229. *Aliphatic Hydroxylamines. Part II.* Autoxidation.*

By David H. Johnson, M. A. Thorold Rogers, and G. Trappe.

The autoxidation of aliphatic hydroxylamines in aqueous alkaline solution has been studied and the effect of catalysts has been demonstrated. Usually, 1½ or 2 atoms of oxygen are absorbed, and peroxidic material is formed. Part of this is hydrogen peroxide, but a part is organic, and progress towards the isolation of the pure organic component has been made. A mechanism, similar in some respects to that now generally accepted for olefinic autoxidation, is considered.

The ready autoxidation of aliphatic hydroxylamines, both primary, $R{\cdot}CH_2{\cdot}NH{\cdot}OH$, and secondary, $R{\cdot}CH_2{\cdot}N(OH){\cdot}CH_2R'$, has been known for a very long time. Indeed, it is difficult to avoid the formation of aldehyde, which has long been recognised as one of the products, during any manipulation of hydroxylamines, especially under alkaline conditions. Behrend and König [1] attribute the first observation to Beckmann. These authors, and Bamberger and Szolayski [2] examined the course of the reaction, and obtained a number of products; they also showed that hydrogen peroxide is formed. Since then the mechanism of autoxidation of the olefins has been extensively studied, but no re-investigation of the autoxidation of hydroxylamines has been undertaken in the light of the work of Farmer, Bolland, Gee, and others.

In this paper we report preliminary results which lead us to formulate a tentative mechanism for the autoxidation which resembles that now generally accepted for olefinic autoxidation. In the later stages our efforts have been concentrated on attempts to isolate the organic peroxides (which are posulated to be intermediates) in a pure state. Although we have failed to achieve this objective, we present evidence that organic peroxides are formed and can be isolated, though the conditions for isolating pure material in quantity require defining more closely.

We have worked almost entirely with *NN*-dialkylhydroxylamines, but no obvious difference in behaviour has been apparent in the few experiments carried out on the monoalkylhydroxylamines, and we believe that the same principles apply. All our autoxidations have been carried out in aqueous solution.

Many of the early experiments [2] were carried out on the readily available mono- or di-benzylhydroxylamine, and the aqueous suspensions were air-blown for long periods. The choice of dibenzylhydroxylamine was unfortunate as it is very insoluble, hence the oxidation is heterogeneous. Bamberger suggested that the oxidation of amines under certain conditions can proceed through the hydroxylamine, and appreciated [3] that the sequence was :

$$\text{Amine} \xrightarrow[\text{Slow}]{(a)} \text{Hydroxylamine} \xrightarrow[\text{Rapid}]{(b)} \text{Primary product} \xrightarrow[\text{Less rapid than } (b)]{(c)} \text{Secondary products}$$

but by the nature of his experiments he allowed the primary products to be further oxidised by stage (*c*) to a complex variety of end-products. We have attempted to overcome this obstacle, and have found that the simple dialkylhydroxylamines are autoxidised in aqueous solution or suspension at pH >7 at room temperature or at 37° at a rate which can be measured very conveniently by following the uptake of oxygen.

Our early experiments were carried out in a Warburg apparatus at 37°.† It was found that :

(1) The rate of oxygen uptake is a function of pH, being very slow at pH 7, and very rapid in the presence of sodium hydroxide (Fig. 1).

(2) In most runs the absorption of oxygen was 1½ atoms per molecule of hydroxylamine.

* Part I, *J.*, 1955, 769.

† In these experiments we were assisted by Dr. J. Madinavietia, whom we cordially thank.

[1] Behrend and König, *Annalen*, 1891, **263**, 210.

[2] Bamberger and Szolayski, *Ber.*, 1900, **33**, 3193.

[3] Bamberger, *Ber.*, 1902, **35**, 4293; Bamberger and Scheutz, *Ber.*, 1901, **34**, 2262; Bamberger and Seligman, *Ber.*, 1902, **35**, 4299; 1903, **36**, 685.

Fig. 1 is typical of many runs. In the presence of excess of sodium hydroxide the oxygen absorption–time curve shows a sharp inflection at a point corresponding to the absorption of $1\frac{1}{2}$ atoms of oxygen, after which a slow absorption continues indefinitely. At pH 9 the curve is normally exponential to the $1\frac{1}{2}$-atom absorption line, but (Fig. 1, curve *b'*) an occasional anomalous curve shows a different stoicheiometry, oxygen uptake ceasing at 1 atom per molecule of hydroxylamine.

(3) The normal curves found when operating at pH 7 or 9 follow first-order kinetics with

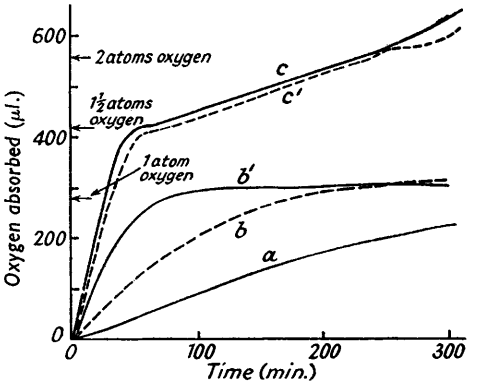


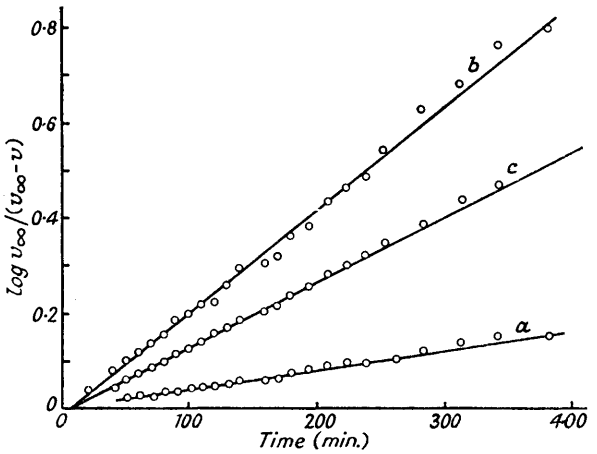
FIG. 1. *Autoxidation of dipropylhydroxylamine in the Warburg apparatus at* 37°.

