# **Electron Spin Resonance Studies in Aqueous Solution:** Fragmentation of Radical Intermediates Derived from $\beta$ -Amino Alcohols

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In acidic aqueous solution, oxidation of the  $\beta$ -amino alcohols  $R_3 \overset{+}{N}CH_2CH_2OH$ , I, and  $R_3 \overset{+}{N}CH_2$ -CHOHCH<sub>3</sub>, II, (R = H, alkyl) using the Ti(III)-H<sub>2</sub>O<sub>2</sub> flow technique gave the radicals  $R_3 \overset{+}{N}CH_2 \overset{+}{C}HOH$ , and  $R_3 \overset{+}{N}CH_2 \overset{+}{C}OHCH_3$ . The spectrum of (CH<sub>3</sub>)<sub>2</sub>  $\overset{+}{N}HCH_2 \overset{+}{C}OHCH_3$  shows restricted rotation about the C<sub>1</sub>--C<sub>2</sub> bond assigned to intramolecular hydrogen bonding.

Under neutral conditions, oxidation of I gave the spectrum of  $CH_2CHO$ , and of II the acetonyl radical  $CH_2COCH_3$ . It is proposed that elimination occurs by deprotonation of the abstraction radical in a hydrogen-bonded conformation, followed by rapid fragmentation to yield the  $\alpha$ -carbonyl radical.

En solution aqueuse acidique, l'oxydation des  $\beta$ -amino alcools  $R_3 \overset{+}{N}CH_2CH_2OH$ , l, et  $R_3 \overset{+}{N}CH_2$ -CHOHCH<sub>3</sub>, II (R = H, alcoyle) en utilisant le système Ti(III)-H<sub>2</sub>O<sub>2</sub> a conduit aux radicaux  $R_3 \overset{+}{N}CH_2$ -CHOH et  $R_3 \overset{+}{N}CH_2 \overset{+}{C}OHCH_3$ . Le spectre de (CH<sub>3</sub>)<sub>2</sub> $\overset{+}{N}HCH_2 \overset{+}{C}OHCH_3$  a révélé une rotation limitée autour du lien  $C_1$ -- $C_2$  attribuable à un enchaînement par liaison hydrogène intramoléculaire.

Dans des conditions neutres, l'oxydation de I a conduit au  $\cdot CH_2CHO$  alors que l'oxydation de II a conduit au radical acétonyle,  $\cdot CH_2COCH_3$ . On suggère que l'élimination s'effectue par déprotonation du radical d'abstraction dans une conformation comportant une liaison hydrogène, puis par fragmentation rapide pour donner le radical  $\alpha$ -carbonyle. [Traduit par le journal]

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### Introduction

In reaction with the hydroxyl radical, many alcohols 1 undergo preferential hydrogen atom abstraction at the  $\alpha$  (carbinol) carbon (eq. 1).

[1] 
$$\begin{array}{c} Y \\ R' \\ R, R' = H, alkyl \\ 1 \end{array} \xrightarrow{OH} \begin{array}{c} OH \\ R' \\ R' \\ R \end{array} \xrightarrow{Y} CHC \xrightarrow{OH} H_{2}O \\ R' \\ R' \\ R \end{array}$$

The secondary radicals 2 have been detected by e.s.r. spectroscopy during radiolysis of aqueous solutions (1), photolysis of alcohols containing hydrogen peroxide (2), and by use of the Ti(III)–  $H_2O_2$  reaction in a rapid flow system (3). When the alcohol bears certain  $\beta$  substituents (notably Cl, Br, and OH), radical 2 may undergo a polar elimination process generating an  $\alpha$ -carbonyl radical 3 and losing the substituent  $Y^-$  (eq. 2) (4, 5).



Acid-catalysis of the elimination of hydroxide ion during oxidation of 1,2-ethanediol (1 R, R' = H, Y = OH) was demonstrated in photolysis studies (2), and in the Ti(III)-H<sub>2</sub>O<sub>2</sub> experiments (4) by e.s.r. observation of radical 5 (eq. 3).

[3] HOCH<sub>2</sub>CHOH 
$$\rightleftharpoons$$
 H<sub>2</sub>OCH<sub>2</sub>CHOH  
4  $\rightarrow$  CH<sub>2</sub>CHO + H<sub>2</sub>O + H<sup>+</sup>  
5

By way of confirmation, a recent pulse radiolysis study indicated this elimination was complete at pH 1.0 immediately following a 5 µs pulse (6).

In the pH 4.0–7.0 range, however, only the abstraction radical 4 was detected in the e.p.r. and pulse radiolysis work. It has been suggested that the rate of the uncatalyzed elimination (eq. 2), was too slow at high steady-state radical concentrations to compete with bimolecular termination (7). Indeed, continuous  $\gamma$  irradiation of neutral aqueous solutions of 1,2-ethanediol containing added  $H_2O_2$  (7) or  $N_2O$  (8) revealed a chain reaction that produced acetaldehyde. It was proposed that at these lower radical concentrations, elimination did occur and that radical 5 propagated the chain. Furthermore, e.s.r. spectra of  $\alpha$ -carbonyl radicals 3 were recorded at pH 4.6 for 1,2-propanediol oxidation (1 R =H,  $R' = CH_3$ , Y = OH) and under neutral conditions for 2,3-butanediol (1 R,  $R' = CH_3$ ,

4009

Y = OH) (5). The observation of deoxy sugars as products of the photolysis (9) and radiolysis (10) of neutral aqueous solutions of carbohydrates was also rationalized by the same reaction sequence (reactions 1, 2).

