A STUDY OF FREE RADICAL 1, 2-ACYL MIGRATIONS

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This is to certify that the

thesis entitled

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ABSTRACT

A STUDY OF FREE RADICAL 1,2-ACYL MIGRATIONS

By E. Jerome Maas

The incomplete information pertaining to 1,2-acyl shifts in free radicals prompted this investigation of keto radicals III and IV; these radicals are structually designed to permit 1,2-acyl migration thus generating radicals V and VI respectively. Experiments show that radical IV undergoes this rearrangement to a much greater extent than radical III; however, triphenyltin and tributyltin hydrides intercept most of radical IV before rearrangement.



t-Butylperlevulinate- \underline{d}_5 (I) and t-butyl-3,3-dimethylperlevulinate (II) were decomposed in 0.25 M solutions of triglyme and phenyl ether at 130-132° for 5 1/2 hours. Greater than 97% decomposition occurred during this time and the carbon dioxide evolution ranged from 60-90% of the theoretical amount.

Decomposition of t-butylperlevulinate- \underline{d}_5 (I) afforded 45% (yield based on mmoles of perester consumed) of a mixture of deuterated 2-butanones (VII and IX) in triglyme and a 42% mixture in phenyl ether; however, the rearranged ketone (IX) constituted no more than 10% of these mixtures.

Decomposition of t-butyl-3,3-dimethylperlevulinate (II) afforded a 23% yield of a mixture of unrearranged ketone [3,3-dimethyl-2-butanone (VIII)] and rearranged ketone [4-methyl-2-pentanone (X)] in triglyme and an 11% yield in phenyl ether; the ratio of rearranged ketone (X) to unrearranged ketone (VIII) was 19 in both solvents. Reaction of radical (IV) with the t-butoxy radical afforded an 11% yield (based on mmoles of perester consumed) of 4-t-butoxy-3,3-dimethyl-2-butanone (XIII) in both solvents.

> 0 CH₃ II I S CH₃-C-CCH₂-O-C(CH₃)₃ CH₃ CH₃ XIII

Triphenyltin and tributyltin hydride reductions of 4-bromo-3,3dimethyl-2-butanone (XI) and 4-chloro-3,3-dimethyl-2-butanone (XII) afforded mixtures of unrearranged ketone [3,3-dimethyl-2-butanone (VIII)] and rearranged ketone [4-methyl-2-pentanone (X)] whose ratio (VIII/X) decreased with decreasing concentrations of the tin hydride.

A STUDY OF FREE RADICAL 1,2-ACYL MIGRATIONS

Вy

E. Jerome Maas

A THESIS

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To my wife, Peg

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HISTORICAL

Free radicals are electron deficient, uncharged, trivalent species which for the most part exist only momentarily during the course of chemical reactions. These reactive intermediates can react by a variety of pathways (1), and in some cases may undergo molecular rearrangement before suffering a terminal reaction. The simplest rearrangement is an intramolecular 1,2-shift (equation A); and although such transformations are well known for carbonium ion intermediates (* = +), the number of authentic free radical examples ($* = \cdot$) is relatively small. In most of

A
$$R_1 R_2 R_3 CCH_2 \longrightarrow R_1 R_2 CCH_2 R_3$$

the known free radical rearrangements the moiety undergoing transfer is an aryl group or a halogen atom, and the 1,2-shift usually proceeds so as to generate a more stable radical.

Diradicals should be considered as a separate topic, since in cases where interaction of the reactions sites can occur (e.g. 1,3 diradicals), a markedly different behavior is observed (2).

Hydrogen and alkyl groups do not normally migrate in free radical 1,2-shifts. Walling states "In most cases where they have been reported alternate explanations are available for the observed results, or the radical nature of the reaction is in doubt" (3). Nonetheless, an apparently unambiguous alkyl group migration has been reported (B). A fragmentation recombination mechanism was proposed for this reaction.

Aryl group migrations take place in preference to any conceivable alkyl shifts, as shown in the following examples:

D $\emptyset C(CH_3)_2 CH_2$ (CH₃)₂ CCH₂ \emptyset (6)

$$F \qquad \emptyset_2^{C(CH_3)CH_2} \cdot \qquad \longrightarrow \qquad \hat{\phi_c(CH_3)CH_2} \emptyset \qquad (8)$$



G

$$J \qquad NO_2 \bigcirc -C(CH_3)_2 CH_2 \cdot \longrightarrow NO_2 \bigcirc -CH_2 \dot{C}(CH_3)_2 \quad (11)$$

These rearrangements usually proceed so as to give the more stable radical, however equations K and L illustrate two cases lacking this driving force.

$$\kappa \qquad \rho CH_2^{14} CH_2^{\cdot} \qquad -\frac{4\%}{4\%} \qquad \rho^{14} CH_2^{\cdot} CH_2^{\cdot} \qquad (12)$$

The facility with which aryl groups undergo 1,2-shifts to radical sites is apparently related to the unsaturation of these groups, since other radicals having homoallylic unsaturation also rearrange if a more stable radical can be formed. The following examples of vinyl and acyl group migrations illustrate this fact.

$$M \quad CH_3CH=CHC(CH_3)CH_2 \cdot - CH_3CH=CHCH_2CHCH_3 \quad (14)$$



 $Q = CH_3COCØ(CH_3)CH_2$ \longrightarrow $CH_3COCH_2C(Ø)CH_3$ (18)

The last case (equation Q) is interesting in that three rearrangement pathways are possible: 1,2-shift of a phenyl, methyl, or acyl group. The preferential migration of the acyl group was unexpected.