(*a*) at pH 7, (*b*) at pH 9, (*b'*) anomalous curve at pH 9 as occasionally found, (*c*) with excess of sodium hydroxide, (*c'*) with excess of sodium hydroxide and added oxalic acid.

respect to the hydroxylamine as measured by oxygen uptake when the stoicheiometry is taken to require absorption of $1\frac{1}{2}$ atoms of oxygen (Fig. 2).

(4) Dipropylhydroxylamine appeared to be autoxidised more rapidly than diethyl- or dibutyl-hydroxylamine, but this result may be without real meaning and a fortuitous consequence, not appreciated at that time, of traces of catalysts. The occasional anomalous or atypical result, such as that shown in Fig. 1, curve *b'*, can also be attributed to chance contamination by catalysts.

FIG. 2. *Logarithmic plot of rates of autoxidation at* pH 7 *of* (a) *diethyl-*, (b) *dipropyl-, and* (c) *dibutyl-hydroxylamine on the assumption of a stoicheiometry requiring the absorption of* $1\frac{1}{2}$ *atoms of oxygen per molecule* (*experiments in Warburg apparatus at* 37°).



(5) There was no induction period in any experiment.

The scale of the early experiments in the Warburg apparatus precluded examination of the products. In later experiments we have carried out the autoxidation using a "Microid wrist-action" shaker, operated at room temperature, the oxygen absorption being measured in a burette. It was found that:

(6) Under these conditions the normal stoicheiometry was different from that found in the Warburg experiments at 37°, and 2 atoms of oxygen were now usually absorbed (Fig. 3), still without induction period.

(7) With this altered stoicheiometry the kinetics remain of first order with respect to the hydroxylamine (Fig. 4).

(8) The rate of oxygen uptake was enormously influenced by added trace-metal catalysts, notably copper and manganese.

(9) Oxygen uptake was entirely arrested by the addition of suitable metal-sequestering agents, but could be started again by the addition of further metal catalysts in excess of the sequestering agent.

(10) The autoxidised solution was peroxidic.

Some qualification and expansion is required for the statements (6)—(10). Just as in the Warburg experiments, results were not always reproducible. The normal stoicheiometry at room temperature would appear to involve 2 oxygen atoms, and indeed when the Warburg experiments were run at 22°, 2 atoms were absorbed (large-scale experiments at 37° were inconclusive). But every now and then, especially when catalysts were added, the stoicheiometry appeared to change to absorption of $1\frac{1}{2}$ atoms or to some intermediate figure. The rate of autoxidation also changed from time to time, without affecting the stoicheiometry. Slow absorption was found in one instance to be a result of

FIG. 3. *Autoxidation of dipropylhydroxylamine hydrogen oxalate* (0·4271 *g.*) *at* 23° *and* 755·7 *mm. in laboratory shaker in presence of excess of sodium hydroxide.*

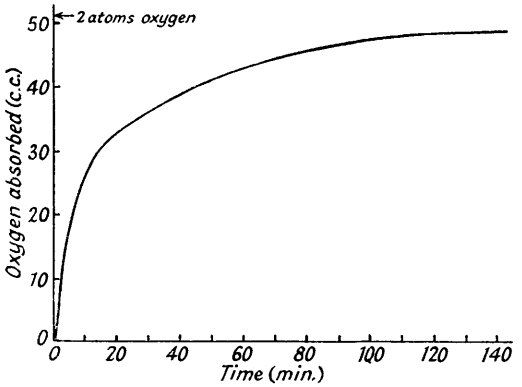
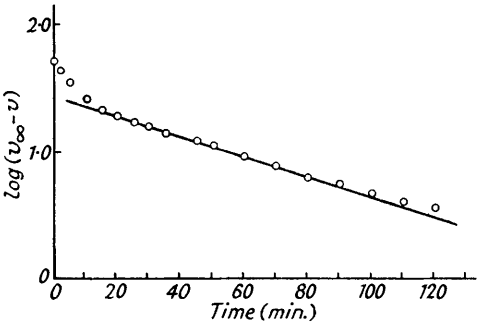


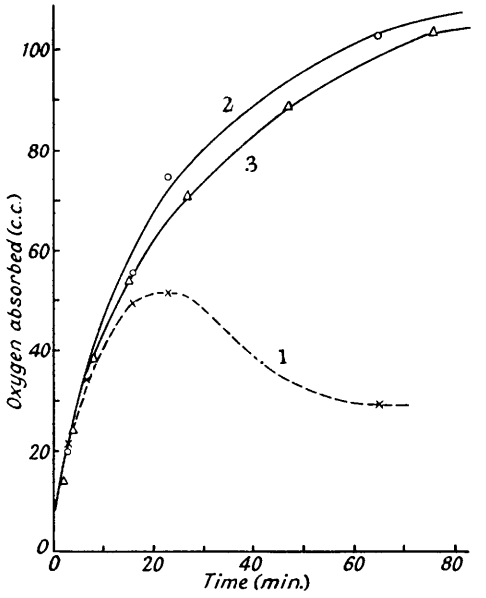
FIG. 4. *Logarithmic plot of the autoxidation of dipropylhydroxylamine in the presence of excess of sodium hydroxide at* 23° *in laboratory shaker, plotted on the assumption of a stoicheiometry requiring the absorption of* 2 *atoms of oxygen per molecule.*



using insufficiently pure oxygen, but other suspected influences were shown to be unimportant; thus, light had no obvious effect on the rate, nor did addition of glass wool or replacement of the glass by a Polythene container. Some further experiments with catalysts are discussed below.

