1}{\mathsf{N}}\mathsf{H}_{a}^{+}$$
 (4)
O-
 $\stackrel{1}{\mathsf{H}_{2}}$ O·
(5) $\stackrel{1}{\mathsf{N}}\mathsf{CH}_{2}$ $\stackrel{1}{\mathsf{N}}\mathsf{CH}_{2}$ $\stackrel{1}{\mathsf{N}}\mathsf{CH}_{2}$ $\stackrel{1}{\mathsf{N}}\mathsf{CH}_{2}$ $\stackrel{1}{\mathsf{N}}\mathsf{CH}_{2}$ (3)

$$Me_{s}C\cdot NO \xrightarrow{TiIII} Me_{s}C\cdot N - O^{-} \xrightarrow{H^{+}} Me_{s}C\cdot NH\cdot O \cdot \qquad (4)$$
(7)

When the N-alkylhydroxylamine was omitted from the reactants, the spectrum observed was that of the radical¹² (7) $[a_{\rm N}(1) = a_{\rm H}(1) = 1.425 \text{ mT}]$ (see later), evidently formed as in reaction (4). However, no adduct from the nitroso-compound could be detected when either hydroxylamine itself or hydrogen peroxide was included instead of an N-alkylhydroxylamine; presumably the amino- and hydroxyl radicals add less rapidly to the nitroso-group than do carbon radicals of the type (2), and this may be related to the weaker dissociation energies of N-N and O-N bonds compared with the C-N bond.

(ii) Nitric oxide as trap. Nitric oxide has been successfully used to trap phenyl and hydroxyalkyl radicals in flow-system experiments.¹³ We found that the use of a neutral solution of sodium nitrite as the third reactant stream in the reduction of each of three N-alkylhydroxylamines by titanium(III) ion in acidic solution gave spectra, the hyperfine splitting constants of which are in Table 2. These are attributed to the nitroxides

TABLE 2

Hyperfine splitting constants (mT) of the radicals (8)

R1	\mathbb{R}^2	$a_{\rm N}(1)$	$a_{\rm N}(2)$	$a_{\beta-\mathrm{H}}$
H	н	1.24	0.28	0·95 (4H)
H	Me	1.29	0.22	0.41(2H)
Me	Me	1.475		

(8), which are evidently formed by successive addition of radicals of the type (2) to the nitric oxide generated from the acidified nitrite.



(iii) t-Butyl methylene nitrone as trap. As we have shown, the nitrone (5) traps the amino-radical, to give an observable concentration of the adduct (6), whereas the nitroso-compound (3) does not. This suggested the possibility that the nitrone (5), unlike the nitrosocompound (3), might successfully trap the alkylaminoradicals (1), assuming that these radicals are the precursors of those of the type (2). However, the use of the nitrone (5) as a trap during the reaction of titanium(III) ion with N-ethylhydroxylamine gave a radical the splitting constants of which $[a_N(1) \ 1.635, \ a_H(2) \ 1.28,$ $a_{\rm H}(1)$ 0.05 mT] are incompatible with the structure (9) derived from the protonated ethylamino-radical but are consistent with the structure (10) (see further below). Further, when N-ethylhydroxylamine was replaced by N-t-butylhydroxylamine [the alkylamino-radical from which cannot be transformed into a radical of type (2)], no radical could be detected.

$$\begin{array}{c} O^{\bullet} & O^{\bullet} \\ \downarrow \\ Et^{\bullet} NH_2 \cdot CH_2 - N - CMe_3 & H_3 N^{\bullet} \cdot CHMe^{\bullet} CH_2 - N - CMe_3 \\ (9) & (10) \end{array}$$

The evidence from the trapping experiments for the mediation of radicals of the type (2) in the reduction of some N-alkylhydroxylamines by titanium(III) ion led us to re-examine the spectra observed in the absence of a trapping agent. Conditions for the reaction were found in which these spectra were intense enough for analysis. E.s.r. parameters for the radicals from three N-alkylhydroxylamines and one NN-dialkylhydroxylamine are in Table 3; in the case of the N-ethyl compound, there were additional, weak resonances indicative of the presence of a second radical. No resonances could be detected with N-t-butylhydroxylamine.

The spectra described in Table 3, each of which was satisfactorily simulated by the quoted data and the observed line-widths, are assigned to the radicals (11)— (14) on three grounds. First, the spectrum of the radical (11) has been observed previously during irradiation of methylammonium alum crystals;14 the isotropic splitting constants could only be measured within relatively wide limits but are in reasonable agreement with those from the spectrum which we have assigned to this radical. Secondly, the hyperfine splitting constants are compatible with these structures. Thus, the large 1:3:3:1quartet splittings in the radicals from N-ethyl- (2.67 mT)and NN-diethyl-hydroxylamine (2.69 mT) are consistent with the presence in each of a methyl group which is bonded to a tervalent carbon atom possessing a significant fraction (ca. 90%) of the unit spin,¹⁵ as in the radicals (12) and (14), respectively. Likewise, the large septet splitting in the radical from N-isopropylhydroxylamine (2.425 mT) is consistent with the presence of two such methyl groups, as in the radical (13); the smaller splitting constant in this case should reflect, at least in part, the greater removal of spin by two methyl groups as compared with one.¹⁵ The numbers of protons with splitting constants in the range 2.2-2.3 mT and 1.5-1.8 mT are in accord with the numbers of protons at-

994

¹² Th. A. J. W. Wajer, A. Mackor, and Th. J. de Boer, *Tetra-*hedron, 1969, **25**, 175. ¹³ A. L. J. Beckwith and R. O. C. Norman, J. Chem. Soc. (B),

^{1969, 403.}

¹⁴ R. P. Kohin and P. G. Nadeau, J. Chem. Phys., 1966, 44,

^{691.} ¹⁵ R. O. C. Norman and B. C. Gilbert, Adv. Phys. Org. Chem., 1967, 5, 53.

tached to the tervalent carbon atom and to the nitrogen atom, respectively, in the radicals (11)—(14); the splitting constants are accordingly assigned in this way and their magnitudes are discussed later.

Thirdly, when acidic solutions containing titanium(III) ions and formic acid, and hydrogen peroxide and formic acid, were mixed with a basic solution of the azomethine (15), the final pH being ca. 2, a spectrum identical with that attributed to the radical (14) was observed. Under these conditions, the radical •CO₂H, which is a strong one-electron reducing agent, is same spectra, although with slightly broader line-widths, were obtained by oxidising the hydroxylamines with either hexacyanoferrate(III) ion in aqueous alkali or cerium(IV) ion in aqueous acid (cf. refs. 12 and 18); they are assigned to the nitroxides (17).

$$R \cdot NH \cdot + R \cdot NH \cdot OH \longrightarrow R \cdot NH_2 + R \cdot NH \cdot O \cdot (6)$$
(16)
(17)

Since a probable mechanism of formation of the nitroxides (17) with the titanium(III)-N-alkylhydroxylamine system involves reaction of the first-formed

TABLE	3
-------	---

	Hyperfin	e splitting o	constants (mT) and g -	factors of the	radicals R ¹ R ²	Ċ•ŇH₂•R³	
Radical	R1	$\mathbf{R^2}$	R ³	$a_{\rm N}(1)$	a_{N-H}	a _{α-H}	$a_{\beta-\mathbf{H}}$	g
(11)	н	\mathbf{H}	\mathbf{H}	0.34	1·825 (3H)	2.31 (2H)		2.0027
(12)	\mathbf{H}	Me	H	0.325	1·725 (3H)	$2 \cdot 27$ (1H)	2.67 (3H)	2.0028
(13)	Me	Me	н	0.285	1.60 (3H)		2.425(6H)	2.0027
(14)	н	Me	Et	0.332	1.50(2H)	2.255 (1H)	2.69(3H)	2.0029

formed;^{9,16,17} formation of the radical (14) according to reaction (5) is to be expected, providing support for our assignment of the spectrum from NN-diethylhydroxylamine to this radical.