Rearrangements involving 1,2-shifts of silicon, sulfur, bromine, and chlorine atoms have also been reported. These atoms all have valence shell d-orbitals which may be used to form a three membered cyclic transition state or intermediate. Some examples of these rearrangements are:

$$R = CH_3, \emptyset \qquad R' = n-Bu, \emptyset, p-CH_3\emptyset \qquad (19)$$

s
$$(CH_3)_3$$
SiSi $(CH_3)_2$ CH₂· \longrightarrow $(CH_3)_3$ SiCH₂Si $(CH_3)_2$ (20)

$$T \quad [(CH_3)_3Si]_2Si(CH_3)S \quad \longrightarrow (CH_3)_3SiSi(CH_3)SSi(CH_3)_3 \quad (21)$$

$$U \qquad (CH_3)_2 CBrCH_2 \cdot - (CH_3)_2 \dot{C}CH_2 Br \qquad (22)$$

W
$$CC1_3CHCH_2Br$$
 \longrightarrow $CC1_2CHC1CH_2Br$ (23)

x
$$cc1_3\dot{c}(cH_3)CH_2Br \longrightarrow \dot{c}c1_2Cc1(cH_3)CH_2Br$$
 (24)

The absence of bonafide alkyl group 1,2-shifts in radical intermediates can be explained if one considers the activation energy for such a shift. Application of a truncated Huckel molecular orbital theory to this system indicates that a cyclic transition state is energetically unfavorable (25-27). The three atomic orbitals involved in the migration are converted into three molecular orbitals; one of these molecular orbitals is bonding and the other two are antibonding. In carbonium ion rearrangements only two electrons are involved in the bonding of the migrating group, and these electrons would occupy the lowest available orbital, which is the bonding orbital. In mono-radicals, however, there are three electrons which must be accomodated and the third electron must occupy the lowest anti-bonding orbital, thereby destabilizing the transition state.

Rearrangements of unsaturated groups such as aryl, vinyl, and acyl do not fall into this category, and can easily be rationalized by three membered cyclic intermediates, e.g.:



We undertook this study to determine whether a 1,2-acyl shift would take place in a system incapable of generating a more favorable radical by rearrangement and to obtain information concerning the rate of acyl shift.

>

INTRODUCTION

Methods of generating suitably substituted 3-ketoradicals (e.g. I and II) were required for this study of free radical acyl rearrangements (equation Y).



The choice of radicals I and II was based on the expectation that I would have a moderate driving force for the rearrangement (i.e. a primary radical going to a tertiary radical), while II would provide a reference measurement in which this driving force is missing.

Common methods of generating radicals include thermal decomposition of peresters (equation Z), thermal decomposition of azo compounds (equation A'), radical initiated decarbonylation of aldehydes (equation B'), decomposition of tertiary alkoxy radicals (equation C') and radical initiated reduction of alkyl halides by tin hydride derivatives (equation D').

Z R-C-0-0-R'
$$\longrightarrow$$
 R'0' + R-C-0' $\xrightarrow{-C0_2}$ R'

A' R-N=N-R \longrightarrow $N_2 + 2R$

B'
$$R-C-H + R'-0$$
 \rightarrow $R'-OH + R-C'$ $-CO$
C' $R-C-O'$ $R' + R_2C=0$
D' $R-X + R_3'Sn'$ \rightarrow $R_3'Sn-X + R'$

The present study of acyl rearrangements in radical intermediates relied heavily on the first method of radical formation, since it is a generally reliable and well-tested procedure and since the necessary β -keto acid precursors (equation E') were known compounds.



RESULTS

A. Syntheses

Preparation of a selectively deuterated levulinic acid was first attempted by treating ethyl-4,4-(ethylenedioxy)-pentanoate with alkaline deuterium oxide in order to form a levulinic acid- \underline{d}_2 having deuterium at the 2-position. Several different bases were used in these reactions but no deuterium was incorporated into the resultant levulinic acid at reflux temperature. When deuterium exchange was attempted in a sealed tube at 150⁰ some deuterium was incorporated into the 2-position, but concomittant cleavage of the ketal occurred and the product was a mixture of deuterated levulinc acids.

These results indicated that the 2-position of levulinic acid was relatively resistant to base catalyzed deuterium exchange, so it seemed that preparation of levulinic acid- \underline{d}_5 might be straightforward. When ethyllevulinate was treated with alkaline deuterium oxide the recovered levulinic acid was found to be largely the \underline{d}_5 -compound; however, significant amounts of \underline{d}_3 -, \underline{d}_4 -, \underline{d}_6 -, and \underline{d}_7 -labled material was also present. Mass spectral analysis of the corresponding perester 2,4-dinitrophenylhydrazone derivative showed deuterium incorporation as follows: 0.6% \underline{d}_0 ; 1.3% \underline{d}_1 ; 2.9% \underline{d}_2 ; 7.6% \underline{d}_3 ; 26.8% \underline{d}_4 ; 44.6% \underline{d}_5 ; 12.4% \underline{d}_6 ; 3.5% \underline{d}_7 .

The preparation of t-butylperlevulinate and substituted perlevulinate esters is difficult to accomplish cleanly due to facile cyclization to

pseudo-esters (equation F'). The presence of the γ -lactone was easily

F'
$$CH_3CCH_2CH_2C-0-OC(CH_3)_3 \xrightarrow{H^+} (CH_3)_3CO-0 \xrightarrow{O} O$$

detected by a strong band at $910cm^{-1}$ in the infrared spectrum; the strong carbonyl stretching absorption at $1785cm^{-1}$ overlapped the perester absorption at $1775cm^{-1}$. Several unsuccessful approaches were tried before the synthesis of t-butylperlevulinate (VIII), t-butylperlevulinate- d_5 (IX), and t-butyl-3,3-dimethylperlevulinate (X) were finally achieved by the following reaction sequence:

$$\begin{array}{c} 0 & R' \\ R - C - CCH_2CO_2H \\ R' \end{array} \qquad \begin{array}{c} 1 & N \rightarrow 2 & C = 0 \\ \hline 1 & N \rightarrow 2 & C = 0 \\ \hline 2 & (CH_3)_3C - 0 - 0H \end{array} \qquad \begin{array}{c} 0 & R' \\ R - C - CCH_2CO_3(CH_3)_3 \\ \hline R - C - CCH_2CO_3(CH_3)_3 \\ \hline R' = 0 \\ \hline R' \end{array}$$

These reactions probably proceed by way of a mixed anhydride of imidazole-N-carboxylic acid and the levulinic acid (equation G'). This anhydride rapidly loses carbon dioxide to form the imidazolide (equation H') which then reacts with t-butylhydroperoxide to give the perester. Unreacted acid was easily recovered and could be recycled.