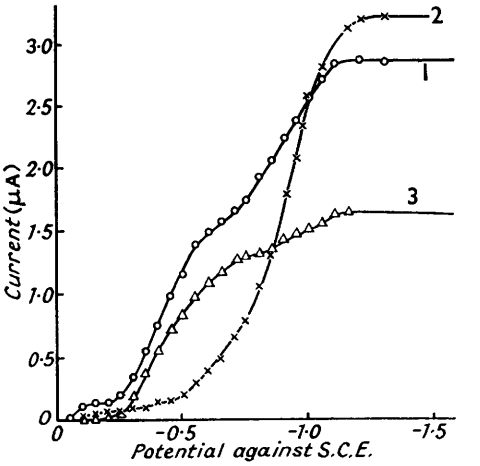
The production of peroxidic material under conditions of controlled oxygen uptake has obvious bearing on the mechanism. We have therefore examined the peroxidic material with care, and conclude that the peroxide activity is due to a mixture of hydrogen peroxide and organic peroxide. When peroxide content is plotted against oxygen absorption (Fig. 5) it is seen that the curve bears a striking resemblance to that found in the autoxidation of benzaldehyde (see, *e.g.*, Waters, " The Chemistry of Free Radicals," Oxford, 1946, p. 237). The peroxide reaches a maximum at a point on the curve between 10 and 30% of the final oxygen absorption. The peroxide content of autoxidised solutions slowly falls when kept, but not to zero, particularly with fully autoxidised solutions. The possibility that the residual activity was organic peroxide, and the labile material was hydrogen peroxide, was supported by polarographic analysis (Fig. 6), the fully autoxidised solution giving a wave which is clearly attributable in part to hydrogen peroxide (half-wave potential —0·9 v; see Kolthoff and Lingane, " Inorganic Polarography," Interscience, New York, 2nd edn., 1952, p. 447), but which had a shoulder at much lower potential. As the total peroxide (iodine titration) decayed, so the shoulder became relatively more and more important, and the wave attributed to hydrogen peroxide less and less dominant. The half-wave potential of the residual peroxide was estimated to lie between —0·40 and —0·45 v (see Fig. 6, curve 3).

FIG. 5. *Comparison of the peroxide content with oxygen absorption during autoxidation of dipropylhydroxylamine at 23° in the presence of excess of sodium hydroxide.*



1, Peroxidic oxygen, expressed as its equivalent in c.c. of oxygen absorbed (1 atom of peroxy-oxygen ≡ 1 mole of oxygen absorbed).
2, Oxygen absorption curve constructed from partial oxidations.
Absorption curve of a typical single autoxidation.

FIG. 6. *Polarogram of autoxidised solution of dipropylhydroxylamine at 23° in presence of sodium hydroxide.*



1, Fresh autoxidised solution.
2, Hydrogen peroxide–oxalate solution of approx. the same peroxide concentration as the autoxidised solution; half-wave potential, — 0·9 v.
3, Autoxidised solution after 3 days.

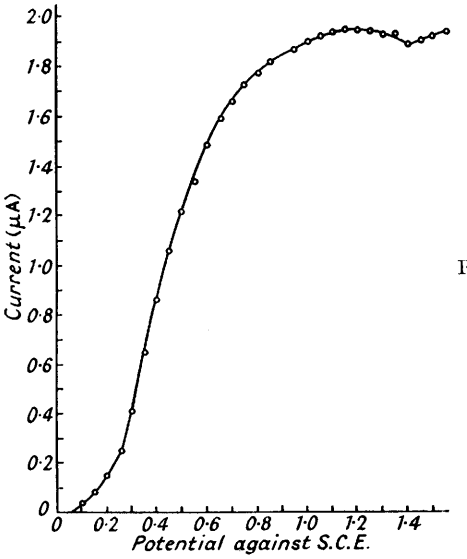


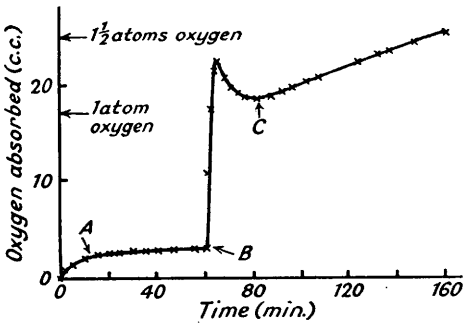
FIG. 7. *Polarogram of the peroxide from dipropylhydroxylamine, after distillation; half-wave potential,* — 0·425 v.

It is surprising that the shoulder only appears in nearly or quite fully autoxidised solutions. It would be unwise to deduce from this that no organic peroxide is present under conditions of partial oxidation, but we confined our further attempts to isolate the peroxide to fully autoxidised material (see Experimental section). They were only partly successful; we isolated a volatile material, boiling up to 70°, highly peroxidic, with a half-wave potential of −0·42 v (Fig. 7), and no sign of the characteristic hydrogen peroxide wave, and giving propionaldehyde and monomethylhydroxylamine on acidification, but analyses were unsatisfactory; organic peroxide is undoubtedly present, but its isolation pure must await detailed physicochemical study, which is being undertaken elsewhere.