$$R^{1} R^{2} R^{3}$$

$$R^{1}R^{2}\dot{C} \dot{N}H_{2} R^{3}$$

$$(11) H H H H$$

$$(12) H Me H$$

$$(13) Me Me H$$

$$(14) H Me Et$$

$$MeCH:NEt + \cdot CO_{2}H \xrightarrow{H^{+}} Me\dot{C}H \cdot \dot{N}H_{2} \cdot Et + CO_{2}$$

$$(15) \qquad (14)$$

The spectrum of the radical (13) from the reaction of N-isopropylhydroxylamine with titanium(III) ion was observed throughout the pH range 0.5-3.1. However, when the pH was increased above 3.1, the signal became extremely weak; at pH 3.9, the resonances due to the nitroxide Me₂CH·NH·O· (see later) were detected, and these became progressively more intense as the pH was further increased. When this reduction was carried out at pH 2 in ca. 90% deuterium oxide, a weaker spectrum was obtained than in water, but the central region of the spectrum showed the resonances expected for the species $\cdot CMe_2 \cdot ND_3^+$ $[a_N(1) \quad 0.285]$, $a_{\rm D}(3)$ 0.25 mT]. It follows that the NH protons exchange rapidly compared with the time-scale of the flow experiments. However, the fact that NH proton splittings are observed for the radicals (11)-(14) indicates a maximum rate for the exchange of ca. 10⁷ s⁻¹.

(b) Reactions in basic solution. When an aqueous solution of titanium(III) ion complexed with either ethylenediaminetetra-acetic acid (EDTA) or tartaric acid at pH 8-9 was mixed with a solution containing a slight excess of an N-alkylhydroxylamine at pH 6-7, so that the final pH was \geq 7, spectra with the hyperfine splitting constants listed in Table 4 were observed. The N-alkylamino-radical (16) with more of the hydroxylamine [reaction (6)], we reduced the concentration of the hydroxylamine in the hope of reducing the relative importance of reaction (6) and thereby detecting the alkylamino-radicals. However, although the observed concentration of the nitroxides (17) duly decreased, no resonances attributable to alkylamino-radicals could be discerned. Instead, with the titanium(III)-EDTA complex as reducing agent, a weak spectrum of the radical formed by abstraction of a hydrogen atom from EDTA¹⁹ was detected; its intensity increased on addition of an excess of EDTA.

When a large excess of N-ethylhydroxylamine was reduced by the titanium(III)-EDTA complex at ca.

TABLE 4

Hyperfine splitting constants (mT) of the radicals (17)

R	$a_{\rm N}(1)$	$a_{\rm N-H}(1)$	$a_{\mathrm{C-H}}$
Me	1.48	1.48	1·48 (3H)
\mathbf{Et}	1.415	1.415	1.415(2H)
Pr^i	1.425	1.425	1·335 (1H) *
$\operatorname{Bu}^{\mathbf{t}}$	1.44	1.39	

* The alternative assignment of the NH and CH splittings is also possible.

pH 7, the spectrum of the nitroxide Et·NH·O· was accompanied by that of a second radical with $a_{\rm N}(1)$ 1.60, $a_{\rm H}(2)$ 1.18, and $a_{\rm H}(1)$ 0.375 mT; the intensity of the latter increased relative to that of the former as the pH was reduced to 4. The a_N value is of the magnitude expected for a nitroxide, and the proton splittings are consistent with a structure of the type (18) in which neither Y nor Z is hydrogen; its structure is derived later. Neither N-methyl- nor N-isopropyl-hydroxylamine gave analogous species under these conditions.

¹⁶ A. L. J. Beckwith and R. O. C. Norman, J. Chem. Soc. (B), 1969, 400.

¹⁷ D. J. Edge and R. O. C. Norman, J. Chem. Soc. (B), 1970, 1083.

 ¹⁸ J. Q. Adams, S. W. Nicksic, and J. R. Thomas, J. Chem. Phys., 1966, 45, 654; C. J. W. Gutch and W. A. Waters, J. Chem. Soc., 1965, 751.
 ¹⁹ R. O. C. Norman and R. J. Pritchett, J. Chem. Soc. (B), 1067, 976.

^{1967, 378.}



The amino-radical is trapped efficiently in basic solution by the aci-anion of nitromethane or nitroethane.⁶ In the hope of trapping alkylamino-radicals (16), we mixed, simultaneously, basic solutions of the titanium(III)-EDTA complex, an N-alkylhydroxylamine, and nitromethane. The hyperfine splitting constants of the resulting radicals are in Table 5, together

Table	5
-------	----------

Hyperfine splitting constants (mT) of the radicals (19)

R	$a_{\rm N}(1)$	$a_{\rm N}(1)$	$a_{\rm CH_s}$	$a_{\rm NH}(1)$	$a_{\rm NMe}$
н	2.55	0.11	0.89	0.05	
Me	2.48	0.15	0.915	0.02	0.01
Et	2.48	0.14	0.925		
\Pr^i	2.50	0.13	0.95		
Bu^t	2.47	0.12	0.92		

with those⁶ for the radical (19; R = H); the spectra were accompanied in all cases except with N-t-butylhydroxylamine by that of the nitromethane radical anion.

The spectra reported in Table 5 have a_N values in the range $2 \cdot 4 - 2 \cdot 6$ mT, as expected for aliphatic nitroalkane radical anions, and the remaining splitting constants are in accord with the structures (19), formed as in reaction (7). Confirmation of these assignments was derived from our finding that the spectrum of a radical with identical splitting constants to that attributed the structure (19; R = Me) was observed when solutions containing, respectively, titanium(III) tartrate, the nitromethane aci-anion, and potassium persulphate and methylamine were mixed simultaneously to give a final pH of ca. 10. Under these conditions, the initially formed sulphate radical anion oxidises the nitromethane aci-anion to the nitromethyl radical²⁰ which is susceptible to nucleophilic attack,²¹ in this case by methylamine, to give the radical anion (19; R = Me) as in reaction (8).

$$R \cdot NH \cdot + CH_2 \cdot NO_2^{--} \longrightarrow R \cdot NH \cdot CH_2 \cdot NO_2^{--}$$
(7)

$$CH_2:NO_2^{-} \xrightarrow{SO_4^{-}} CH_2:NO_2 \xrightarrow{MeNH_2} Me:NH:CH_2:NO_2^{-} (8)$$

When nitroethane was substituted for nitromethane, with use of the same N-alkylhydroxylamines as for the experiments in Table 5, no spectra attributable to adducts of the type $R \cdot NH \cdot CHMe \cdot NO_2^{--}$ were observed. Instead, the spectra of the (\pm) - and meso-isomers of the radical anion $(20)^{21}$ were recorded, together (except with N-tbutylhydroxylamine) with that of the nitroethane radical anion; the relative concentrations of the isomers of the radical anion (20) were the same in each case and also the same as when, under other conditions, the two are generated by reaction (9).^{20,21}

$$Me\dot{C}H\cdot NO_{2} + MeCH: NO_{2}^{-} \longrightarrow MeCH-CHMe$$

$$MeCH-CHMe$$

$$MeCH-$$

When N-methyl-, N-ethyl-, or N-isopropyl-hydroxylamine was reduced with titanium(III) tartrate at pH 7-8 in the presence of the nitrone (5), the spectra described in Table 6 were obtained. The nitrogen splitting con-

TABLE 6

Hyperfine splitting constants (mT) of the radicals H₂N·CR¹R²·CH₂·NBu^t·O· \mathbb{R}^2 Radical R1 $a_{\rm N}(1)$ $a_{\beta \cdot \mathbf{H}}(2)$ $a_{\gamma-\mathrm{H}}(1)$ н н (21)1.641.37 (22)н 1.28Me 1.6350.05(23)Me 1.63 1.20Me

stants indicate that these are due to nitroxide radicals, and the patterns of proton splitting constants are consistent with the structures (21)—(23), respectively, but not with species of the type R·NH·CH₂·NBu^t·O· (formed from alkylamino-radicals). When t-nitrosobutane was used in place of the nitrone, only the spectrum of the radical Me_aC·NH·O· was observed. With N-t-butylhydroxylamine, there was no e.s.r. absorption with either trapping agent.