The β -halo ketones 4-bromo-, and 4-chloro-3,3-dimethyl-2-butanone were prepared by the following scheme:



However, most of the 4-chloro-2-butanone was prepared by another route:



Plans to use 4-bromo-3,3-dimethyl-2-butanone as a precursor to 3,3-dimethyllevulinic acid were unsuccessful because the Grignard reagent from the corresponding ketal bromide led only to the counled bisketal shown in equation I'. Fortunately the dimethyl levulinic acid could be prepared from 2,2-dimethylsuccinic acid, as shown in equation J' (28).



II. Perester Pyrolysis

A. Analytical Methods

The carbon dioxide evolved during perester decomposition was collected in an ascarite trap after volatile organic compounds had been condensed from the effluent gases. A preliminary wash of the perester pyrolysis mixture by aqueous NaHCO₃ failed to disclose any acidic products. Unreacted perester was then determined by the method of Silbert and Swern (29), whereby perester is decomposed by a catalytic amount of ferric ion in the presence of excess iodide ion; the iodine liberated in this reaction is titrated with a standard thiosulfate solution. The following mechanism has been proposed:

(1)
$$Fe(III) + I^{-} \longrightarrow Fe(II) + I^{-}$$

(2) $Fe(II) + RCO_{3}C(CH_{3})_{3} \longrightarrow (CH_{3})_{3}CO^{-} + RCO_{2}^{-} + Fe(III)$
(3) $(CH_{3})_{3}CO^{-} + H_{2}O \longrightarrow (CH_{3})_{3}COH + HO^{-}$
(4) $HO^{-} + I^{-} \longrightarrow HO^{-} + I^{-}$
(5) $2I^{-} \longrightarrow I_{2}$

In all cases the amount of unreacted perester was less than 1%. The presence of triglyme or phenyl ether in the mixture necessitated mechanical stirring during the titrations; however, the accuracy of the measurements was apparently not affected by either solvent.

The absence of carboxylic acids and unreacted perester permitted the work-up procedure to be simplified. Immediately after pyrolysis the solvent was distilled through a spinning band column and the early fractions and pot residue were analyzed by vapor phase chromatography and/or column chromatography.

B. Reaction Products

1. Unreacted Perester and Products from the t-Butoxy Radical

Pyrolysis of a 0.25M solution of perester in phenyl ether or triglyme at $130-132^{\circ}$ for 5 1/2 hours resulted in greater than 97% perester decomposition. The t-butoxy radical gave t-butanol and acetone which were swept from the pyrolysis flask into the dry ice traps. The ratio of t-butanol to acetone was 252 in triglyme and decreased to 1.1 in phenyl ether.

2. Carbon Dioxide

The amount of carbon dioxide collected in the ascarite traps ranged from 60% to 90% of the theoretical quantity, and the rate of gas evolution was often sporadic. Because of this variance, the original plan for monitoring the course of the reaction by carbon dioxide evolution was abandoned, and kinetic measurements were made by determining the unreacted perester remaining in aliquots of a 0.25M phenyl ether solution being heated at 130-132°.

A graph of (total perester)/(unreacted perester) versus time in minutes was plotted for t-butylperlevulinate, t-butyl-3,3-dimethylperlevulinate, and t-butyl-3-phenyl-3-methylperlevulinate (Figure 1). Only t-butylperlevulinate (k = $2.75 \times 10^{-4} \text{sec}^{-1}$) showed simple first order kinetic behavior for most of the reaction. Both t-butyl-3,3-dimethylperlevulinate (k = $3.46 \times 10^{-4} \text{sec}^{-1}$) and t-butyl-3-phenyl-3-methylperlevulinate (k = $2.71 \times 10^{-4} \text{sec}^{-1}$) appear to suffer induced decomposition in the early stages of pyrolysis (see dotted lines Figure 1).





3. Cage Products

A previous study of the pyrolysis of t-butyl-3-phenyl-3-methylperlevulinate showed that 23% to 26% of the recombination product 4-t-butoxy-3-phenyl-3-methyl-2-butanone was formed in the course of the reaction (18). Similar recombination products were anticipated in this work; however, only the dimethyl perlevulinate ester yielded such a compound (4-t-butoxy-3,3-dimethyl-2-butanone). The keto ether 4-t-butoxy-3,3-dimethyl-2-butanone (XXIV) (11% yield based on mmoles perester) was identified from its ir (Figure 2) and nmr (Figure 3) spectra and by a carbon-hydrogen-nitrogen microanalysis of its 2,4-dinitrophenylhydrazone derivative.

The absence of 4-t-butoxy-2-butanone (XXV) among the pyrolysis products from t-butylperlevulinate was unexpected. It is possible that this keto ether may have undergone $\boldsymbol{\beta}$ -elimination to methyl vinyl ketone. No methyl vinyl ketone was found among the volatile products; however, methyl vinyl ketone polymerizes readily and could be removed by reaction with other radicals present in the reaction mixture.

4. Rearranged Products

The monomeric rearranged products formed in these pyrolyses experiments were recovered from the dry ice traps along with acetone and t-butanol, and the yields (based on mmoles starting perester) of these simple ketones were obtained by vapor phase chromatography analysis. Pyrolysis of t-butylperlevulinate yielded 2-butanone in 46.4% yield when triglyme was the solvent and 42.5% yield when phenyl ether was the solvent.