Catalysts in the Autoxidation Process.—The action of copper and manganese in promoting autoxidation of nitrogenous substances has analogies; thus Audrieth and Mohr [4] have shown the great effect of copper in promoting autoxidation of hydrazine.

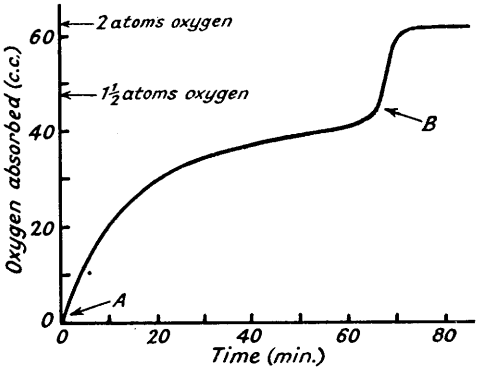
Cobalt, which has little or no positive catalytic effect, causes a characteristic trough in the absorption curve at or about the point of maximum absorption (Fig. 8). This is found regardless of the order in which the copper and cobalt are added, or of the stage in the oxidation. The failure of cobalt to catalyse aqueous autoxidations is not unexpected.[5] Audrieth and Mohr [4] found vanadate to be a good catalyst for hydrazine oxidation; we find it to be without effect in our autoxidations. Sulphite had no effect, but β-naphthol had a marked positive effect, and was itself partially oxidised to yellow-brown material of unknown structure. Baryta would appear at first sight to be acting merely as an alkali, but with monopropylhydroxylamine at room temperature and with dipropylhydroxylamine at 37° it showed a remarkable break in the rate of oxygen uptake, the absorption suddenly increasing very considerably, at which point the solution became yellow (Fig. 9).

FIG. 8. *Autoxidation of dipropylhydroxylamine hydrogen oxalate* (0·2812 *g.*) *at* 20° *and* 761·5 *mm. in the presence of excess of sodium hydroxide.*



At point *A*, cobalt acetate (1 mg.) was added.
At point *B*, copper acetate (1 mg.) was added.
(The gas evolution leading to trough *C* is characteristic of the presence of cobalt.)

FIG. 9. *Autoxidation of monopropylhydroxylamine at* 22·5° *and* 774 *mm. in the presence of excess of baryta.* (The curve for the autoxidation of dipropylhydroxylamine at 37° in the presence of excess of baryta is similar.)



At point *A*, barium peroxide began to be precipitated.
At point *B*, the solution darkened considerably.

Mechanism.—In earlier work it has been assumed that two hydrogen atoms are removed by a mechanism unspecified to give (I), which is presumed to hydrolyse to the aldehyde and

$$R{\cdot}CH_2{\cdot}N(O){:}CHR \quad (I) \qquad R{\cdot}CH_2{\cdot}N(OH){\cdot}CH(OH)R \quad (II) \qquad R{\cdot}CH_2{\cdot}N(OH){\cdot}CH(O{\cdot}OH)R \quad (III)$$

to hydroxylamine. This dehydrogenation process is of the type postulated by Wieland [6] for many biological oxidations, including the oxidation of amines and amino-acids.

[4] Audrieth and Mohr, *Ind. Eng. Chem.*, 1951, **43**, 1774.
[5] Bawn and Williamson, *Trans. Faraday Soc.*, 1951, **47**, 743.
[6] Wieland, "On the Mechanism of Oxidation," Yale Univ. Press, 1932, p. 87; see also Green, "Mechanism of Biological Oxidation," Cambridge, 1940, pp. 87, 143.

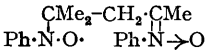
The mechanism of the autoxidation of hydroxylamines can be considered in two stages:

(1) *The primary process.* Our results show: (*a*) That the rate of autoxidation is a function of pH, so that it is reasonable to assume that an ionic species is involved. (*b*) That the rate of autoxidation is trace-metal catalysed, and because of this, and by analogy with other autoxidation systems, we can say that a radical or one-electron system is involved. These two criteria can be accommodated satisfactorily in the equations

$$R{\cdot}CH_2{\cdot}N(OH){\cdot}CH_2R \xrightarrow{OH^-} R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH_2R\ (IV) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH_2R \xrightarrow[+H^+]{O_2} R{\cdot}CH_2{\cdot}N(O{\cdot}){\cdot}CH_2R\ (V) + HOO{\cdot} \quad . \quad . \quad . \quad . \quad (2)$$

There is ample evidence for the formation of radicals such as (V), and, provided that there is no α-hydrogen atom, they are stable. For instance, Teuber and Jellinek [7] have reviewed the literature on Frémy salt $(^-O_3S)_2NO{\cdot}$; Gilman and McCrachen [8] examined the radical $Ph_2NO{\cdot}$, and Banfield and Kenyon [9] made the compound



(2) *Subsequent reaction.* When there is a free α-hydrogen atom a nitrosyl compound is not isolated, and it follows from the products of the oxidation that an α-carbon atom must be oxidised. One of the simplest of several processes which will accommodate these facts is:

$$\underset{(V)}{R{\cdot}CH_2{\cdot}N(O{\cdot}){\cdot}CH_2R} + \underset{(IV)}{R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH_2R} \longrightarrow \underset{(VI)}{R{\cdot}CH_2{\cdot}N(O^-){\cdot}\dot{C}HR} + R{\cdot}CH_2{\cdot}N(OH){\cdot}CH_2R \quad (3)$$

The further behaviour of the radical-ion (VI) may be expected to depend on its life in the particular environment. The two extreme possibilities, low stability and short life, and comparative high stability and long life (compared, *e.g.*, to that of a simple alkyl radical), can be taken in turn.