(c) Reactions in the presence of maleic acid and related compounds. The reduction of N-methyl-, N-ethyl-, or N-isopropyl-hydroxylamine with titanium(III) ion in acid solution or with titanium(III)-EDTA in neutral solution (pH 7—8), in the presence of maleic acid, gave radicals derived from the maleic acid; however, no e.s.r. absorption was detected when N-t-butylhydroxylamine was used.

With N-methylhydroxylamine, at pH 1.8, the spectrum showed the presence of two radicals. The one present in the greater concentration was characterised by two doublet splittings (2.06 and 1.15 mT) of which the larger is in the range of α -proton splittings of species formed by addition of a radical to maleic acid.¹³ There are two radicals of the this type which could be formed under the reaction conditions, namely, (24) from the alkylamino-radical Me·NH₂⁺⁺, and (25) from the α -aminoalkyl radical ·CH₂·NH₃⁺. In order to distinguish between these possibilities, we studied the oxidation of N-methylaspartic acid with the hydroxyl radical in acidic solution. The spectrum observed had $a_{\rm H}(1) 2.04$, $a_{\rm H}(1)$ 1.34 mT, consistent with its being due to the radical (24) with splitting from the α - and β -protons, respectively; moreover, this radical is expected to be formed faster than its isomers by reaction of N-methylaspartic acid with the electrophilic hydroxyl radical.¹⁵ Since the splitting constant for the β -proton is significantly different in this case from that of the radical derived from

D. J. Edge, R. O. C. Norman, and P. M. Storey, J. Chem. Soc. (B), 1970, 1096.
 N. H. Anderson, M. McMillan, and R. O. C. Norman, J.

Chem. Soc. (B), 1970, 1075.

N-methylhydroxylamine, we attribute to the latter structure (25).

	,		R1	R²
Me•NH2•CH•CO2H	H ₃ N·CR ¹ R ² ·CH·CO ₂ H	(25)	н	Н
	-	(26)	Н	Me
(24) •ĊH•CO₂H	•ĊH•CO₂H	(27)	Me	Me

Only two resonances, separated by 0.1 mT, were discerned for the radical present in smaller concentration. We believe that this is part of the spectrum of the radical (28), the other two resonances of which were obscured by those of the radical (25); the full spectrum is observed when either *N*-ethyl- or *N*-isopropyl-hydroxylamine is used (see below).

With N-ethylhydroxylamine, at pH 2.2, the spectrum showed the presence of two radicals. That in smaller concentration had splitting constants (Table 7) charac-

TABLE 7

Hyperfine splitting constants (mT) of the radicals

	H ₃ N•CR ¹ R	² ·CH(CO ₂ H	I)∙CH(CO₂H)
Radical	\mathbb{R}^1	\mathbb{R}^2	$a_{\alpha \cdot \mathrm{H}}(1)$	$a_{\beta-\mathbf{H}}(1)$
(25)	н	\mathbf{H}	2.06	1.15
(26)	H	\mathbf{Me}	$2 \cdot 10$	0.95
(27)	Me	Me	2.03	0.85

teristic of adducts of maleic acid and is assigned, by analogy to the major spectrum from the N-methyl compound, the structure (26). The other $[a_{\rm H}(2) 0.64,$ $a_{\rm H}(1) 0.11$ mT, g 2.0035] is believed to be the species (28), for reasons discussed elsewhere.²² When the pH was reduced, the observed concentration of the adduct (26) increased relative to that of the radical (28). When the pH was raised, the opposite effect was observed; the adduct (26) could barely be discerned at pH 2.7. Further successive increases in the pH to 5 brought about changes in the structure of the radical (28) which are discussed in the following Paper.



N-Isopropylhydroxylamine in acid solution behaved similarly to the N-ethyl compound, giving a radical



characterised as (27) by its splitting constants and analogy with the behaviour of the *N*-methyl compound, and also the radical (28). For a given pH, the observed concentration of the adduct (27) relative to that of (28) was lower than the corresponding ratio of the radicals (26) and (28) from *N*-ethylhydroxylamine.

Reactions at pH 7-8 in the presence of maleic acid gave the following results. With N-methylhydroxylamine, the spectrum had $a_{\rm H}(1)$ 2.045 and $a_{\rm H}(1)$ 1.075 mT, attributable to the radical (30), the splitting constants being ascribed to the α - and β -protons, respectively; the same spectrum was obtained when maleic acid was replaced by fumaric acid. With N-ethylhydroxylamine, the predominant observed species had $a_{\rm H}(2)$ 0.66, $a_{\rm H}(1)$ 0.06 mT, attributable to the radical (29),²² and there were weak resonances attributable to the adduct (31) $[a_{\rm H}(1) \ 2.00, \ a_{\rm H}(1) \ 0.79 \text{ mT}$, ascribed to the α - and β-protons, respectively]; when maleic acid was replaced by fumaric acid, the spectrum of the adduct (31) was more intense and no other radical could be detected. With N-isopropylhydroxylamine, the radical (29) was present but there were no resonances attributable to an adduct; in contrast, when maleic acid was replaced by fumaric acid, the principal resonances were those of the adduct (32) $[a_{\alpha \cdot H} 2 \cdot 01, a_{\beta \cdot H} 0 \cdot 55 \text{ mT}]$ and the spectrum²² of a radical formed by one-electron reduction of fumaric acid was very weak.

The spectrum observed during the reaction of N-isopropylhydroxylamine with titanium(III) ion in the presence of diethyl maleate at ca. pH 3 was that of the radical (33) $[a_{\rm H}(2) 0.64, a_{\rm H}(5) 0.13 \text{ mT}]$;²² its intensity



decreased when the pH was reduced, but the adduct (34) was not detectable. However, evidence for the formation of this radical was obtained by analysis of the products formed when titanium(III) chloride solution was added dropwise to a stirred solution of N-isopropylhydroxylamine and diethyl maleate at ca. pH 1. After work-up, the lactam (35) was isolated in 7% yield; it presumably arises from the radical (34) as in reaction (10).



(d) Reactions in the presence of nitroalkanes in acid solution. The radicals (28) and (29) are products of the one-electron reduction of maleic acid; they have also been generated with the radicals $\cdot CO_2H$ and $\cdot CO_2^-$ as ²² N. H. Anderson, D. J. Edge, R. O. C. Norman, and P. R. West, following paper.

J. Chem. Soc. (B), 1971

reducing agents.²² In order to explore further the oneelectron reducing capacity of the titanium(III)-N-alkylhydroxylamine system in acid solution, we included a nitroalkane^{17,23} as a third reactant stream.

With 2-nitropropane and N-ethylhydroxylamine, there was only weak absorption, although this nitrocompound is efficiently reduced by hydroxy- or alkoxysubstituted carbon radicals at pH 1.8.23 However, when 2-methyl-2-nitropropane was used, the spectra of two radicals were recorded; one was identical with that assigned to the species (4; $R^1 = H$, $R^2 = Me$) (Table 1) and the other $[a_N(1) 2.80, a_H(1) 0.45 \text{ mT})$ was also obtained when the nitroalkane was reduced with the radical \cdot CO₂H and is assigned to the radical (36) (cf. ref. 17). When N-ethylhydroxylamine was replaced by the N-methyl analogue, only the spectrum of the radical (36) was observed, but with N-isopropylhydroxylamine there was no detectable absorption.