Pyrolysis of t-butyl-3,3-dimethylperlevulinate (X) in triglyme resulted in a 23.4% yield (based on mmoles perester) of a ketone mixture



Figure 2. Infrared spectrum of 4-t-butoxy-3,3-dimethyl-2-butanone (neat).





consisting of 95% rearranged ketone (4-methyl-2-pentanone) and 5% 3,3dimethyl-2-butanone. When this perester was pyrolysed in phenyl ether, an 11.7% yield of a ketone mixture composed of 95% 4-methyl-2-pentanone and 5% 3,3-dimethyl-2-butanone was obtained.

Efforts to determine the extent of acetyl rearrangement in the 2-butanone obtained from the pyrolysis of the deuterium labeled t-butylperlevulinate were complicated by the rather broad distribution of deuterium in the perester itself. Mass spectral analysis of the ketone showed a range of deuterium incorporation (Table I) very similar to that observed for the perester, and it is clear that over 30% of the sample has less deuterium than desired (d_5) while 20% has more deuterium. The ratio of hydrogen atoms to deuterium atoms in this mixture is 0.67, while pure 2-butanone- \underline{d}_5 has a 0.60 ratio. Despite this difficulty, the nmr spectrum of the labeled 2-butanone can be interpreted so as to set an upper limit on the amount of rearrangement.

TABLE I				
Deuterium Distribution in the 2-Butanone From the Pyrolysis of Isotopically Labeled t-Butylperlevulinate in Triglyme				
Deuterium Incorporation	(Per Cent) Concentration	Deuterium and Hydrogen Units (Based on 800 Total)		
		Deuterium	Hydrogen	
d 2 d3 d4 d5 d6 d7	1.6 7.4 24.3 46.3 16.5 <u>3.4</u> 99.5	3.2 22.2 97.2 231.5 99.0 23.8 476.9	9.6 37.0 97.2 138.9 33.0 <u>3.4</u> 319.1	

TABLE II			
Proton Distribution in Labeled 2-Butanone			
Source of 2-Butanone	Area of Pro	oton Resonance S	Signal
	CH ₃ — C (a)	о — Сн ₂ — (b)	СН ₃ (с)
Perester Pyrolysis in Triglyme Perester Pyrolysis in Diphenyl Ether	0.60 ⁺ .08 0.69 ⁺ .06	0.22 ⁺ .01 0.25 ⁺ .02	3.0 3.0

Table II shows the relative areas of the three distinct proton resonance signals in the nmr spectrum of the labeled 2-butanone. The chemical shifts of these signals are: (a) γ 7.94, (b) γ 7.61, and (c) γ 8.98. Now, if the 2-butanone consisted entirely of <u>d</u>₅-labeled molecules with hydrogen located only on groups b and c, the ratio of b/c would be zero in the absence of any rearrangement and would rise to two if the substrate were completely rearranged (see equation K'). In the likely



event that rearrangement proceeds through a symmetrical intermediate or causes complete equilibration of the two radicals the maximum b/c ratio

would be unity. From these considerations it is a simple matter to relate the b/c ratio to the mole fraction of rearrangement (x) as follows: b/c = 2x/3-x. The b/c ratios from the two experiments listed in Table II thus point to 11.9% rearrangement in diphenyl ether and 10.6% rearrangement in triglyme.

The assumption that all the labeled butanone is \underline{d}_5 is of course not correct, and the major error in the previous calculations is that hydrogen atoms remaining at b due to incomplete exchange are counted as hydrogen atoms from rearrangement. This clearly leads to an exaggerated value for the mole fraction of rearrangement, and the actual amount of rearrangement must be less than 11% (perhaps even zero).

The next step in this data analysis is to ascertain whether the mass spectral data (Table I) and the nmr intensities (Table II) for the 2butanone obtained from labeled perester pyrolysis in triglyme are mutually consistent with a degree of rearrangement ranging from 0-11%. In order to do this, the isotopic composition at each position in the 2-butanone (i.e. a, b, and c) is given in terms of the hydrogen and deuterium units defined in Table I (i.e. positions a and c will have three hundred units each, while b has two hundred units). The distributions given in Table III depend upon the following assumptions:

1) If there is no rearrangement, all the deuterium units in 2-butanone- \underline{d}_5 are at positions a and b. The extra hydrogen in d_2 , d_3 , and d_4 -labeled ketone will be at positions a and b, while the extra deuterium in the d_6 and d_7 compounds is at c.

2) If 10% of the methylene hydrogen units at c rearrange to b, a reasonable a/b hydrogen ratio is obtained only if <u>all</u> the extra hydrogen in the sample (i.e. the 44 hydrogen units associated with the d₂, d₃, and

d, labeled ketone) is located at position a.

3) The distribution of hydrogen and deuterium for a 5% rearrangement of methylene groups lies midway between the 0% and 10% extremes.

TABLE III Calculated Hydrogen-Deuterium Distributions			
Extent of Rearrangement	Hydrogen and Deuterium Distribution		
	<u>a</u>	<u>b</u>	<u>c</u>
0%	32H, 268D	12H, 188D	277H, 23D
5%	38H, 262D	15H, 185D	268H , 3 2D
10%	44H, 256D	18H, 182D	259H , 41D

Since the total number of hydrogen and deuterium units remains unchanged for the three cases listed in Table III, we can judge their relative merits by comparing the ratio of hydrogen atoms in positions a, b, and c with the experimental values given in Table II. These are 0.35 : 0.13 : 3.0 for 0% rearrangement; 0.43 : 0.15 : 3.0 for 5% rearrangement and 0.51 : 0.21 : 3.0 for 10% rearrangement. Although none of these examples fit the observed ratio (0.60 : 0.22 : 3.0) exactly, it is clear that the best agreement is for 10% rearrangement. The unique assumption that isotopic exchange in the levulinic ester precursor is complete at the methylene group (b) but incomplete at the acetyl methyl group (a) becomes less outrageous if one assumes that the inductive effect of the carboxyl group greatly enhances the acidity of the methylene protons.