An apparent change in this established mechanism of elimination has been reported in the case of quaternary N-methyl derivatives of 2aminoethanol. Electron spin resonance studies on the  $\gamma$  irradiation of crystalline choline chlo-

ride (1 R, R' = H, Y =  $(CH_3)_3N$ —) (11), and on the oxidation of its aqueous solutions in the Ti(III)-H<sub>2</sub>O<sub>2</sub> systems (5) both assigned  $(CH_3)_3N^{+}$  as the only observed fragmentation or elimination radical. Homolysis of the  $\beta$  C—N bond was proposed to account for cation radical formation (eq. 4). Interest in the solid state radiolysis arose from the efficient chain production of acetaldehyde and trimethylamine hydro-

[4]  $(CH_3)_3 \overset{+}{N}CH_2 \dot{C}HOH \rightarrow (CH_3)_3 \overset{+}{N} + CH_2 = CHOH$ ⇒  $CH_3CHO$ 

chloride ( $G = 55\,000$ ) (12, 13).

In solution at pH 1.0, 2-hydroxyethyltriethylammonium chloride (1 R, R' = H, Y =  $(CH_3CH_2)_3N$ ) also gave the cation radical spectrum (5). However, under the same conditions other 2-aminoethanol derivatives (Y =  $^{+}NH_3$ ,  $CH_3NH_2$ ,  $(CH_3)_3NH$ ) gave only the abstraction radicals 2. The results are unexpected in view of the usual tendency of a quaternary nitrogen substituent to be eliminated as the amine moiety, just as predicted on the basis of the previously observed elimination reactions (reaction 2).

In this paper we report an e.s.r. study on the oxidation of both 2-aminoethanol (1 R, R' = H,

 $Y = NH_3$  and 1-amino-2-propanol (1 R =

 $CH_3$ , R' = H,  $Y = NH_3$ ) and related *N*-alkyl derivatives, in both acidic and neutral solution. Conditions are established under which the established polar radical elimination pathway (reaction 2) is operative for these substrates.

### Experimental

#### General

For the aqueous flow experiments, a Varian E-6S X-band e.s.r. spectrometer was equipped with a commercial all-quartz two-entry T-mixing chamber (Varian model E-249) having a specified mixing volume of  $2.5 \times 10^{-3}$  ml. The flat sample cell is an integral part of the device, providing a total reacting volume to the view point of 0.080 ml. Flow rates for the two reactant solutions of 150 ml per min were generated by gravity feed, and controlled by a water aspirator applied to the exit tubing. A Gilmont #13 "Compact" flowmeter was inserted in each stream. Hyperfine splitting constants (h.f.s.) were measured to  $\pm 0.1$  G, and g values to  $\pm 0.0002$  employing Fremy's salt ( $a_N = 13.0$  G, g = 2.0052) as a standard (14). Alternatively, direct comparison was made to the 'CH<sub>2</sub>OH radical ( $a_{CH_2} = 17.57$  G, g = 2.0032) generated during the flow experiment by addition of a large excess of methanol as co-substrate (15).

pH measurements (to  $\pm 0.1$  units) were made on all reactant and effluant solutions. Water from the building supply was routinely used after determining that its substitution for distilled water made no detectable change in the nature or quality of the spectra that were obtained. Commercially available aminoalcohols and inorganic reagents were of Fisher Certified Reagent or Aldrich reagent grade unless otherwise specified. In the amine syntheses, n.m.r. spectra were recorded on a Perkin–Elmer R12A instrument employing CCl<sub>4</sub> solvent and TMS as internal standard, or D<sub>2</sub>O with TMS external.

#### Flow Experiments

#### (a) Acidic Conditions

In the oxidation of the aminoalcohols at pH 2.0, one reactant stream contained 0.02 M titanium(III) chloride (Fisher Reagent, 20% solution) adjusted to pH 2.0 with concentrated sulfuric acid; and the other stream contained 0.1 M hydrogen peroxide (Fisher Certified, 30% solution), and 0.5 M alcohol substrate, acidified to pH 2.0 with concentrated sulfuric acid. All solutions were deaerated with oxygen-free nitrogen gas for at least 15 min prior to reaction. Titanium(III) stock solution was not added until after degassing to minimize oxidation of the metal ion.