Me₃C-N (36) OH

Reaction Mechanisms.—As we shall show in the sequel. the results we have described are consistent with the paths outlined in the Scheme (except that nitrogen atoms neutral solution [by fumarate anion and the nitrone(5)]. In this context, it is notable that when amines trapped in an adamantane matrix are irradiated with X-rays, only α -aminoalkyl radicals are observed,²⁴ and it has also been reported that the radical \cdot NMe₂, formed by γ -irradiation of dimethylamine, changes into the radical •CH₂•NHMe even at 77 K.25 Under our conditions, rearrangement may occur by way of proton transfers as in reaction (11); the second step in this sequence is analogous to the conversion of aminium radical cations into a-aminoalkyl radicals which has been suggested as an intermediate step in the Polonovski reaction,²⁶ the electrochemical oxidation of tertiary amines,²⁷ and the reaction of tertiary amine N-oxides with iron(II) ion.²⁸

$$R^{1}R^{2}CH\cdot NH \cdot \underbrace{\overset{H^{+}}{\longleftarrow}}_{R^{1}R^{2}CH \cdot \dot{N}H_{2}} \cdot \underbrace{\overset{-H^{+}}{\longleftarrow}}_{R^{1}R^{2}\dot{C} \cdot NH_{2}} \underbrace{\overset{H^{+}}{\longleftarrow}}_{H^{+}} R^{1}R^{2}\dot{C} \cdot \overset{+}{N}H_{3} (11)$$

Since *N*-t-butylhydroxylamine, which cannot give an α -aminoalkyl radical via step (d), yields the nitroxide Me₃C·NH·O· in basic solution, we infer that this and the related nitroxides (17) are formed from alkylaminoradicals as in step (b) and not by reactions involving α -aminoalkyl radicals.



shown as unprotonated will be protonated under conditions of suitable pH; see later).

Evidence for the occurrence of step (a) is derived from the successful trapping of alkylamino-radicals by the aci-anion of nitromethane in basic solution. It is apparent that these radicals are extremely short-lived since their spectra were not observed under any of the conditions used. There is evidence of at least two modes of destruction (rearrangement and hydrogen-atom uptake) and the likelihood of a third (one-electron reduction).

Rearrangement to α -aminoalkyl radicals, step (d), evidently occurs readily, for these radicals were both observed directly in acid solution and were trapped efficiently in both acid solution [by t-nitrosobutane, nitric oxide, maleic acid, and the nitrone (5)] and

In strongly acidic solution, the nitroxides are not observed. With N-isopropylhydroxylamine, the nitroxide Me₂CH·NH·O· is detected at pH 3.9, increasing in concentration above this pH, while the radical •CMe₂•NH₃⁺ decreases in concentration as the pH is raised above 3.1. Possibly, the protonated nitroxide is more rapidly destroyed than its conjugate base (in which the spin is delocalised on to the nitrogen atom), while the species •CMe₂•NH₃⁺ is less rapidly destroyed than its conjugate base •CMe2•NH2 (which is particularly susceptible to one-electron oxidation; see later).

The one-electron reduction of alkylamino-radicals by titanium(III) ion, step (c), is to be anticipated, especially in acid solution; thus, there is evidence for the reduction of tertiary amine radical cations to the corresponding tertiary amines by iron(II) ion.28 In accord with expectation, isopropylamine was isolated, as its 2,4-dinitro-

²⁶ M. Polonovski and M. Polonovski, Bull. Soc. chim. France,

²³ M. McMillan and R. O. C. Norman, J. Chem. Soc. (B), 1968,

^{590.} ²⁴ D. E. Wood and R. V. Lloyd, J. Chem. Phys., 1970, 52,

^{3840.} ²⁵ G. V. Pukhal'skaya, A. G. Kotov, and S. Ya. Pshezhetskii, 1066 171 1380 Doklady Akad. Nauk S.S.S.R., 1966, 171, 1380.

 ²⁰ M. FORDOVSKI and C. K. Mann, J. Org. Chem., 1969, **34**, 1821.
 ²⁷ P. J. Smith and C. K. Mann, J. Org. Chem., 1969, **34**, 1821.
 ²⁸ J. P. Ferris, R. D. Gerwe, and G. R. Gapski, J. Org. Chem., 1969. 1968, **33**, 3493.

phenyl derivative, from the reaction of N-isopropylhydroxylamine with titanium(III) ion.

One-electron reduction of alkylamino-radicals is probably also responsible for the formation of the radical ·CHMe·NO₂, and thence^{20,21} the dimeric radical anion (20), in the reaction between the titanium(III)-N-alkylhydroxylamine system and the *aci*-anion MeCH·NO₂⁻; this *aci*-anion is known to be susceptible to one-electron oxidation by the sulphate radical anion.²⁰ In contrast, the *aci*-anion CH₂·NO₂⁻ preferentially reacts with the alkylamino-radicals by addition, the difference probably arising in part because the latter *aci*-anion is the more reactive of the two in addition processes (as it is towards the hydroxyl radical²⁹) and in part because the former, containing the electronreleasing methyl substituent, more readily releases one electron to an oxidant.

Radicals in which the tervalent carbon atom is bonded to a hydroxyl or alkoxyl substituent are effective oneelectron reducing agents; the property is attributable to the stability conferred by the substituent on the resulting carbonium ion.⁷ Analogous behaviour, step (e), would therefore be expected of (unprotonated) α -aminoalkyl radicals, since the unshared pair of electrons on the adjacent nitrogen atom should stabilise the carbonium ion (H₂N·CR₂ \longrightarrow H₂⁺N·CR₂) even more effectively than that on an adjacent oxygen atom. The following evidence for this behaviour is derived from the present study.

First, the nitromethane or nitroethane radical anion is observed during reaction of the titanium(III)-EDTA-N-alkylhydroxylamine system with the corresponding nitro-compound in basic solution when alkyl = Me, Et, or Pri, but not But. A potential reducing agent from this system is the radical formed from EDTA by abstraction of a hydrogen atom,¹⁹ and indeed this radical (presumably formed from EDTA and an alkylaminoradical) was itself observed when the concentration of EDTA was increased and the nitroalkane was excluded. However, if this radical were responsible for reduction under our conditions, then we should have expected the nitromethane radical anion to be formed with the use of N-t-butylhydroxylamine, contrary to observation. It is therefore probable that one-electron reduction is by the α -aminoalkyl radicals which can be formed from all the N-alkylhydroxylamines used except the t-butyl compound.