5. Solvent Products

Several solvent incorporated products were obtained from the reactions in phenyl ether. These products appear to arise from a combination of a methyl radical (from the t-butoxy radical) and/or a keto radical (from perester decompostion) with a phenyl ether molecule. This combination produced ortho, meta, and para substituted products. Both methylated and higher alkylated phenyl ethers were separated by vapor phase chromatography and identified by spectroscopic analysis. The ir and nmr spectra were consistent with the structural assignments; however, it could not be determined whether rearrangement of the 3-keto radical had occurred before combination with the solvent.

Several solvent derived products were also formed when triglyme was the pyrolysis solvent. These compounds could be separated by vapor phase chromatography, and each proved to have some carbonyl incorporation. One of the products also had a hydroxyl function. These compounds were not studied further.

III. Halide Decomposition

A. Analytical Methods

The triphenyltin hydride reductions were carried out by heating the reactants in sealed ampoules. These were then cooled to 0° overnight before being opened. The cooling served to precipitate most of the triphenyltin compounds, and the remaining solution was then analyzed by vapor phase chromatography.

B. Reaction Products

Reaction of 4-bromo-3,3-dimethyl-2-butanone with 0.55M triphenyltin hydride at 132° resulted in formation of a ketone mixture composed of 96% 3,3-dimethyl-2-butanone and 4% 4-methyl-2-pentanone. No starting keto halide was evident in the mixture. A similar reaction of 4-chloro-3,3-dimethyl-2-butanone with 0.43M triphenyltin hydride gave a ketone mixture composed of 90% of 3,3-dimethyl-2-butanone and 10% of 4-methyl-2-pentanone. Again no starting material remained. The decrease in the ratio of unrearranged to rearranged ketone from 24 to 9 in these two experiments corresponds to the decrease in tin hydride concentration. Reduction of 4-bromo-3,3-dimethyl-2-butanone with a 0.36M concentration of the less reactive tri-n-butyltin hydride (30) gave an even smaller ratio (5.5) of unrearranged ketone (3,3-dimethyl-2-butanone) to rearranged ketone (4-methyl-2-pentanone).

DISCUSSION

The question of whether intramolecular 1,2-acyl shifts can occur in free radicals can no longer be argued. Extensive rearrangement of the 3-methyl-3-phenyl-2-ketobutyl radical (XXI) was reported by Curtis Karl (18); and in this work, rearrangement of the 3,3-dimethyl-2-ketobutyl radical (I) is clearly well established. These two studies have several similar features and one important difference.



The product distribution from radicals I or XXI, generated by tertbutyl perester decomposition at 130-132°, was remarkably insensitive to changes in the solvent, although the rate of carbon dioxide evolution from I was faster in triglyme than in diphenyl ether. Of course, the ratio of t-butyl alcohol to acetone (both from the t-butoxyradical) did rise in a striking fashion when a perester decomposition in diphenyl ether solution was repeated in p-cymene or triglyme (these latter solvents provide a much better source of abstractable hydrogen than diphenyl ether); however, the relative amounts of rearranged ketones and unrearranged t-butoxyketones were not significantly affected. Apparently the initially formed primary radicals undergo cage recombination with a
t-butoxy radical (equation M') or rearrangement to a longer-lived tertiary radical (equation L') more rapidly than they participate in hydrogen abstraction from nearby solvent molecules.

$$M' \qquad CH_{3}C-C-CH_{2}^{\circ} + (CH_{3})_{3}CO^{\circ} \qquad \xrightarrow{fast} CH_{3}C-C-CH_{2}^{\circ} - OC(CH_{3})_{3}$$

$$I \qquad R = R' = CH_{3} \qquad XXIV \qquad R = R' = CH_{3}$$

$$XXIII \qquad R = R' = H \qquad XXV \qquad R = R' = H$$

The major difference in the fate of these two radicals (I and XXI) is that XXI leads to considerable dimer formation (coupling of rearranged radical XXII) while I does not. This is not surprising in view of the relatively long life expected for the tertiary benzylic radical XXII.

Experiments in which radical I was generated by triphenyl tin hydride reduction of 4-chloro, and 4-bromo-3,3-dimethyl-2-butanone (31) established that a 0.55M concentration of the stannane was sufficient to intercept over 95% of I before rearrangement to III. This result was not completely unexpected since Wenkert <u>et al.</u> (32) recently reported that tri-n-butyltin hydride reacted with 2-dichlormethyl-2-methylcyclohexanone to give 2-chloromethyl-2-methylcyclohexanone.

The rate of acetyl rearrangement (i.e. $I \rightarrow III$) can be roughly estimated from the known absolute rate constant for hydrogen abstraction from triphenyl tin hydride by t-butyl radicals at 25° (k = $5 \times 10^{6} M^{-1} sec^{-1}$). Since the present work involves hydrogen abstraction by primary alkyl radicals at 132° this rate value represents a lower limit for hydrogen abstraction and consequently a probable upper limit for acyl rearrangement. Thermal decomposition of t-butyl perlevulinate (V) in diphenyl ether or triglyme proceeded smoothly at 130-132° and yielded methyl ethyl ketone as one of the major volatile products. Unexpectedly, no trace of the corresponding cage recombination product [4-t-butoxy-2-butanone (XXV)] could be found. The addition of authentic keto ether to the product mixture clearly established that this compound would have been detected had it been present. The elimination product, methyl vinyl ketone, was also absent, but would probably have polymerized under the reaction conditions.

The almost negligible rearrangement observed during decomposition of deuterium labeled t-butylperlevulinate constitutes one of the most important facts revealed by this study. In order to grasp the implications of this result, it is necessary to first consider three plausible mechanisms for 1,2-acyl shifts to radicals (Scheme 1). The first



Scheme 1

mechanism (A) is a two step process involving fragmentation to an olefin and an acetyl radical followed by a fast recombination step; the second mechanism (B) proceeds in two steps through a cyclopropoxy radical intermediate; and the third mechanism (C) is a single step process, having extensive odd electron delocalization in the transition state.