(a) *Low stability and short life.* The probable step in this case is the loss of a further electron to the metal catalyst, to any radicals which approach, or to dissolved oxygen; the product will be the nitrone (I):

$$R{\cdot}CH_2{\cdot}N(O^-){\cdot}\dot{C}HR\ (VI) \xrightarrow{-e} R{\cdot}CH_2{\cdot}N(\rightarrow O){=}CHR\ (I) \quad . \quad . \quad . \quad . \quad . \quad (4)$$

This, presumably, must be the mechanism when hydroxylamines are oxidised by metal oxides in organic media [if, indeed, (VI) is an intermediate in such cases]. The resultant overall process is the familiar dehydrogenation oxidation, and no organic peroxide should be formed.

(b) *High stability and long life.* If the system is reluctant to lose its unpaired electron it may survive long enough to combine with other radicals, *viz.*, hydroperoxy, oxygen, and possibly hydroxyl; dimerisation is improbable because of the negative charge.

(i) Combination with HO·O· will form the hydroperoxide (III) in its ionised form (III*a*) in one step:

$$R{\cdot}CH_2{\cdot}N(O^-){\cdot}\dot{C}HR\ (VI) + HO{\cdot}O{\cdot} \longrightarrow R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH(O{\cdot}OH)R\ (III\textit{a}) \quad . \quad . \quad (5)$$

(ii) Combination with oxygen will give the radical (VII), and from this point it seems safe to draw on the analogy with the currently accepted mechanism for olefin autoxidation:

$$R{\cdot}CH_2{\cdot}N(O^-){\cdot}\dot{C}HR\ (VI) + O_2 \longrightarrow R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH(OO{\cdot})R\ (VII) \quad . \quad . \quad (6)$$

$$R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH(O{\cdot}O{\cdot})R + R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH_2R \longrightarrow R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH(O{\cdot}OH)R\ (III\textit{a}) + R{\cdot}CH_2{\cdot}N(O^-){\cdot}\dot{C}HR\ (VI) \quad . \quad (7)$$

(iii) Combination with HO·, if present, would lead to the formation of the hydroxy-hydroxylamine (II), the hydrated form of the nitrone. The existence of significant amounts

[7] Teuber and Jellinek, *Chem. Ber.*, 1952, **85**, 95.
[8] Gilman and McCrachan, *J. Amer. Chem. Soc.*, 1927, **49**, 1052.
[9] Banfield and Kenyon, *J.*, 1926, 1612.

of hydroxyl radical would presumably depend on the presence of metal catalysts, able to react suitably with hydrogen peroxide; thus Fe^{++} would give a reagent of Fenton type:

$$R{\cdot}CH_2{\cdot}N(O^-){\cdot}\dot{C}HR + HO{\cdot} \longrightarrow R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH(OH)R \longrightarrow R{\cdot}CH_2{\cdot}N(O){=}CHR \quad (8)$$

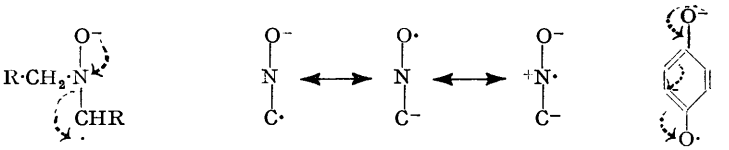
A further possible route to a hydroperoxide is:

$$R{\cdot}CHO + R{\cdot}CH_2{\cdot}NH{\cdot}OH \overset{OH^-}{\rightleftharpoons} R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH(OH)R + H_2O_2 \longrightarrow R{\cdot}CH_2{\cdot}N(O^-){\cdot}CH(O{\cdot}OH)R\ (III\textit{a}) + H_2O \quad (9)$$

but we have found only traces of organic peroxide when hydrogen peroxide reacts with the aqueous alkaline condensation product of propionaldehyde and monoalkylhydroxylamine.

Fortunately, Rogers [10] has found independent evidence of (VI) as an intermediate so that this last possibility does not represent the main reaction sequence and the evidence is strongly in favour of the concept of (VI) being relatively stable.

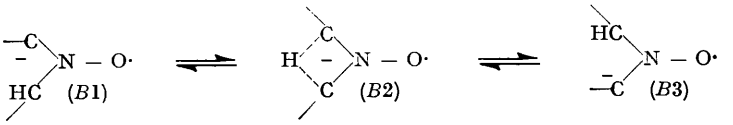
The Structure and Stability of the Radical-ion (VI).—Having postulated a stability for the radical-ion (VI) which is greater than that of typical alkyl radicals, some structural rationalisation of the stability is required. In terms of resonance this can be expressed as (*A*), this representing the canonical forms (A_1), (A_2), (A_3). Such a system has some



(*A*) (A_1) (A_2) (A_3) (*B*)

analogy with the semiquinones, which may be written as in (*B*). The two systems are not entirely analogous, however, because the radical-charge separation in (*B*) is even (four atoms), whereas in (*A*) it is odd (one atom); but the *p*-phenylene unit is here regarded as a whole. It is not, of course, suggested that the radical-ion (VI) has a stability comparable with that of the semiquinones.