Secondly, radicals formed by one-electron reduction of maleic acid and its anions (acid solution and pH 7-8), t-nitrosobutane (pH 7-8), and 2-methyl-2nitropropane (acid solution) were observed with the use of N-methyl-, N-ethyl-, or (except in the last case) N-isopropyl-hydroxylamine but not with the N-t-butyl compound, the inference again being that α -aminoalkyl radicals are the electron donors. The formation of the radical (4; $\mathbb{R}^1 = \mathbb{H}$, $\mathbb{R}^2 = \mathbb{M}e$) from N-ethylhydroxyl-

amine and the nitro-compound presumably follows disproportionation¹⁷ of the radical (36), as in reaction (12).

$$2\operatorname{Me}_{3}C-N \xrightarrow{\bigcirc} -\operatorname{Me}_{s}C\cdot\operatorname{NO}_{2} \\ \bigcirc H \xrightarrow{\longrightarrow} \operatorname{Me}_{3}C\cdot\operatorname{N}_{\circ} \\ (36) \xrightarrow{\longrightarrow} \operatorname{Me}_{3}C-N \xrightarrow{\bigcirc} \operatorname{Me}_{3}C-N \xrightarrow{\frown} \operatorname{Me}_{3}C-N \xrightarrow{+} \\ H \xrightarrow{+} M \xrightarrow{+}$$

In the cases of reaction of maleic acid (or its anions) and t-nitrosobutane, one-electron reduction evidently competes, in a pH-dependent way, with the addition by the α -aminoalkyl radical. Thus, t-nitrosobutane gives adducts in acid solution but the product of one-electron reduction, Me₃C·NH·O·, at pH 7-8, and maleic acid gives both adducts and one-electron reduction products in ratios which decrease as the pH is raised. This no doubt reflects the increasingly significant removal of the electron-donating α -aminoalkyl radical (to give its conjugate acid, which is unlikely to be an effective donor) as the pH is lowered. It is not possible to estimate the pK_a values of protonated α -aminoalkyl radicals since nothing is known of the relative rates of donation by these radicals and addition by their conjugate acids. However, since electron transfer is observed at a pH as low as ca. 2, it is likely that the pK_a values are much lower than those of the parent amines; this is to be expected because of the stabilisation energy which should be associated with the delocalised structures of α -aminoalkyl radicals (R¹R²Ċ- $\ddot{N}H_2 \leftrightarrow R^1R^2\ddot{C}-\dot{N}H_2$).

The occurrence of step (e) should give protonated imines and thence, by solvolysis, carbonyl compounds [step (f)]. In accord with this, acetone was isolated, as its 2,4-dinitrophenylhydrazone, from the reaction of titanium(III) ion with N-isopropylhydroxylamine. In acidic solution, the yield of acetone was greater than 50%both when the titanium(III) ion was added slowly to the hydroxylamine and when the reverse method of addition was employed, the latter result suggesting that step (d) is relatively efficient compared, for example, with step (c). However, in basic solution the addition of the hydroxylamine to titanium(III) ion in the presence of tartaric acid as a sequestering agent gave less than 4%of acetone. This is presumably because step (c) is relatively more efficient under these conditions, in accord with earlier evidence that titanium(III) tartrate is a more powerful one-electron reducing agent than titanium(III) chloride in acid solution.²¹

Some aldehydes and ketones react rapidly enough with hydroxylamine under our flow-system conditions to form adducts of the type $R^1R^2C(OH)\cdot NH\cdot OH$ and thence the nitroxides $R^1R^2C(OH)\cdot NH\cdot O$ which can be detected by their e.s.r. spectra; likewise, with acetone and *N*-methylhydroxylamine, the spectrum of the radical $Me_2C(OH)\cdot NMe\cdot O$ is observed.⁶ Analogous reactions would be expected with the carbonyl compounds such as acetone which are formed under the conditions we have employed; in particular, the radical (18; Y, $Z \neq H$) might be formed from *N*-ethylhydroxylamine *via* acetaldehyde, according to steps (g) and (h), and

²⁹ R. O. C. Norman and P. M. Storey, J. Chem. Soc. (B), 1971, 1009.

therefore be the species (37) [reaction (13)]. To seek evidence for this, we included acetaldehyde in the reagents giving the radical (18); in accord with our suggestion, this resulted in an increase in the observed concentration of the radical (18) relative to that of the radical Et·NH·O. Moreover, when N-methylhydroxylamine was employed instead of the N-ethyl compound, again with the inclusion of acetaldehyde, a radical was observed with $a_{\rm N}(1)$ 1·62, $a_{\rm H}(3)$ 1·41, and $a_{\rm H}(1)$ 0·55 mT, consistent with the structure (38).

Et•NH•OH	+ √H₂
$\begin{array}{c} H_{3}O \\ \hline \\ -NH_{4}^{+} \end{array} \begin{array}{c} \text{MeCH:O} \\ \hline \\ HO \\ \end{array} \begin{array}{c} \text{Et·N+OH} \\ \hline \\ HO \\ \end{array} \begin{array}{c} -H \\ HO \\ \end{array} \end{array}$	(13)
Me•N-CHMe O• OH (38)	

Radicals analogous to (37) were not observed when either N-methyl- or N-isopropyl-hydroxylamine was used. In the former case, this is probably because the formaldehyde formed by step (f) is hydrated and unreactive towards N-methylhydroxylamine;⁶ in accord with this view, the addition of formaldehyde in place of acetaldehyde in the experiment described above which leads to the radical (37) caused no change in the spectrum. In the latter case, it is possible that step (g)occurs so much less readily with acetone and N-isopropylhydroxylamine than with acetaldehyde and N-ethylhydroxylamine that the nitroxide is not generated rapidly enough for detection.

Further information about the relative importance of some of the steps in the Scheme was sought by a study of the stoicheiometry of the reaction of titanium(III) ion with N-isopropylhydroxylamine. If the process consisted essentially of reactions (14)-(16), the stoicheiometric ratio would be $[Ti^{III}]$: $[Pr^{I} \cdot NHOH] = 1: 0.5$, whereas if the oxidation of α -aminoalkyl radicals [step (e)] was important [by any of reactions (17)-(19)], a smaller value would be expected. The values found were $1:0.9\pm0.1$ for acidic solution, irrespective of whether the hydroxylamine was added to the reducing agent or vice versa, and $1:0.5 \pm 0.05$ for basic solution [use of titanium(III) tartrate], suggesting that step (e) is important under the former conditions but not under the latter; this is in accord with the evidence obtained from the yields of acetone under the two sets of conditions. Of possible oxidation paths for α -aminoalkyl radicals, reactions (17)-(19), the first two are unlikely to be significant because of the relatively weak oxidising power of titanium(IV) ion, at least for α -hydroxyalkyl radicals,⁹ and the relatively low probability of radicalradical interaction. On the other hand, the third is reasonable by analogy with the one-electron reduction (20) of hydrogen peroxide by α -hydroxyalkyl radicals^{9,30} (see later). However, this reaction leads to a new alkylamino-radical and thence another α -aminoalkyl radical, so that a chain reaction would occur and a very small

value for the stoicheiometric ratio would, in principle, be possible; the fact that this is not the case indicates that the average chain length cannot be long.

$$Me_{2}CH\cdot NH\cdot OH \xrightarrow{Till1, H^{+}} Me_{2}CH\cdot NH_{2} \cdot$$
(14)

$$Me_{2}CH\cdot NH_{2} \cdot \longrightarrow Me_{2}CH\cdot NH_{2}$$
(15)

$$Me_{2}CH\cdot NH_{2} \cdot \xrightarrow{-H^{+}} Me_{2}\dot{C}\cdot NH_{2} \xrightarrow{H^{+}} Me_{2}\dot{C}\cdot NH_{3} \xrightarrow{TiIII} Me_{2}CH\cdot NH_{2} \quad (16)$$

$$Me_{2}\dot{C}\cdot NH_{3} + Ti^{IV} \longrightarrow Me_{2}C = \overset{+}{N}H_{2} + Ti^{III}$$
(17)

$$Me_{2} \dot{C} \cdot NH_{2} + Me_{2}CH \cdot \dot{N}H_{2} \cdot \longrightarrow Me_{2}C = \dot{N}H_{2} + Me_{2}CH \cdot NH_{2} \quad (18)$$

$$Me_2C = NH_2 + Me_2CH + NH + OH^-$$
 (19)

$$R^{1}R^{2}\dot{C}\cdotOH + H_{2}O_{2} \longrightarrow R^{1}R^{2}C = OH + OH + OH^{-}$$
 (20)