#### (b) Neutral Conditions

After deaerating a 0.02 *M* solution of disodium ethylenediaminetetraacetate, titanium(III) chloride was added to a final concentration of 0.02 *M*; and the pH adjusted to 7.5 with concentrated NH<sub>4</sub>OH (d = 0.880). The second solution was made 0.5 *M* in organic substrate, 0.1 *M* in hydrogen peroxide, and adjusted to pH 7.5 with concentrated sulfuric acid. It should be noted that a reduction in the pH of the effluant solution to pH 6.5–7.0 is observed. (In this work we have ensured that the results reported at pH 2.0 for the abstraction radicals do not qualitatively change in the range 1.5–2.5 unless specified. Similarly eliminations reported at pH 7.0 have been verified in the range 6.0–8.0.)

### (c) Reduction with the Formic Acid Radical COOH

The reduction of chloroacetone ClCH<sub>2</sub>COCH<sub>3</sub> and the aminoketone (CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>COCH<sub>3</sub> via the oxidation of formic acid was carried out using an all-glass mixing device that allows the simultaneous mixing of three reactant streams. The design has been previously described by Norman and co-worker (16). In these experiments, one stream contained 0.02 M titanium(III) chloride and 0.5 M formic acid, the second 0.1 M hydrogen peroxide, and the third 0.5 M organic substrate. All solutions were adjusted to pH 2.0 prior to reaction.

TABLE 1. Hyperfine splitting constants for the radicals  $R_3NCH_2CHOH$ ;\*  $R = H, CH_3, HOCH_2CH_2$ 

	Aminoalcohol	a <sub>CHa</sub>	a <sub>сн2</sub> р	a <sub>N</sub>	a <sub>on</sub>	<i>a</i> <sub>NH</sub> <sup>+</sup>
6	<sup>+</sup> NH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OH	18.0	11.6	10.5	1.0	†
7	CH <sub>3</sub> <sup>+</sup> NH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OH	18.6	11.0	11.0	1.0	0.8(2H)
8	(CH <sub>3</sub> ) <sub>2</sub> <sup>+</sup> NHCH <sub>2</sub> CH <sub>2</sub> OH	19.0	9.9	12.0	1.4	1.4(1H)
9	(CH <sub>3</sub> ) <sub>3</sub> NCH <sub>2</sub> CH <sub>2</sub> OH	19.7	8.5	13.6	1.8	_
10	<sup>+</sup> NH <sub>2</sub> (CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	18.5	10.9	11.0	1.1	1.1(2H)
11	<sup>+</sup> NH(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>3</sub>	19.1	9.7	11.9	1.2	1.2(1H)

\*g-Values of all radicals were  $2.0032 \pm 0.0002$ . †No further resolved splitting, line width 0.5 G.

#### (d) Spectral Simulation

A program (QCPE 160) was used that allowed simulation of two or more radicals with different g-value and line width.<sup>1</sup>

#### Preparation of Aminoalcohols

(i) 2-Hydroxyethyltriethylammonium Chloride

2-Chloroethanol (40.0 g, 0.5 mol) and triethylamine (25.0 g, 0.25 mol) were heated under reflux for 7 h. On cooling, two layers formed. The lower layer, containing the desired quaternary salt and excess 2-chloroethanol, was washed repeatedly with ether, and the resulting syrup recrystallized from ethanol-ether to yield 30 g (0.18 mol; n.m.r. (D<sub>2</sub>O): 8.76 (9H, t, J = 7.5 Hz), 5.67 (6H, q, J = 7.5 Hz), 5.77 (2H, m), and 5.10 (2H, m).

(ii) 2-Hydroxypropyltrimethylammonium Chloride

A solution of N,N-dimethylamino-2-propanol (50.0 g, 0.49 mol) in 500 ml of absolute ethanol was heated under reflux (Dry Ice - acetone condenser) while chloromethane was bubbled through the mixture until an aliquot no longer showed (CH<sub>3</sub>)<sub>2</sub>N-n.m.r. absorption. After cooling the reaction mixture (Dry Ice - acetone), anhydrous ether was added until precipitation ceased. Recrystallization (ethanol-ether) and vacuum desiccation (10 h) gave the hygroscopic salt (69 g, 0.45 mol), m.p. 163-165° (lit. (17)  $165^{\circ}$ ; n.m.r. (D<sub>2</sub>O): 6.90 (9H, s), 8.86 (3H, d, J = 7.0 Hz), 6.59 (s) and 6.78 (d, J = 0.5 Hz) total 2H, and 5.65 (1H, m).

#### (iii) 1-(N-methylamino)-2-propanol and

1-(N-methyl,N-(2-hydroxypropyl)-amino)-2-propanol Both amines were isolated from the reaction of propylene oxide and methylamine. Propylene oxide (40 g, 0.7 mol) and methylamine (28 g, 0.33 mol), the latter added as the 40% aqueous solution, were heated under reflux for 30 min. On distillation (1 atm) 1-(N-methylamino)-2-propanol was collected at 148-150° (10 g, 0.11 mol); n.m.r.  $(D_2O)$ : 7.83 (3H, s), 8.97 (2H, d, J = 7.0 Hz), 7.62 (2H, d, J = 7.0 Hz), and 6.23 (1H, sextet, J = 7.0Hz). 1-(N-methyl, N-(2-hydroxypropyl)amino)-2-propanol was collected at 225 °C (28 g, 0.19 mol); n.m.r. (D<sub>2</sub>O):

8.41 (6H, d, J = 7.0 Hz), 5.57 (2H, sextet, J = 7.0 Hz), and 7.17 (7H, m,  $CH_3$ —N and  $CH_2$ ). Prolonged reflux led to increased yields of tertiary amine, but no attempt to optimize the yields of the respective amines has been made.