A further structure which might contribute to the enhancement of stability can be derived from (A_2) and (A_3), when the negative charge on the carbon atom may be expected to result in co-ordination with a neighbouring hydrogen atom:



(*B*1) (*B*2) (*B*3)

There is some experimental support for these tautomeric forms. It has been found that *N*-ethyl-*N*-methylhydroxylamine and *N*-methyl-*N*-propylhydroxylamine, autoxidised under the conditions described, give substantially only formaldehyde. Now this could be the result if the radical oxidation stage (equation 3) were much more rapid on a methyl than on an ethyl or propyl radical. But if this were the case the rate of autoxidation of dimethylhydroxylamine should be much greater than that of the higher homologues. For reasons already given, no accurate figures for the rates can yet be given, but certainly the rate of autoxidation of dimethylhydroxylamine is not greatly different from that of the higher homologues, and the difference is not enough to account for the great preponderance of formaldehyde found in the oxidation of the unsymmetrical hydroxylamines. But if (*B*2) represents a further canonical form of (VI), the aldehyde formed from the oxidation of an unsymmetrical hydroxylamine should not be consequent on relative oxidation rates of the two alkyl groups.

Experimental

Materials.—The dialkylhydroxylamines were made by the methods of Part I (*loc. cit.*). They were normally stored and used as the hydrogen oxalates, these being the simplest non-hygroscopic salts. Experiment showed that oxalic acid has no effect on the oxidation rates

[10] Rogers, *Chem. and Ind.*, 1953, 1033; and forthcoming publication.

(*e.g.*, Fig. 1, effect of adding further oxalic acid). Monopropylhydroxylamine was made by Beckmann's method.[11] Rates of autoxidation varied with the batch, probably owing to presence of traces of metal catalysts. Sodium hydroxide solutions were generally made by dilution of filtered concentrated solutions of flake sodium hydroxide; solutions made from commercial pellets usually gave slow autoxidation rates. Oxygen was of pure anæsthetic quality.

Autoxidation in the Warburg Apparatus.—Unless otherwise stated all experiments were carried out at 37°. Agitation was kept at a rate which experiment showed was not critical, and small alterations had no effect on the oxygen-absorption curve. All flasks contained 2 c.c. of solution of the oxalate, and the centre cup was filled with 2N-sodium hydroxide. Sodium hydroxide or buffer solution (0·2 c.c.) was added from the side arm. For experiments at pH 7, phosphate buffer (0·25M) was made up in 0·25N-sodium hydroxide, and for experiments at pH 9, borax buffer (0·3M) in 0·25N-sodium hydroxide was used. The available alkali neutralised the oxalic acid, and trial showed that the appropriate pH was attained and maintained throughout the experiment.

Normal practice [12] for equilibration and calculation was observed. The gas phase was air, and calculation showed that the oxygen depletion was negligible.

Autoxidation in the Larger-scale Apparatus.—A 250 c.c. flask connected to a gas burette was shaken vigorously by a "Microid wrist-action" shaker; failure to shake vigorously enough accentuates the initial deviation from the straight-line first-order plot (Fig. 4). The apparatus was not kept in a thermostat and experiments were usually carried out at room temperature; up to 1 g. of hydroxylamine could be handled in this way, and in a few experiments, a larger shaker was used which would permit experiments on a 10 g. scale. In general the concentration was higher the larger the scale. A few experiments at 37° were conducted with the whole apparatus enclosed in a cabinet, heated electrically with an industrial fan dryer. The alkali, or buffer, was added by temporarily removing the lead from the burette. The gas phase was oxygen but no special precautions were taken to remove residual air. The apparatus was in diffuse daylight.

Effect of Catalysts.—Aqueous solutions of copper acetate have shown marked acceleration of oxygen uptake at all pH studied; in concentrations of about 1 : 100,000 the oxygen absorption in the presence of sodium hydroxide was too rapid for measurement, and the almost imperceptible uncatalysed absorption at pH 7 was much increased. The stoicheiometry and general shape of the absorption curve with copper and sodium hydroxide present were not regularly reproducible.

In a series of autoxidations, the rate of absorption was noted when 2N-sodium hydroxide (3 c.c.) was added to dipropylhydroxylamine (400 mg. of hydrogen oxalate) in water (30 c.c.) containing the following substances: Manganese dioxide (100 mg.) and manganese acetate (1 mg.), much increased rate; β-naphthol (10 mg.), much increased rate, and oxidation of the β-naphthol to a yellow-brown substance; colloidal platinum, protected by polyvinyl chloride (100 mg.), much increased rate. Silver nitrate (10 mg.), hydrogen peroxide (30%; 1 mg.), and benzoic acid (100 mg.) had no effect (no hydroxybenzoic acid was isolated from the last of these). Benzoyl peroxide (10 mg.), sodium sulphite (10 mg.), ferrous sulphate (10 mg.), and ammonium vanadate (1 mg.) appeared to depress the rate somewhat. Cobalt acetate (1 mg.) appeared to depress the rate (Fig. 8) and, in certain circumstances already discussed, caused a break in the curve.

When the autoxidation of dipropylhydroxylamine (280 mg.) in aqueous solution (30 c.c.) at pH 9, containing 1 mg. of copper acetate, was interrupted by addition of the following metal-sequestering agents, the oxygen uptake ceased: salicylaldoxime (15 mg. in aqueous alcohol), sodium diethyldithiocarbamate (30 mg. in water), and "Cupron" (30 mg. in ethanol), in the first two cases, abruptly, in the last, slowly. The uncatalysed autoxidation was also inhibited by these reagents. In each case the addition of copper ions in large molar excess over the sequestering agent resulted in further oxygen uptake.

The experiment represented by Fig. 2 demonstrates the first-order character of the reaction but the linearity is not much affected by the stoicheiometry. The experiment was made before the importance of the catalytic effect was fully appreciated, and the relative rates must be taken with reserve. Nevertheless, because dipropylhydroxylamine appeared to be most rapidly oxidised, it has been selected for the later experiments.

[11] Beckmann, *Annalen*, 1909, **365**, 205.
[12] Dixon, "Manometric Methods as applied to the Measurement of Cell Respiration and Other Processes," Camb. Univ. Press, 1943.