The analogy between reactions (19) and (20) prompted us to study the stoicheiometry of the titanium(III)hydrogen peroxide system in the presence of various alcohols to seek further information about the latter (the evidence for which has so far been gained by other means^{9,30}). When titanium(III) ion was added slowly to hydrogen peroxide in acidic solution, the observed stoicheiometric ratio was $[Ti^{III}]$: $[H_2O_2] = 2: 1\cdot 1 \pm 0\cdot 1$, as expected on the basis of reactions (21) and (22). In contrast, when methanol, ethanol, or isopropyl alcohol was included with the peroxide, the observed values were $2: 2\cdot 4, 2: 2\cdot 6$, and $2: 3\cdot 4 \pm 0\cdot 1$, respectively. That these values are greater than unity is consistent with the occurrence of reactions (23) and (20) in succession; moreover, the increase in the values in the order $MeOH < EtOH < Pr^{i}OH$ is in accord with the effect of methyl substituents in promoting the capacity for oneelectron donation of the corresponding radicals as evidenced in other reductions.⁷ However, it is apparent that, as with the titanium(III)-N-isopropylhydroxylamine reaction, the chains are, on average, short.

$$\mathsf{T}\mathsf{i}^{\mathbf{III}} + \mathsf{H}_{2}\mathsf{O}_{2} \longrightarrow \mathsf{T}\mathsf{i}^{\mathbf{III}} + \mathsf{O}\mathsf{H} + \mathsf{O}\mathsf{H}^{-}$$
(21)

$$Ti^{III} + OH \longrightarrow Ti^{IV} + OH^{-}$$
(22)

$$\cdot OH + R^{1}R^{2}CH \cdot OH \longrightarrow R^{1}R^{2}\dot{C} \cdot OH + H_{2}O$$
(23)

 α -Aminoalkyl Radicals from Amines.—Like the hydroxy-group in an alcohol, the amino-group in an aliphatic amine would be expected to activate the adjacent C-H bond towards abstraction by the electrophilic hydroxyl radical, thereby giving an α -aminoalkyl radical directly. However, we could not detect e.s.r. absorption during the reaction of titanium(III) tartrate with hydrogen peroxide in the presence of methylamine or ethylamine at pH 12.

Since some α -aminoalkyl radicals have been successfully trapped by t-nitrosobutane during the photo-

³⁰ C. E. Burchill and I. S. Ginns, Canad. J. Chem., 1970, 48, 1232.

reduction of benzophenone in the presence of the corresponding amines,³¹ we included this nitrosocompound in our oxidation system. Spectra were then observed from both methylamine $[a_N(1) 1.63, a_N(1) 0.175,$ $a_{\rm H}(2)$ 0.98, $a_{\rm H}(2)$ 0.04 mT] and ethylamine [$a_{\rm N}(1)$ 1.48, $a_{\rm N}(1)$ 0.125, $a_{\rm H}(1)$ 0.175, $a_{\rm H}(2)$ 0.05 mT], although the predominant radical (ca. 5:1) present in each case was the nitroxide Me₂C·NH·O·. The spectra are assigned to the radicals (39; R = H or Me, respectively), the larger and smaller nitrogen splittings being attributable to the nitroxide and amino nitrogen atoms, respectively, the very small triplet splitting to the amino protons, and the remaining triplet (methylamine) or doublet (ethylamine) to the CH protons adjacent to the nitroxide function. Support for the assignments was sought by mixing titanium(III) ion and N-ethylhydroxylamine at pH 2 to give the radical •CHMe•NH₃⁺ and then introducing base and t-nitrosobutane at a second mixing point to give a final pH of ca. 11 so as to form the radical (39;

R = Me; as expected, the same spectrum was observed as from the titanium(III) tartrate-hydrogen peroxideethylamine reaction.*

Our failure to detect α -aminoalkyl radicals themselves from the oxidation of amines, together with the evidence for their formation from the trapping experiments, suggests that they are very readily oxidised by hydrogen peroxide [reaction (24)]. This would be consistent with the evidence described earlier for step (e) in the Scheme and for reaction (20), coupled with the expectation that the carbonium ion which develops during reaction (24) should be more effectively stabilised by the α -aminogroup than is that developing during reaction (20) by the α -hydroxy-group.

$$R^{1}R^{2}\dot{C}\cdot NH_{2} + H_{2}O_{2} \longrightarrow R^{1}R^{2}\dot{C} \stackrel{\frown}{\longrightarrow} NH_{2} + \cdot OH + OH^{-}$$
(24)

Hyperfine Splitting Constants.—The following are the more notable features of the hyperfine splitting constants which we have listed.

In the radicals (4) and (8), the larger nitrogen splitting is assigned to the nitrogen nucleus in the nitroxide function and the smaller to that in the β -amino-group, as in other β -amino-nitroxides.⁶ In each group of radicals, there is a large reduction in the splitting constant for the β -proton(s) when \mathbb{R}^2 is changed from H to Me in the generalised structure (40; $\mathbb{R}^1 = H$, $\mathbb{R}^3 = Bu^t$ or α aminoalkyl); evidently the one β -C-H bond in the latter case makes, on average, a larger dihedral angle with the π -system of the nitroxide function than do the two C-H bonds in the former, so that hyperconjugative interaction is reduced.⁷ At the same time, the splitting constant of the amino-group nitrogen nucleus is also slightly smaller for the methyl-substituted radicals; moreover, it is so small that it could not be resolved when a second methyl group was introduced [as estimated from the line-widths, splittings of <0.1 and <0.05 mT would have been resolved in the radicals (4) and (8) $(R^1 = R^2 = Me)$, respectively]. Since the average dihedral angle for the β -C-N bond decreases as that for a β -C-H bond increases towards 90°, it appears that the amino-nitrogen splitting is not maximal for a dihedral angle of 0°. Now, in the related radicals (40; $R^3 = H$), the amino-nitrogen splittings are significantly larger than in the radicals (40; $\mathbb{R}^3 = \mathbb{B}u^t$ or α -aminoalkyl) (e.g., 0.30 and 0.22 mT for 40; $R^3 = H$; $R^1 = H$, $R^2 = Me$ and $R^1 = R^2 = Me$, respectively), and it has been suggested that the nuclei acquire spin by way of an internally hydrogen-bonded system represented by the structure (41).⁶ It is probable, therefore, that, because of steric interactions with the group \mathbb{R}^3 , the radicals (40; $\mathbb{R} = \mathbb{B}u^t$ or α -aminoalkyl) do not readily adopt conformations corresponding to (41).

In the radicals (19) (except for R = H), (22), and (23), the central resonance of the triplet splitting due to the methylene protons was broadened with respect to the wing resonances, indicating that the interconversion of preferred conformations arising from rotation about the C-nitro or C-nitroxide bond is occurring at a rate comparable with the hyperfine splitting interval between the two protons in a particular conformation.