### (iv) N,N-Dimethylamino-2-propanone

The reaction of bromoacetone with aqueous dimethylamine by the method of Craig et al. (18) gave N,Ndimethylamino-2-propanone in 40% yield, b.p. 115° (lit. (18) 114°); n.m.r. (CCl<sub>4</sub>): 7.79 (6H, s), 7.07 (2H, s), and 7.94 (3H, s).

## Results

### 2-Aminoethanol and Related Compounds

### (i) Hvdrogen Abstraction Radicals

In acidic aqueous solution, all the aminoalcohols under consideration are in the protonated form. The deactivating effect of a  $-N(R)_3$  substituent (R = alkyl or H) on hydro-

gen abstraction by the electrophilic OH radical is consistent with the exclusive observation of the

radicals R<sub>3</sub>NCH<sub>2</sub>CHOH at pH 2.0. In Table 1, the hyperfine splitting constants (h.f.s.) for a series of these abstraction radicals show a pattern of low  $\beta$  hydrogen h.f.s. constants (10–13 G) and relatively large  $\beta$  nitrogen splitting (10-12

G).<sup>2</sup> In the case of the radical  $CH_3NH_2CH_2$ -CHOH, we report for the first time the resolution of the NH and OH h.f.s. constants for radicals of this type. The fine structure consists of a doublet  $(a_{OH}(1H) = 1.0 \text{ G})$  of triplets  $(a_{\rm NH_2}^+ (2H) = 0.8 \text{ G})$  recorded in a spectrum with line width < 0.1 G. In the pH range indi-

<sup>&</sup>lt;sup>1</sup>By B. S. Snowden Jr. and E. T. Strom of Mobile Research and Development Corporation, Dallas.

<sup>&</sup>lt;sup>2</sup>Agreement to within experimental error is noted with values published after the completion of this work by Norman and co-workers for compounds (6-9) (5).

# CAN, J. CHEM, VOL. 51, 1973

cated no other resonances are observed for these compounds, while signal intensity is near the maximum observed using the flow technique. In particular repeated attempts to observe the

radical  $(CH_3)_3 N^+$  from choline chloride oxida-

tion  $(R_3 N - = (CH_3)_3 N - )$  were unsuccessful.<sup>3</sup>

(ii) Secondary Elimination Radicals

(a) Acetaldehyde Radical ·CH<sub>2</sub>CHO

Oxidation of the aminoalcohols 6-8 and 10 (Table 1) at pH 6.5-7.5 (effluant) provided spectra dominated by the ·CH<sub>2</sub>CHO radical. Previously unreported in neutral aqueous solution, this species has spectral parameters unchanged from those at pH 1.0 (4), namely  $a_{CH}(2H) = 19.0 \text{ G}, g = 2.0045$ , and a line width of 1.0 G. In addition, one detects weaker resonances from the radicals 12-14 associated with generation of  $\cdot$ CH<sub>2</sub>CHO in aqueous solution (5).<sup>4</sup>

$$\cdot$$
CH<sub>2</sub>CH(OH)<sub>2</sub> HOCH<sub>2</sub>CHOH O=CHCH<sub>2</sub>CH<sub>2</sub>CHOH  
12 13 14

At pH 6.5–7.5, spectra of sufficient intensity to interpret have not yet been observed for triethanolamine 11 and the quaternary ion  $(CH_3)_3$ -

NCH<sub>2</sub>CH<sub>2</sub>OH, 9. However, for all of the compounds 6-11, the abstraction radical spectrum

(e.g. R<sub>3</sub>NCH<sub>2</sub>ĊHOH) does not persist under conditions where ·CH2CHO and related species are detected (pH > 5.0).

(b) Fragmentation of

 $(CH_3CH_2)_3 \overset{+}{N}CH_2\dot{C}HOH$ At pH 1.6, the triethyl quaternary ion (CH<sub>3</sub>- $CH_2$ )<sub>3</sub> $NCH_2CH_2OH$  gave an intense spectrum attributed to  $(CH_3CH_2)_3 N^+$   $(a_N(1) = 20.2 \text{ G},$  $a_{CH}$ ,(6H) = 22.1 G) as previously reported (5).<sup>5</sup> At pH 2.5-4.0, a complex spectrum appeared dominated by the radical  $\cdot CH_2CH(OH)_2$  12  $(a_{CH}, (2H) = 22.4 \text{ G}, a_{CH}(1H) = 18.7 \text{ G}, g =$ 2.0025); with weaker lines clearly assigned to the species HOCH<sub>2</sub>ĊHOH 13  $(a_{CH}, (2H) = 9.4 \text{ G},$  $a_{CH}(1H) = 18.0 \text{ G}, a_{OH}(1H) = 1.0 \text{ G}, g = 2.0032$ and O=CHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CHOH 14 ( $a_{CH}(1H) = 15.2$ G,  $a_{CH_2}(2H) = 20.2$ ,  $\gamma CH_2$  splitting unresolved, g = 2.0032). In striking contrast to choline, no spectra of simple abstraction radicals are identified at pH 1.5-2.5.