Hydrogenation of the Product of Autoxidation of Dipropylhydroxylamine.—Dipropylhydroxylamine hydrogen oxalate (501·9 mg.) was autoxidised in aqueous solution (30 c.c.) containing 2N-sodium hydroxide (4·0 c.c.). When uptake of oxygen was complete (2 atoms per molecule) the solution was hydrogenated with 5% palladium on carbon catalyst; 105·1 c.c. of hydrogen were taken up (Calc. for 4H per mole: 120·4 c.c.). The filtered solution was steam-distilled, and from the distillate was obtained dipropylamine as its picrate (15 mg.), m. p. 97—98°.

Hydrogenation of Monopropylhydroxylamine–Propionaldehyde Mixture.—A solution of the hydroxylamine hydrogen oxalate (402 mg.) in water (30 c.c.) containing 2N-sodium hydroxide (3·0 c.c.) was added dropwise to a solution of propionaldehyde (0·8 g.; freshly distilled) in water (20 c.c.),with stirring. At the end of 1 hr. the solution was not appreciably reducing in the triphenyltetrazolium chloride test. The solution was hydrogenated in the same way as in the previous experiment, and by steam-distillation there was isolated dipropylamine as its picrate (15 mg.), m. p. 97—98°.

Aqueous alkaline solutions of monopropylhydroxylamines are autoxidised as readily as those of the dialkyl series. When an alkaline solution of monopropylhydroxylamine was mixed with propionaldehyde, and the mixture kept for 1 hr., it was autoxidised very slowly. This is consistent with the suggestion that there has been reaction to form $Pr{\cdot}N[CH(OH){\cdot}CH_2{\cdot}CH_3]{\cdot}OH$. When copper (as acetate) was added, autoxidation proceeded more rapidly.

Determination of Total Peroxide in Autoxidised Solutions of Dipropylhydroxylamine.—A stream of carbon dioxide was passed through glacial acetic acid ("AnalaR"; 25 c.c.) in a 250 c.c. conical flask for 5 min. With the gas stream continuing, sodium iodide solution (60%; 2 c.c.) was added, followed by the peroxide solution (10 c.c.) under examination. The flask was tightly stoppered and kept for 30 min., and the liberated iodine was titrated with 0·1N-sodium thiosulphate. Blank titres were always less than 0·1 c.c. All determinations were carried out in duplicate, and agreement was satisfactory.

Polarographic Measurements.—A Tinsley automatic polarograph was used, with saturated calomel reference electrode. The peroxidic solution (0·5 c.c.), adjusted previously to pH 8 by saturation with carbon dioxide (conveniently by the addition of solid carbon dioxide), was added to 0·1N-lithium chloride solution (15 c.c.) in the cell, and dissolved oxygen was removed by passing a slow stream of nitrogen for 20 min. immediately before a determination. Condenser current blanks were obtained with appropriate blank solutions.

Hydrogen Peroxide and Organic Peroxide Content of Fully Autoxidised Dipropylhydroxylamine.—Three typical experiments illustrate the results, which were qualitatively reproducible:

Solution A: Dipropylhydroxylamine hydrogen oxalate solution (0·24 M; 20 c.c.) was mixed with 0·5N-sodium hydroxide (40 c.c.) and autoxidised to completion; 1·86 g.-atoms of oxygen were taken up, $t_{\frac{1}{2}} = 28$ min. Total peroxide was determined at once, and again after 3 and 6 days. The corresponding polarograms are shown in Fig. 6, which also shows the polarogram for a solution of hydrogen peroxide of similar concentration (trial and error).

Solution B: Dipropylhydroxylamine hydrogen oxalate solution (0·72 M; 20 c.c.) was mixed with N-sodium hydroxide (60 c.c.) and autoxidised to completion; 1·91 g.-atoms of oxygen were taken up. The low value for peroxide content (see Table 1) is characteristic of the more concentrated solution.

TABLE 1. *Peroxidic oxygen content of typical autoxidised solutions of dipropylhydroxylamine.*

	Atoms peroxy-O / Mols. hydroxylamine		Atoms peroxy-O / Mols. hydroxylamine
Solution A: freshly autoxidised	0·290	Solution B: freshly autoxidised	0·06
after 3 days	0·189	Solution C: freshly autoxidised	0·21
after 6 days	0·165		

Solution C: A typical chance slow oxidation. (The quality of the potassium hydroxide used was considered to be responsible.) Dipropylhydroxylamine hydrogen oxalate solution (0·097M; (50 c.c.) mixed with 2N-potassium hydroxide (10 c.c.) absorbed 1·83 g.-atoms of oxygen per mole of hydroxylamine, $t_{\frac{1}{2}} = 54$ min. The peroxidic content was rather lower than in the typical fast oxidation.

The Peroxide Content and Characteristic Polarograms of Partially Autoxidised Dipropylhydroxylamine.—It was considered impracticable to determine oxygen uptake and peroxidic content at intervals during a single experiment, so that a number of autoxidations, in identical conditions, were used to make a composite curve. Values of $t_{\frac{1}{2}}$ were very similar in all

experiments, in which the same apparatus and stock solutions were used throughout the series. In each case dipropylhydroxylamine oxalate (1·0 g.) in water (20 c.c.) and N/2-sodium hydroxide (40 c.c.) was autoxidised to the degree required, whereupon the shaking was stopped and the solution adjusted to pH 8 by solid carbon dioxide and made up to 100 c.c. with water. In order to obtain a closer approximation of the peroxide content at the time of interrupting the autoxidation, the determination was repeated on each sample several times, at intervals, whereby an allowance for the decay of the peroxide was made by back extrapolation. In Fig. 5 a composite and a typical oxygen-uptake curve are shown, together with a composite peroxide-content curve corrected for decay. Polarograms taken at each point showed only the characteristic wave for hydrogen peroxide until almost complete oxidation (1·73 atoms of oxygen per molecule), when the shoulder associated with organic peroxide appeared (Fig. 6).