Fragmentation-recombination mechanisms have been proposed for some 1,2-bromo shifts (22b) and for the rearrangement of the camphenyl radical (4). The latter rearrangement required a high temperature (255-290°), and was aided by the bicyclic nature of the substrate which prevented the fragments from drifting apart. Because of the lower temperature employed in the present study and because no evidence of fragment separation was obtained, it is unlikely that the acyl rearrangements proceed by mechanism A. The most damaging argument against this mechanism, however, is that if such a fragmentation-recombination process were to operate when R_1 and R_2 are alkyl or aryl substituents it should continue to function when R_1 and R_2 are hydrogen or deuterium atoms. Thus, the very limited rearrangement observed in the latter case is inconsistent with mechanism A.

Mechanism B appeared at first to be the most reasonable pathway for the acyl rearrangements studied here, since it parallels similar mechanisms proposed for the rearrangement of aryl and vinyl groups (e.g. 9, 12, 13). However, an argument related to that used against mechanism A also damages the credibility of mechanism B. The formation of the cyclopropoxy radical intermediate is the key step in mechanism B. Cyclopropoxy radicals are known to undergo rapid (almost concerted) ring opening to Υ -keto radicals (33); consequently, once the cyclopropoxy radical has formed rearrangement is assured. This first step should not,

however, be seriously affected by variations in R_1 and R_2 . In other words the increase in radical stability, occurring as a result of rearrangement when R_1 and R_2 are alkyl or aryl substituents, should not greatly influence the formation of the cyclopropoxy intermediate. As noted previously, the experimental results do not agree with this conclusion.

The only mechanism (Scheme 1) that clearly predicts the influence of R_1 and R_2 on the extent of acyl rearrangement is C. Because of the delocalization of the unpaired electron in the transition state, it is possible for the stability of the rearranged radical to modulate the activation energy of the rearrangement. When R_1 and R_2 are hydrogen or deuterium, the rate of rearrangement is so slow that it cannot compete with hydrogen abstraction from solvent or substrate. When R_1 and R_2 are alkyl or aryl groups, the rate of rearrangement is increased to such an extent that it occurs to the exclusion of any direct hydrogen abstraction, except for the special case in which triphenyl tin hydride was added.

EXPERIMENTAL

I. General

Melting Points

Melting points were determined with a Hoover "Uni-Melt" melting point apparatus and are uncorrected. All melting points were obtained in open capillaries and are recorded in degrees centigrade.

Spectra

Infrared spectra were obtained with a Perkin-Elmer 237B grating spectrophotometer. Proton magnetic resonance spectra were measured with a Varian Model A-60 or a Varian Model HA-100 high resolution spectrometer. All nmr spectra were recorded using tetramethylsilane as an internal standard. The mass spectra were obtained with a Hitachi Perkin-Elmer Model RMU-6 spectrometer.

Gas Chromatography

Vapor phase chromatographic analyses were performed with a Varian Aerograph A-90P3 chromatograph or a Varian Aerograph 1200 chromatograph. Preparative work was carried out with the Varian Aerograph A-90P3 chromatograph. Relative peak areas were determined by the triangulation method.

Elemental Analysis

All elemental analyses were performed by the Spang Microanalytical Laboratory, Ann Arbor, Michigan.

II. Syntheses

A. General Perester Preparation Method

The l,l'-carbonyldiimidazole was dissolved in dry tetrahydrofuran, distilled directly into the reaction flask, and an equimolar amount of the levulinic acid in tetrahydrofuran was added dropwise to the stirred solution. Gas evolution ceased after ca. thirty minutes, and following a one hour interval, an equimolar amount of freshly distilled t-butyl hydroperoxide was added dropwise with stirring. The reaction mixture was stirred at ambient temperature for two days, following which the solvent was removed under vacuum, keeping the temperature below 50° .

The residue was taken up in ethyl ether and washed successively with ice cold 10% H₂SO₄, ice cold 10% Na₂CO₃, and water. The ether solution was dried (MgSO₄) and concentrated under vacuum, and the residue was held under vacuum overnight to remove any residual t-butyl hydroperoxide. Distillation under high vacuum yielded the perester in yields ranging from 40% to 60%.

B. Preparation of t-Butylperlevulinate

1.8g (11.1 mmole) of 1,1'-Carbonyldiimidazole, 1.3g (11.2 mmole) of freshly distilled levulinic acid, and 1.0g (11.1 mmole) of freshly distilled t-butyl hydroperoxide were combined according to the general procedure outlined above. Distillation afforded 0.99g (53%) of t-butylperlevulinate: bp 79-80⁰ (0.001mm); ir (Figure 4) 2970, 1775, 1720, 1368, 1185, 1110, and 825cm^{-1} ; nmr (Figure 5) τ 8.73 (s, 9H), 7.88 (s, 3H), τ 7.42 (q, 4H); 2,4-dinitrophenylhydrazone, mp 135⁰, parent ion at m/e 368 in the mass spectrum.



Figure 4. Infrared spectrum of t-butylperlevulinate (neat).





Anal. Calcd for
$$C_{15}H_{20}N_4O_5$$
: C, 48.91; H, 5.47; N, 15.21
Found: C, 48.84, H, 5.43; N, 15.17

C. Preparation of t-Butylperlevulinate- \underline{d}_5

1. Preparation of Levulinic Acid-d5

28.8g (0.2 mole) Ethyl levulinate was mixed with 30g (0.22 mole) potassium carbonate dissolved in 100ml D_2^0 and refluxed for forty-eight hours under a nitrogen atmosphere. The mixture was then concentrated under vacuum and fresh D_2^0 was added to the residue. After refluxing an additional twelve hours methylene chloride was added to the cooled mixture which was then carefully neutralized (concentrated HCl) with stirring and cooling. The aqueous layer was extracted several more times with methylene chloride and the combined extracts were dried (MgSO₄) and concentrated, affording 24.3g (100%) of levulinic acid-<u>d</u>₅.