# 1-Amino-2-Propanol and Related Compounds

### (i) Hydrogen Abstraction Radicals

In Table 2, h.f.s. constants are given for the

radicals  $R_3$ NCH<sub>2</sub>ĊOHCH<sub>3</sub> (R = H, alkyl) observed during the oxidation of the corresponding alcohols at pH 2.0–4.5. In the spectra from 16-18, the N-H hydrogen splittings are again resolved, but no splitting due to the OH group can be detected. However, at pH 2.0 in water, no splitting due to hydroxyl hydrogen is detected for the radical (CH<sub>3</sub>), COH a good model for 16–18. In the spectra of 17 and 18 severe broadening of the central lines of the B-hydrogen triplet creates the impression of a single (doublet) splitting. Indeed this apparent anomaly in the spectrum from 17 led us to examine the oxidation of 18. Computer simulation shows the spectra to be compatible with splitting from two  $\beta$ -hydrogens only if the central lines of each triplet are assigned a higher line width (0.8 G) than the remaining resonances. The phenomenon is analyzed in terms of hindered rotation (see Discussion).

### (ii) Secondary Elimination Radicals

At pH 6.5-7.5, the dominant signal from 15-18 was the acetonyl radical  $\cdot CH_2COCH_3$  $(a_{CH}, (2H) = 19.7 \text{ G}, a_{CH}, (3H) = 1.1 \text{ G}, g =$ 2.0042). The central quartet is resolved, but has a line width twice as great as the wing multiplets. The drastic simplification of the spectrum makes evident in each case a weaker spectrum of radi-

cals of the type  $CH_2CHOHCH_2NR_3$  (g = 2.0025), mostly appearing as an unresolved quartet with broadened center lines (a(3H) =

22.7  $\pm$  0.5 G). Only in the case of NH<sub>3</sub>CH<sub>2</sub>-CHOHCH, was further resolution possible  $(a_{CH}, (2H) = 22.4 \text{ G}, a_{CH}(1H) = 24.0 \text{ G}).$  The line width of the wing resonances was still 1.3 G, evidently due to an unresolved  $\gamma$  hydrogen splitting (compare  $\cdot$ CH<sub>2</sub>CHOHCH<sub>3</sub>,  $a_{CH_3}(3H) =$ 0.8 G) (19). However, referring to ·CH<sub>2</sub>-

4012

<sup>&</sup>lt;sup>3</sup>Simulated spectra of the (CH<sub>3</sub>)<sub>3</sub>NCH<sub>2</sub>CHOH species with low percentage intensities of the resonances from

 $<sup>(</sup>CH_3)_3$ N' $(a_{CH}, (9H) = 28.6 \text{ G}, a_N(1) = 20.3 \text{ G})$  were used to evaluate the experiments.

<sup>&</sup>lt;sup>4</sup>In neutral solution, we suggest ·OH addition to CH<sub>2</sub>=CHOH in the continuing secular equilibrium is the likely source of 12 and 13 with 14 arising from ·CH<sub>2</sub>CHO addition to the enol as previously suggested (5).

<sup>&</sup>lt;sup>5</sup>The lack of observation of  $(CH_3)_3 \overset{\tau}{N}$  from choline oxidation in this work must then be attributed to not achieving the exact conditions of the earlier study (5).

	Aminoalcohol	a <sub>BCH3</sub>	а <sub>всн2</sub>	a <sub>N</sub>	a <sub>N-H</sub> +
15	<sup>+</sup> NH₃CH₂CHOHCH₃	21.3	11.6	9.7	·†
16	CH <sub>3</sub> <sup>+</sup> NH <sub>2</sub> CH <sub>2</sub> CHOHCH <sub>3</sub>	21.9	11.0	11.0	1.0(2H)
17	(CH <sub>3</sub> ) <sub>2</sub> <sup>+</sup> NHCH <sub>2</sub> CHOHCH <sub>3</sub>	21.7	9.9‡	12.5	1.4(1H)
18	(CH <sub>3</sub> CHOHCH <sub>2</sub> )(CH <sub>3</sub> ) <sup>+</sup> NHCH <sub>2</sub> CHOHCH <sub>3</sub>	21.5	9.8‡	12.5	1.4(1H)

Hyperfine splitting constants for the radicals  $R_3$  NCH<sub>2</sub>COHCH<sub>3</sub>;\* R = H, CH<sub>3</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>)OH

 ${}^{*}g$ -Values were 2.0032  $\pm$  0.0002. +No further splitting was resolved.  $\pm$ The center lines of the triplet splitting are broadened and detected only in the outer multiplets.

CHOHCH<sub>2</sub>OH as a model  $(a_{CH_2}(2H) = 22.3 \text{ G},$  $a_{\text{CHOH}}(1\text{H}) = 24.6 \text{ G}$  (5), the above assignment seems appropriate.