It was pointed out earlier that the methyl-group splittings in the radicals (12)—(14) show that a very large proportion of the unit spin is on the (formally) tervalent carbon atom. Treatment of the data by Fischer's correlative method³² shows that the ammonio-group is ineffective at delocalising the spin; the spin-withdrawing parameter, expressed as a percentage, is 0.8, 2.0, and 0.1 as derived from (12), (13), and (14), respectively, which may be compared with³² 8% for a methyl substituent and 16% for hydroxyl. It can also be inferred, at least for the radicals (12) and (14) which contain both α - and β -protons, that the protonated amino-group does not induce bending at the tervalent carbon atom; thus, the ratio $a(\beta-Me)/a(\alpha-H)$ is 1.18 for the former radical and 1.19 for the latter, these values being in the range consistent with coplanar species and significantly

^{*} On the basis of these results, it is probable that the small triplets in the spectra observed during the photoreduction of benzophenone in the presence of t-nitrosobutane and propylamine or butylamine are due to the amino protons in the adducts corresponding to (39), and not to the γ -methylene protons as was suggested.³¹

 ³¹ I. H. Leaver and G. C. Ramsay, *Tetrahedron*, 1969, 25, 5669.
 ³² H. Fischer, Z. Naturforsch., 1964, 19a, 866; 1965, 20a, 428.

smaller than the values for radicals such as •CHMe•OH which, from independent evidence, are known to be distorted from planarity.33

EXPERIMENTAL

A Varian E-3 spectrometer, with 100 kHz modulation and an X-band klystron, was employed in conjunction with Varian-type perspex mixing chambers⁶ which enabled (i) two solutions to be mixed, (ii) three solutions to be mixed simultaneously, or (iii) two solutions to be mixed followed by a third, and a fourth if required, after a time interval of ca. 0.02 s; the total flow rate in experiments involving N-alkylhydroxylamines was ca. 120 ml min⁻¹ and in other experiments it was ca. 200 ml min⁻¹. Splitting constants were measured to within ± 0.01 mT, the calibration of the spectrometer being checked by comparison with p-benzosemiquinone in ethanol ($a_{\rm H}$ 0.237 mT) from time to time. g-Factors were measured to within ± 0.0001 by comparison with an aqueous solution of Fremy's salt (g 2.0055) which was contained in a capillary attached to the aqueous sample cell, or with a radical having a known g-factor, where one was also present.

Materials. N-Alkylhydroxylamines were prepared by reduction of the corresponding nitroalkane with zinc dust (1.67 mol scale), following the literature method for Nmethylhydroxylamine with some modifications.34,35 The zinc oxide and unchanged zinc dust were filtered off at the end of the reaction and washed thoroughly with water $(2 \times 800 \text{ ml})$; the combined filtrate was acidified (conc. HCl) and evaporated to ca. 500 ml under reduced pressure at 90°. The 1H n.m.r. spectra of the solutions thus obtained (after dilution with D₂O) showed the N-alkylhydroxylamine hydrochlorides to be pure, discounting the presence of ammonium chloride. Unless otherwise stated these solutions were used for the e.s.r. experiments after appropriate dilution. The concentrated solutions were estimated by basification with a known volume of aqueous ammonia and titration into an alkaline solution of titanium(III) tartrate. The end-point was indicated by the disappearance of the dark blue colour of the titanium(III) tartrate complex, the accuracy of this method (ca. $\pm 5\%$) being sufficient for solutions used in the e.s.r. experiments. Crystalline Nalkylhydroxylamine hydrochlorides were isolated from the concentrated solutions described above, following the literature method for the isolation of N-methylhydroxylamine hydrochloride.34

t-Nitrosobutane (2-methyl-2-nitrosopropane) was prepared from t-butylhydroxylamine.³⁶ t-Butyl methylene nitrone was obtained from t-nitrosobutane by treatment with diazomethane;¹¹ the n.m.r. spectrum of the crude product indicated it to be essentially pure. N-Ethylethylidenamine was prepared by reaction of acetaldehyde with ethylamine,37 N-methylaspartic acid was prepared by the literature method,38 and 2-methyl-2-nitropropane was obtained by oxidation of t-butylamine.39 Titanium(III) chloride solution was technical grade and all other materials were laboratory reagent grade.

E.s.r. Experiments.—In the experiments described below

- J. Meisenheimer and L.-H. Chou, Annalen, 1939, 539, 78.
 W. D. Emmons, J. Amer. Chem. Soc., 1957, 79, 6522.

in which three reactant solutions were used, the solutions were mixed simultaneously unless otherwise stated.

(a) Reactions of N-alkylhydroxylamines in acidic solution. Solution (i) contained titanium(III) chloride (0.008M) and sulphuric acid (1-3 ml/l) and solution (ii) contained the N-alkylhydroxylamine hydrochloride (0.05-0.1M) and hydrochloric acid to bring the pH to ca. 1.5. In trapping experiments, a third solution contained one of the following: t-nitrosobutane (ca. 0.2 g/l, prepared by dissolving the nitroso-compound in a little hot acetone and diluting the solution with warm water), sodium nitrite (1 g/l), t-butyl methylene nitrone (ca. 0.2 g/l), maleic acid (10 g/l), fumaric acid (10 g/l), diethyl maleate (4 ml/l in hot water), or a nitroalkane (ca. 3 ml/l in warm water). For experiments at pH 2-6, solution (i) contained titanium(III) chloride (0.008M) and (+)-tartaric acid (1.5 g/l) and solution (ii) contained the N-alkylhydroxylamine hydrochloride (0.05-0.1M) and ammonia to bring the solution to the appropriate pH. In experiments with maleic acid, ammonia was also added to this solution. When NN-diethylhydroxylamine was used, solution (i) contained titanium(III) chloride (0.016M) and sulphuric acid (1 ml/l), and solution (ii) contained NN-diethylhydroxylamine (0.1M) and sulphuric acid (20 ml/l).

(b) Addition of the amino-radical to t-butyl methylene nitrone. Solution (i) contained titanium(III) chloride (0.008m) and sulphuric acid (3 ml/l), solution (ii) hydroxylamine hydrochloride (10 g/l) and sulphuric acid (5 ml/l), and solution (iii) t-butyl methylene nitrone (ca. 0.2 g/l).

(c) Reaction of the radical •CO₂H with N-ethylethylidenamine. Solution (i) contained titanium(III) chloride (0.016M), formic acid (20 ml/l), and sulphuric acid (3.3 ml/l), solution (ii) contained hydrogen peroxide (100-vol) (2 ml/l), formic acid (20 ml/l), and sulphuric acid (3.3 ml/l), and solution (iii) contained N-ethylethylidenamine (10 ml/l). The same spectrum was obtained in lower intensity when solutions (i) and (ii) were mixed before the introduction of solution (iii) in the two-stage mixing cell.

(d) Experiment in D_2O . Solution (i) contained titanium-(III) chloride $(12\frac{1}{2}\% \text{ w/v}, 2.5 \text{ ml})$ and sulphuric acid (0.25)ml) in ca. 90% deuterium oxide (250 ml) and solution (ii) contained N-isopropylhydroxylamine hydrochloride (2.8 g) and sulphuric acid (0.25 ml) in the same solvent (250 ml). It was only possible to scan the centre part of the spectrum with these amounts of the reactants.

(e) Reactions of N-alkylhydroxylamines in alkaline solution. Solution (i) contained titanium(III) chloride (0.008M), (+)-tartaric acid (1.5 g/l) or EDTA (6 g/l), and ammonia to give the appropriate pH, and solution (ii) contained the N-alkylhydroxylamine (0.01-0.1M) at pH 6-7. For experiments with an excess of EDTA, a third solution contained EDTA (20 g/l) and ammonia to give ca. pH 10. The passage of nitrogen through the solutions for 15 min immediately before the experiments did not affect the results. For experiments involving the aci-anions of nitromethane or nitroethane, solution (i) was as above, with EDTA as chelating agent, solution (ii) was as above, and a third solution contained the nitroalkane (3.3 ml/l) and ammonia (d 0.880, 3.3 ml/l) and had been allowed to stand for 10 min before use. For trapping experiments with

³³ A. J. Dobbs, B. C. Gilbert, and R. O. C. Norman, J. Chem. Soc. (A), 1971, 124. ³⁴ E. Beckmann, Annalen, 1909, **365**, 204.

³⁷ K. N. Campbell, A. H. Sommers, and B. K. Campbell, J. Amer. Chem. Soc., 1944, 66, 82.