2. <u>Preparation of t-Butylperlevulinate-d₅</u>

Reaction of 23.7g (0.193 mole) levulinic acid- \underline{d}_5 , 32g (0.197 mole) 1,1'-carbonyldiimidazole, and 17.4g (0.193 mole) of t-butylhydroperoxide was accomplished as described and afforded 22g (59%) t-butylperlevulinate- \underline{d}_5 : bp 84-85⁰ (.001mm); ir (Figure 6) 2985, 1775, 1705, 1370, 1105, and 850cm⁻¹; nmr (Figure 7) τ 7.56 (s, 1.95H), and τ 8.76 (s, 9H); 2,4dinitrophenylhydrazone mp 134⁰ and parent ions at m/e 368 (0.6%), 369 (1.2%), 370 (2.6%), 371 (6.7%), 372 (23.5%), 373 (41.6%), 374 (17.9%), and 375 (5.9%) in the mass spectrum.



Figure 6. Infrared spectrum of t-butylperlevulinate- \underline{d}_{6} (neat).





D. Preparation of t-Butyl-3,3-dimethylperlevulinate

1. Preparation of 3,3-Dimethyllevulinic Acid

Employing the procedure of Baumgarten and Gleason (28) 1,1-dimethylsuccinic acid was successively converted to its anhydride; 1,1-dimethyl-2-carbethoxypropionic acid; 1,1-dimethyl-2-carbethoxypropionyl chloride; ethyl-5-(bis-carbethoxy)-3,3-dimethyllevulinate; ethyl-3,3-dimethyllevulinate; and finally to 3,3-dimethyllevulinic acid.

2. Preparation of t-Butyl-3,3-dimethylperlevulinate

Reaction of 16.6g (0.115 mole) of 3,3-dimethyllevulinic acid, 10.7g (0.119 mole) of t-butylhydroperoxide, and 18.65g (0.115 mole) of 1,1'carbonyldiimidazole was effected in 200ml of tetrahydrofuran and gave 10.8g (40%) of t-butyl-3,3-dimethylperlevulinate: bp 93-94⁰ (200μ); ir (Figure 10) 2980, 1770, 1700, 1355, 1080, and $850cm^{-1}$; nmr (Figure 11) τ 7.43 (s, 2H), 7.88 (s, 3H), 8.73 (s, 9H), and τ 8.79 (s, 6H); 2,4-dinitrophenylhydrazone, mp 121-122⁰, parent ion at m/e 396 in the mass spectrum.

Anal. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10; N, 14.13 Found: C, 51.64; H, 6.13; N, 14.20.

E. Preparation of 2-Butanone-d₅

7.2g (0.1 mole) 2-Butanone was mixed with 12ml D_2^0 and 0.1g $K_2^{CO}_3$, refluxed for seven days under a nitrogen blanket, and then concentrated under vacuum. The residue was taken up in 12ml D_2^0 and refluxed two more days under nitrogen. A portion of the mixture was separated on the vapor phase chromatograph: parent ions at m/e 75 (2.82%), 76 (11.27%),



Figure 8. Infrared spectrum of 3,3-dimethyllevulinic acid (neat).

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Figure 10. Infrared spectrum of t-buty1-3,3-dimethy1perlevulinate (neat).





77 (81.69%), and 78 (4.23%); 2,4-dinitrophenylhydrazone, mp 112-113°.

F. Preparation of 4-Bromo-3,3-dimethyl-2-butanone

1. Preparation of Ethyl-3-keto-2,2-dimethylbutanoate

Employing the procedure of Marshall and Cannon (34), 2.67g (0.11)mole) of NaH was mixed with 40ml dry benzene and 40ml azeotropically dried dimethylformamide. Then 17.4q (0.11 mole) of ethylacetoacetate was added dropwise and stirred one hour. 13.2g (0.093 mole) of Methyl iodide was introduced dropwise and the reaction mixture was heated on the steam bath for three hours and stirred at ambient temperature overnight. Ethanol was added to destroy excess sodium hydride and was followed by addition of 50ml water. The two layers were separated, the water layer was acidified, and the aqueous layer was extracted several times with ethyl ether. The ether extracts were combined with the benzene, water washed, dried $(MgSO_4)$, and concentrated. The residue was reacted as before with the exception that the aqueous layer was adjusted to a basic pH. Distillation of the reaction product afforded 9.7q (56%) of ethyl-3-keto-2,2-dimethylbutanoate: bp 34-35° (0.5mm); ir (Figure 12) 1715, 1265, 1120, and 1155cm⁻¹; nmr (Figure 13) τ 5.87 (q, 2H), 7.9 (s, 3H), 8.78 (t, 3H), and τ 8.70 (s, 6H).

2. Preparation of Ethyl-3,3-(ethylenedioxy)-2,2-dimethylbutanoate

130g Ethyl-3-keto-2,2-dimethylbutanoate was mixed with 300ml benzene, 100ml ethylene glycol, and 0.1g p-toluene sulfonic acid, and then refluxed for thirty-six hours. Water was removed from the reaction mixture by means of a Dean-Stark trap. Distillation of the



Figure 12. Infrared spectrum of ethyl-3-keto-2,2-dimethylbutanoate (neat).







Figure 14. Infrared spectrum of ethyl-3,3-(ethylenedioxy)-2,2-dimethylbutanoate (neat).





reaction mixture afforded 159.9g (91%) of ethyl-3,3-(ethylenedioxy)-2,2-dimethylbutanoate: bp 98-100° (14mm); ir (Figure 14) 1720, 1270, 1125, and 1045cm⁻¹; nmr (Figure 15) γ 5.95 (q, 2H), 6.12 (s, 4H), 8.72 (s, 3H), 8.80 (t, 3H), and γ 8.82 (s, 9H).