Both at pH 2.0 and at pH 7.0, oxidation of

the quaternary cation  $(CH_3)_3$   $^{+}NCH_2CHOHCH_3$  gives the same spectrum, assigned as  $(CH_3)_3$ -

NCH<sub>2</sub>CHOHĊH,  $(a(3H) = 22.7 \pm 0.5, g =$ 2.0025).

### Reduction of a-Substituted Ketones

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The oxidation of formic acid (0.5 M) in the presence of the aminoketone cation,  $(CH_3)_2$ -

NHCH<sub>2</sub>COCH<sub>3</sub> was undertaken as a route to the anomalous abstraction radical from alcohol 17 via one-electron reduction of the carbonyl group by  $\cdot$ CO<sub>2</sub>H. At pH 2.0, reduction did occur to give a weak spectrum of the desired abstraction radical, but also an equal intensity of the acetonyl radical. At pH 4.0 only the radical ·CH<sub>2</sub>COCH<sub>3</sub> was observed. When chloroacetone replaced the aminoketone as substrate, acetonyl radical was again the sole species observed at pH 4.0. Evidently the intermediate anion radical eliminates the  $\beta$  substituent in a process closely akin to the eliminations from alcohol abstraction radicals (see Discussion).

### Discussion

The anomalously low  $\beta$  h.f.s. constants that are observed for organic  $\pi$  radicals of the type YCH, CHX have been analyzed by Norman and co-workers (20) in a wide-ranging general treatment. Observing that the phenomenon was restricted to cases where Y was an electron acceptor and X had an available electron pair, he proposed a preferred conformation of the radical that gained stabilization as a result of this sub-

stitution pattern. Employing the radical NH<sub>3</sub>-

CH<sub>2</sub>ĊHOH from 2-aminoethanol as an example, the conformation 19 with dihedral angle  $\theta = 60^{\circ}$ is consistent with the observed value of  $a_{BCH_2}$ -(2H) = 11.6 G. In some instances, even lower

4013



 $\beta$ CH<sub>2</sub> h.f.s. constants are observed; for example  $a_{CH_2}(2H) = 8.5 \text{ G}$  for the choline derived radical (CH<sub>3</sub>)<sub>3</sub>NCH<sub>2</sub>ĊHOH. Further lowering beyond that predicted by 19 is attributed to the electron delocalization shown in structures 20 and 21, a model that suggests planarity

$$(CH_{3})_{3}\overset{+}{N} CH_{2}\dot{C}HOH \leftrightarrow (CH_{3})_{3}N \dot{C}H_{2}CH \stackrel{+}{=} \overset{+}{O}H 20 \\ \leftrightarrow (CH_{3})_{3}N \overset{+}{C}H_{2} \stackrel{+}{=} CH \stackrel{+}{=} OH 21$$

at the  $\alpha$ -carbon and a distortion from tetrahedral geometry at the  $\beta$ -carbon (20). Furthermore, the relatively large  $\beta$ -nitrogen h.f.s. constants are accommodated. Such stabilization would make **19** a preferred conformation.

In the present work, further examples of low  $\beta$ -hydrogen and large  $\beta$ -nitrogen h.f.s. values are noted in the radicals  $CH_3\dot{C}OHCH_2\dot{N}H_3$  and  $CH_3\dot{C}OHCH_2NH_2CH_3$  (Table 2, 15, 16). More-

### CAN. J. CHEM. VOL. 51, 1973

over radicals of the type  $R_2NHCH_2\dot{C}OHCH_3$ (Table 2, 17, 18) have marked broadening of the center lines of  $\beta$ -hydrogen triplets. In consequence we suggest an additional factor that plays a role in determining radical conformation where intramolecular hydrogen-bonding is possible.

Consider  $NH_3CH_2CHOHCH_3$ , having as one preferred conformation the hydrogen bonded form 22 prior to hydrogen abstraction. One predicts then conformers 23 and 24 will result if intramolecular hydrogen bonding continues as a significant factor in the radical. By focussing





attention on one of the  $\beta$  hydrogens, H<sub>A</sub>, we can project a value of  $a_{\beta CH_2}$  for conformation 23. Applying the McConnell relationship (eq. 5),

$$[5] a_{\rm H} = B_0 + B\cos^2\theta$$

we set  $B_0 \simeq 0$  and B = 42.6 following the basic approach taken by Norman and co-workers (20).<sup>6</sup> Then with  $\theta = 30^\circ$ ,  $a_{H_A} = 31.95$ . In conformation **24**, we assume  $\theta = 0$  for  $H_A$  yielding  $a_{H_A} =$ 0 in the approximation. For equal but preferred population of just these two conformations, one predicts  $a_{CH_2}(2H) = 15.98$  G. Clearly, the observed value ( $a_{CH_2}(2H) = 11.6$ ) is somewhat lower, just as often noted for the alternative hypothesis based on conformation **19** (20). In the hydrogenbonded model, the further depression in  $a_{6CH_2}$  is ascribed to distortion of the  $\beta$  carbon tetrahedral geometry towards planarity by net displacement of the amino group toward C- $\alpha$ , energetically compensated for by retention of the optimum

hydrogen-bonding between NH<sub>3</sub> and OH.