 ³⁹ A. Zilkha and M. D. Bachi, J. Org. Chem., 1959, 24, 1096.
 ³⁹ N. Kornblum and R. J. Clutter, J. Amer. Chem. Soc., 1954, 76, 4494.

t-nitrosobutane, t-butyl methylene nitrone, maleic acid, and fumaric acid, solution (iii) was as in (a), except that in the case of maleic and fumaric acids, ammonia was added to bring the third solution to the required pH.

(f) Oxidations with iron(III) ion. Solution (i) contained potassium hexacyanoferrate(III) (0.5 g/l) and ammonia (d 0.880, 2 ml/l), and solution (ii) was as in (e).

(g) Oxidations with cerium(IV) ion. Solution (i) contained cerium(IV) ammonium nitrate (2 g/l) and solution (ii) contained the N-alkylhydroxylamine hydrochloride (0·1M) and hydrochloric acid to give *ca.* pH 4.

(h) Experiment with sulphute radical anion. Solution (i) contained titanium(III) chloride (0.016M), (+)-tartaric acid (3 g/l), and ammonia (d 0.880, 6 ml/l), solution (ii) contained potassium persulphate (5 g/l) and methylamine (0.5M), and solution (iii) contained nitromethane as in (e).

(i) Experiments with added aldehydes. Solution (i) contained titanium(III) chloride (0.008M), EDTA (6 g/l), and ammonia (d 0.880, 4 ml/l), solution (ii) contained N-methylor N-ethyl-hydroxylamine hydrochloride (0.1M), and solution (iii) contained (a) no aldehyde, (b) formaldehyde (38% w/v, 1 ml/l), or (c) acetaldehyde (1 ml/l).

(j) The trapping of α -aminoalkyl radicals from amines. Solution (i) was as in (e) with tartaric acid as chelating agent, solution (ii) contained hydrogen peroxide (100-vol) (1 ml/l) and the amine (0.5M), and solution (iii) contained t-nitrosobutane (0.5 g/l).

(k) Formation of the radical (37) from N-ethylhydroxylamine. The two-stage mixer was used. Solution (i) contained titanium(III) chloride (0.008M) and (+)-tartaric acid (1.5 g/l), solution (ii) contained N-ethylhydroxylamine hydrochloride (0.1M) and hydrochloric acid to give ca. pH 2, solution (iii) contained ammonia (d 0.880, 100 ml/l), and solution (iv) contained t-nitrosobutane (0.5g/l).

Addition of the Radical •CMe₂•NH₃⁺ to Diethyl Maleate: Isolation of 2-Ethoxycarbonyl-3,3-dimethylbutyrolactam (35).—An excess (60 ml) of titanium(III) chloride solution $(12\frac{1}{2}\% \text{ w/v})$ was added dropwise during 1 h to a stirred solution of N-isopropylhydroxylamine hydrochloride (22 g), diethyl maleate (20 ml), and hydrochloric acid (5 ml) in 50%aqueous methanol (400 ml) under nitrogen. The solution was extracted with chloroform (4 \times 50 ml), made alkaline with sodium hydroxide, and again extracted with chloroform $(4 \times 50 \text{ ml})$. The second combined extract was dried and evaporated. Purification by chromatography on alumina followed by recrystallisation from benzenelight petroleum (b.p. 60-80°) gave the lactam (2.5 g, 7%), m.p. 57° (Found: C, 58.0; H, 8.1; N, 7.3. C₉H₁₅NO₃ requires C, 58·35; H, 8·1, N, 7·6%); m/e 185(M); τ 8·81 (3H, s, Me), 8·70 (3H, t, J 7·6 Hz, CH₂-Me), 8·52 (3H, s, Me), 7·9-6·6 (3H, ABC system, CH-CH₂), 5·80 (2H, q, J 7·6 Hz, CH_2Me), 2.0 (1H, s, NH).

The Isolation of Acetone and Isopropylamine from the Reaction of N-Isopropylhydroxylamine with Titanium(III) Ions.—An acidic solution of titanium(III) chloride (0.20M, 10.0 ml) was added dropwise to a stirred acidic solution of N-isopropylhydroxylamine hydrochloride (0.100M, 10.0 ml), which had previously been deoxygenated by passing nitrogen through it for 10 min. After the addition was complete, an excess of 2,4-dinitrophenylhydrazine in acidic methanol was added and the mixture was set aside for 30 min. The precipitate was recrystallised from aqueous

ethanol to give acetone 2,4-dinitrophenylhydrazone (135 mg), m.p. 128°, identical with an authentic sample. When the solution of N-isopropylhydroxylamine hydrochloride was added to the solution of titanium(III) chloride, acetone 2,4-dinitrophenylhydrazone (156 mg) was isolated following a similar procedure. Isopropylamine was isolated by the following method. Titanium(III) chloride solution was added to N-isopropylhydroxylamine hydrochloride solution, in the same manner as described above, but on twice the scale. Tartaric acid (1 g) was added to the solution, followed by concentrated aqueous sodium hydroxide to make the solution strongly basic. The mixture was distilled until ca. 20 ml distillate, containing all the isopropylamine, had been collected. Addition of an excess of fluoro-2,4dinitrobenzene and sodium hydrogen carbonate, following the literature method,40 gave the crude product which was purified by t.l.c. (Kieselgel G nach Stahl, eluant benzenechloroform (3:1)] and recrystallised from benzene-light petroleum (b.p. 80-100°) to give N-2,4-dinitrophenylisopropylamine (61 mg), m.p. 94° (lit., 40 94-95°), identical with an authentic sample. When a similar procedure was followed except that the N-isopropylhydroxylamine hydrochloride solution was added to the titanium(III) chloride solution, N-2,4-dinitrophenylisopropylamine (136 mg) was again isolated.

Determination of the Stoicheiometry of the Reaction of Titanium(III) Ions with N-Isopropylhydroxylamine.—A solution of titanium(III) chloride (10.0 ml, 0.191M) was added dropwise to a stirred acidic solution of N-isopropylhydroxylamine (10.0 ml, 0.100M) under nitrogen. The excess of titanium(III) chloride was determined by titration with standard iron(III) ammonium sulphate (0.100M) with ammonium thiocyanate as an internal indicator. The stoicheiometry of the reaction was found to be $[Ti^{III}]: [Pr^{i}NHOH] = 1: 0.9 \pm 0.1$. When the addition was carried out in the inverse manner, the stoicheiometry was found to be the same, within experimental error.

A deoxygenated alkaline solution of *N*-isopropylhydroxylamine (0.050M) was added dropwise to a stirred alkaline solution containing titanium(III) tartrate (0.0100 mol) under nitrogen. The solution was acidified and the excess of titanium(III) ion was determined as before. The stoicheiometry of the reaction was found to be $[Ti^{III}]$: $[Pr^{i}\cdot NHOH]$ = 1: 0.5 ± 0.05.

Determination of the Stoicheiometry of the Reaction of Titanium(III) Chloride with Hydrogen Peroxide in the Presence of Added Alcohols.—A solution of titanium(III) chloride (15.0 ml, 0.201M) was added dropwise during ca. 2 min to a stirred solution of aqueous hydrogen peroxide (10.0 ml, 0.077M) and sulphuric acid (0.1 ml) under nitrogen. The excess of titanium(III) ion was determined by titration with standard iron(III) ammonium sulphate, with ammonium thiocyanate as an internal indicator. The experiment was repeated, with 10.0 ml aliquots of titanium(III) chloride solution and with 10.0 ml of each of methanol, ethanol, and isopropyl alcohol added to the hydrogen peroxide solution.

The award of an I.C.I. Fellowship to one of us (N. H. A.) is gratefully acknowledged.

[0/2066 Received, December 7th, 1970]

⁴⁰ H. Bräuniger and K. Spangenberg, *Pharmazie*, 1957, **12**, 335.