Separation of Organic Peroxide and Hydrogen Peroxide.—It was shown that, on distillation under reduced pressure, and unlike hydrogen peroxide under the same conditions, the peroxidic activity of a fully autoxidised dipropylhydroxylamine solution at pH 8 (sodium hydrogen carbonate) passed over partially into the distillate, which now gave a polarogram entirely lacking the wave due to hydrogen peroxide, but showing a new wave with a half-wave potential of −0·425 v (Fig. 7). Dipropylhydroxylamine hydrogen oxalate (10·0 g.) in water (200 c.c.) and 0·5N-sodium hydroxide (400 c.c.), autoxidised to completion, was saturated with carbon dioxide by solid carbon dioxide and partially distilled (155 c.c. collected) at 11 mm., a trap cooled to about −40° being used. The degree of concentration obtained is shown by the titre (c.c. of 0·1N-sodium thiosulphate) per c.c. of the original solution (3·20), the distillate (8·54), and the residue (1·38).

Isolation of Organic Peroxide.—The isolation from the distillate was normally carried out at once, but the peroxidic activity and the characteristic polarographic wave did not alter during several days at laboratory temperature. The distillate from two oxidations, each on 10 g., was extracted repeatedly with ether (20 × 20 c.c.) and the combined extracts were dried (K_2CO_3); hydrogen peroxide in ether is completely removed by this treatment. The ether was removed by passing a stream of dry air through until the issuing gases showed marked peroxidic activity to acidified starch–iodide paper. The gas stream was passed into a receiver, cooled by a freezing mixture, and as it was markedly peroxidic the process was repeated on the condensate. The combined residues were fractionated at atmospheric pressure through a short column (Table 2).

TABLE 2. *Typical fractionation of organic peroxide from dipropylhydroxylamine.*

Fraction	B. p.	Remarks	Fraction	B. p.	Remarks
1	Below 38°	Ether	4	48·5—67°	Strongly peroxidic
2	39—41·5	Mainly ether	5	67—71	0·16 g., strongly peroxidic
3	41·5—48·5	,,	6	71—72	0·23 g., ,, ,,

The material from fractions 5 and 6, and similar material from several other preparations of a similar nature in some of which the concentration procedure was omitted, was extraordinarily volatile. It had a sharp pungent smell, and when it was warmed a carbylamine-like smell developed; propionaldehyde-like smell was not detected until the liquid was acidified, but it then developed immediately. It showed little reducing action towards triphenyltetrazolium chloride but, when acidified, immediately developed strong reducing characteristics. It gave a strong purple-red ferric reaction in methanol, and a polarogram identical with that of the undistilled material (half-wave potential = −0·425 v). On reaction with 2 : 4-dinitrophenylhydrazine in warm 2N-hydrochloric acid, the dinitrophenylhydrazone of propionaldehyde was immediately precipitated (m. p. and mixed m. p.), and with aqueous oxalic acid the oxalate of monopropylhydroxylamine (m. p. and mixed m. p.) was isolated. When a mixture of acrylonitrile and the peroxide was warmed on the steam-bath, the acrylonitrile polymerised.

Many attempts were made to get reproducible analytical results which could be correlated with any imagined peroxide structure. To avoid loss during the sweeping-out operation in the nitrogen determination, the sample was either cooled in carbon dioxide in a U-tube during this stage, or was sealed in a capillary, which was subsequently crushed by means of a plunger.* Despite these precautions, all results for nitrogen, except one, have been under half the expected, and results generally were very erratic. Azeotropes with ether are a possible complication.

Other methods of isolation were tried. The preliminary separation from hydrogen peroxide

* The modifications to the standard procedure were kindly carried out by Mr. R. Rothwell, whom we thank.

may be omitted, and the total oxidation product neutralised and extracted with ether, and the hydrogen peroxide extracted by anhydrous potassium carbonate. The method has no advantage. Finally, attempts were made to isolate the organic peroxide as sodium salt. The autoxidised solution was evaporated to dryness at about 0·1 mm., leaving a peroxidic residue. Alternatively, the water-distilled material (see p. 1102) was treated with excess of sodium hydroxide and evaporated under reduced pressure. In both cases the residue was strongly peroxidic, and remained so for months, but it did not show any sign of the polarographic wave associated with organic peroxide. It contained nitrogen, and had some of the properties to be expected, but attempts to purify it failed.

Autoxidation of Ethylmethyl- and of Methylpropyl-hydroxylamines.—The autoxidation was carried out, without added catalyst, at room temperature on the 0·5 g. scale. The resultant solution was made slightly acid, and mixed with an aqueous alcoholic solution of dimedone. The mixture was kept overnight, and the precipitate was then collected and dried. It was treated with glacial acetic acid under the conditions for separating formaldehyde from its homologues.[13] In each case only a trace of the higher homologue was isolated, and the anhydride of the formaldehyde derivative was obtained in a pure state.

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IMPERIAL CHEMICAL INDUSTRIES LIMITED,
DYESTUFFS DIVISION, RESEARCH DEPARTMENT,
HEXAGON HOUSE, BLACKLEY, MANCHESTER, 9. [*Received, March 26th,* 1955.]

[13] Hopkin and Williams Ltd., " Organic Reagents for Organic Analysis," 1944.