The hypothesis accommodates the observation of a selective line broadening in the 1-(N,Ndimethylamino)-2-propanol abstraction radical.<sup>7</sup> We propose 25 as the stable conformation of the substrate leading to 26 as one conformation of the radical.<sup>8</sup> First, the n.m.r. spectrum of the cation 25 in aqueous hydrochloric acid (pH 2.0)



shows two distinct *N*-methyl resonances at 6.47 (CH<sub>3</sub>(A)) and 6.37 (CH<sub>3</sub>(B)), each split by a single proton (N—H, J = 2 Hz). Secondly, the magnitude of the N—H splitting (e.s.r.) for **26**  $(a_{\rm NH}^+ = 1.4 \text{ G})$  is compatible with direct interaction of the hydrogen with the oxygen atom bonded to the alpha carbon. For example, in the maleic acid reduction radical **27**, the bridging hydrogen has  $a_{\rm H}(1) = 1.1$  G, and is not exchange broadened at pH 1.0 (21).



Indeed, both the observation of large  $\beta$ -nitrogen h.f.s. and NH splitting throughout the series of radicals from the aminoalcohols is consistent with population of hydrogen-bonded conformations. Broadening of the center line of the triplets is compatible with slow interconversion

4014

<sup>&</sup>lt;sup>6</sup>Calculated from  $a_{CH_3} = 21.3$  G in CH<sub>3</sub>COHCH<sub>2</sub>NH<sub>3</sub> with  $\langle \cos^2 \theta = 1/2 \rangle$  for a freely rotating methyl group.

<sup>&</sup>lt;sup>7</sup>The authors acknowledge a referee's suggestions in interpretation of this phenomenon.

 $<sup>^{8}</sup>$ In analogy to 23 and 24, an equivalent enantiomeric conformation exists.





SCHEME 1

of the equivalent conformers on the e.s.r. time scale.

In support of the interpretation we note that the phenomenon is observed for two distinct substrates and that one of the radicals  $(CH_3)_2$ -

NHCH<sub>2</sub> $\dot{C}OHCH_3$  has been generated by an independent route (reduction of *N*,*N*-dimethyl-amino-2-propanone).

Clearly for radicals such as  $CH_3OCH_2$ -CHOCH<sub>3</sub>, only the Norman analysis in terms of conformations of the type **19** is appropriate (20). We propose that *in addition* conformations of the type **23** and **24** are populated in the aminoalcohols and contribute to lowered  $\beta$ -hydrogen h.f.s. values. For highly hindered cases, restricted rotation in the radical can be observed as a line broadening effect.

### Elimination Processes in β-Aminoalcohol Abstraction Radicals

The observation of  $\alpha$  carbonyl radical spectra in the pH range 6.5–7.5 is compatible with deprotonation of an abstraction radical, followed by rapid fragmentation of its conjugate base. The sequence is outlined in Scheme 1 for (CH<sub>3</sub>)<sub>2</sub>NHCH<sub>2</sub>COHCH<sub>3</sub> adopting the proposed

intramolecularly hydrogen-bonded conformation. For the mechanism to be operative, it is clearly necessary that the  $pK_a$  of the abstraction radical be markedly lower than that of the amine precursor. Presently available data from e.s.r. studies during irradiation of alcohols indicate that the  $pK_a$  of an  $\alpha$ -alcohol radical is lower by from 4-8 units in comparison with that of the alcohol substrate (22). For instance, 2-propanol has  $pK_a = 17.1$ , while  $(CH_3)_2\dot{C}OH$  has  $pK_a$ 12.03. Even more striking is the acidity of  $(CF_3)_2$ - $\dot{C}OH$ ,  $pK_a = 1.7$ . Similarly, chloral hydrate and

6] 
$$CCl_3C - H \xrightarrow{OH} CCl_3C - H + H_2O pK_a = 10.0$$
  
OH OH

[7] 
$$CCI_3C$$
,  $OH \longrightarrow CCI_3 - C$ ,  $H_2O \ pK_a = 6.2$   
OH

its abstraction radical show the same trend (reactions 6, 7) (23). Moreover, the effect of an electron-withdrawing  $R_3^+N$ -group on alcohol radical acidity should be comparable to that of the CCl<sub>3</sub> group. For example, betaine, (CH<sub>3</sub>)<sub>3</sub>-<sup>+</sup> N—CH<sub>2</sub>COOH (pK<sub>a</sub> = 1.83) is a stronger acid

than acetic acid,  $CH_3COOH$  (p $K_a = 4.75$ ). By analogy, then, the abstraction radical from

 $(CH_3)_2$ NHCH<sub>2</sub>CHOHCH<sub>3</sub> (p $K_a = 9.3$ ) will have a p $K_a$  value at least as low as 6.0. Elimination is clearly in evidence in solutions p $H \ge 6.0.9$ 

Using pulse radiolysis Henglein and coworkers have observed the conversion of the 1,2-dihydroxyethyl radical  $CH_2OH\dot{C}HOH$  to acetaldehyde radical  $\cdot CH_2CHO$  at pH 8.5 (reaction 8) (6).

[8] HOCH<sub>2</sub>CHOH 
$$\rightarrow$$
 HOCH<sub>2</sub>CHO<sup>-</sup>  $\rightarrow$   
·CH<sub>2</sub>CHO + OH<sup>-</sup>

We consider the  $\beta$ -aminoalcohol radical elimination to be an analogous reaction via the conjugate base of the initial abstraction radical. In summary, e.s.r. observation of a significant steady state population of the  $\alpha$ -carbonyl radicals at pH 7.0 probably reflects a significantly faster rate of elimination of the deprotonated radical than of the acid form at pH 2.0. If such is the case then under *in vivo* conditions (*e.g.* pH 7.3), radicals from biologically important 2-aminoethanol derivatives (serine, choline) may eliminate in competition with repair even by efficient hydrogen transfer agents.

The observation of the acetonyl radical from reduction of N,N-dimethylamino-2-propanone is fully consistent with the proposed elimination. First, Fessenden and co-worker have demonstrated that the reducing radical  $\cdot CO_2H$  is not active in direct deamination reactions that would yield the  $\alpha$ -carbonyl radical directly (*e.g.* reaction 9) (24).

$$[9] \cdot CO_2H + (CH_3)_2NHCH_2COCH_3 \xrightarrow{} \\ \cdot CH_2COCH_3 + (CH_3)_2NH + CO_2 + H^+$$

Observation of the  $\cdot$ CH<sub>2</sub>COCH<sub>3</sub> species at higher acidity than in aminoalcohol oxidation can be understood in terms of direct formation of the deprotonated intermediate **28** by electron transfer to the carbonyl group (21). Fragmentation is then assumed to occur before the protonation equilibrium can be established (eq. 10).



# Spectra of $R_3 N^{+}$ in Quaternary Cation Oxidation

Spectra of sufficient intensity to analyze were

not achieved for  $(CH_3)_3NCH_2CHOHCH_3$  oxidation at pH 1.0 and 7.0 or for choline cation oxidation at pH 7.0. At pH 1.0 only the radical  $(CH_3)_3NCH_2\dot{C}HOH$  was observed from choline. However, for both cations at pH 1.0 and 7.0 we have observed that trimethylamine hydrochloride and acetone or acetaldehyde, respectively, are the major products of photolysis of their aqueous solutions containing  $H_2O_2$  (25). Accordingly, further efforts to identify the elimination radicals by e.s.r. particularly at pH 7.0 are being made prior to speculation on the mechanism in these instances.

In the case of  $(CH_3CH_2)_3$   $^+NCH_2CH_2OH$ , the radical  $(CH_3CH_2)_3$   $^+N$  was observed at pH 1.6. However, at pH 2.5–4.0 the spectra of  $CH_2$ - $CH(OH)_2$  and associated species were recorded, with no trace of cation radical remaining. By analogy to previous considerations (5) we postulate the usual heterolysis (reaction 11). In order to accommodate

[11]  $(CH_3CH_2)_3NCH_2\dot{C}HOH \rightarrow$ 

$$[(CH_3CH_2)_3N CH_2CH=OH] \rightarrow$$

$$(CH_{3}CH_{2})_{3}NH + \dot{C}H_{2}CHO$$

the appearance of the cation radical at pH 1.6, either a change in mechanism (homolysis of the C—N bond) (reaction 4) or electron-transfer from the amine to the radical in a cage reaction is required (reaction 12).

[12] 
$$(CH_3CH_2)_3N: + \dot{C}H_2CH=OH \rightarrow$$

(CH<sub>3</sub>CH<sub>2</sub>)<sub>3</sub>N' + CH<sub>2</sub>==CHOH



<sup>&</sup>lt;sup>9</sup>Clearly if elimination from the deprotonated form were highly favored kinetically, reaction could be observed at a pH one or two units lower than the actual  $pK_a$ .

Clearly the protonated amine is not an oxidizable species, so only transfer from the amine is viable. *Tertiary* amines are readily oxidized, *e.g.* tri-*n*-propylamine in acetonitrile at  $E_p =$ -0.87 V (26). Henglein has recently measured the reducing potential of the *neutral* acetaldehyde radical  $\dot{C}H_2CHO$  as -0.75 V by polarographic current measurements during pulse irradiation (6). If one admits only a modest increase in reducing potential for the protonated

form  $\dot{C}H_2CHOH$  in close proximity to the amine, an electron transfer is clearly possible. Walling and El-Taliawi (27) have demonstrated reduction of  $\dot{C}H_2COCH_3$  by ferrous ion in the Fenton reagent oxidation of acetone (reaction 13), another example of reduction of  $\alpha$ -carbonyl radicals.

[13]  $\cdot CH_2COCH_3 + Fe^{II} \rightarrow CH_2COCH_3 + Fe^{III}$ 

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We favor the electron-transfer as preferable to postulating a complete change in mechanism over such a narrow range of pH, but clearly more examples of such cation radical generation would be desirable.

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