3. Preparation of 3-Keto-2,2-dimethylbutanol

6.45g (0.27 mole) Lithium aluminum hydride was mixed with 150 ml of tetrahydrofuran that had been freshly distilled. The mixture was chilled, 62.5g (0.31 mole) of ethyl-3,3-(ethylenedioxy)-2,2-dimethylbutanoate was added dropwise, and then the reaction was refluxed for two days. After cooling, 7 ml water was added followed by 7 ml 15% NaOH and 21 ml water. The resulting white solid was filtered and washed several times with ethyl ether. The ether was combined with the tetrahydrofuran filtrate, dried $({\rm MgSO}_4)\,,$ and concentrated on the rotary evaporator. The residue was stirred overnight in a 50:50 mixture of acetone and water containing a catalytic amount of acid, and then this solution was extracted several times with methylene chloride. The extracts were washed successively with water, $10\%NaCO_3$, and water, dried (MgSO₄), and concentrated. Distillation of the residue afforded 32.1g (88%) of 3-keto-2,2-dimethylbutanol: bp 78-79° (14mm); ir (Figure 16) 3400, 2950, 1710, 1475, 1375, 1120, and 1035 cm^{-1} ; nmr (Figure 17) 7 5.82 (s, 1H), 6.53 (s, 2H), 7.91 (s, 3H), and **7** 8.92 (s, 6H).

4. Preparation of 3-Keto-2,2-dimethyl-butyl tosylate

31.0g (0.267 mole) 3-Keto-2,2-dimethylbutanol was added dropwise as a solution in 60 ml pyridine to a solution of 67g (0.351 mole) p-toluenesulfonyl chloride in 60 ml pyridine. The mixture was stirred for forty-



Figure 16. Infrared spectrum of 3-keto-2,2-dimethylbutanol (neat).





Figure 18. Infrared spectrum of 3-keto-2,2-dimethylbutyl tosylate (neat).





eight hours, poured into a mixture of ice and water, and extracted several times with methylene chloride. The combined extracts were washed successively with cold 10% H_2SO_4 , cold 10% $NaCO_3$, and water, dried (MgSO_4), and concentrated. The resulting oil crystallized from pentane affording 43.3g (82.5%) 3-keto-2,2-dimethyl-butyl tosylate: mp 56°; ir (CCl_4) (Figure 18) 2950, 2800, 1710, 1600, 1360, 1245, 1175, 1100, 975, 850, 745, and 730cm⁻¹; nmr (CCl_4) (Figure 19) τ 2.50 (q, 4H), 6.09 (s, 3H), 7.53 (s, 2H), 7.96 (s, 3H), and τ 8.91 (s, 6H). Anal. Calcd for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71 Found: C, 57.72; H, 6.53

5. Preparation of 4-Bromo-3,3-dimethyl-2-butanone

In the manner of Leriverend and Conia (35), 35.6g (0.132 mole) of 3-keto-2,2-dimethylbutyl tosylate, 73g (0.84 mole) of lithium bromide, and 500 ml of 2-butanone are refluxed for forty-eight hours. The mixture is cooled, filtered, poured into water, and extracted several times with ethyl ether. The combined ether extracts are dried (MgSO₄) and concentrated. Distillation of the residue afforded 23.5g (95%) of 4-bromo-3,3-dimethyl-2-butanone: bp 79° (18mm); ir (Figure 20) 2980, 1705, 1470, 1350, 1248, and 1150cm⁻¹; nmr (Figure 21) τ 6.48 (s, 2H), 7.84 (s, 3H) and τ 8.76 (s, 6H); parent ions at m/e 178 and 180 in the mass spectrum.

G. Preparation of 4-Chloro-3,3-dimethyl-2-butanone

Employing the procedure of DePuy, et al. (36), mesityl oxide was reacted with hydrazine hydrate to give 3,5,5-trimethyl-2-pyrazoline. This pyrazoline was reacted with lead tetraacetate to afford 3-acetoxy-3,5,5-trimethyl-l-pyrazoline, which was thermally decomposed to 1,2,2-



Figure 20. Infrared spectrum of 4-bromo-3,3-dimethyl-2butanone (neat).







Figure 22. Infrared spectrum of 4-chloro-3,3-dimethyl-2butanone (neat).





trimethyl-cyclopropyl acetate in quantitative yield. This cyclopropyl acetate led to 1,2,2-trimethyl-cyclopropanol which was cleaved to the desired 4-chloro-3,3-dimethyl-2-butanone by the action of t-butyl-hypochlorite: bp 25° (0.5mm); ir (Figure 22) 2980, 1710, 1470, 1355, 1105, and 765cm⁻¹; nmr (Figure 23) τ 8.78 (s, 9H), 7.84 (s, 3H), and τ 6.37 (s, 2H); parent ions at m/e 134 and 136 in the mass spectrum.

H. Preparation of Triphenyltin Hydride

Utilizing the method of Kuivila and Beumel (37), 1.56g (40.9 moles) of lithium aluminum hydride and 38.5g (100 mmoles) of triphenyltin chloride were added to 150ml of cold, anhydrous ether. The mixture was stirred at ice bath temperatures for 15 minutes, at room temperature for three hours, and then was slowly hydrolyzed with 100ml of water. The ether layer was separated, washed with two 100ml portions of ice-water, dried (MgSO₄), and distilled. The triphenyltin hydride was distilled, using an oil bath preheated to 200°, with varying yields (77-85%).

III. Thermal Decomposition Procedure

A. In Phenyl Ether

1. Purification of Phenyl Ether

Phenyl ether was washed with 10% KOH, followed by a saturated NaCl solution, and then dried over anhydrous sodium sulfate. Distillation afforded 99.9% pure ether (v.p.c.). When this solvent was heated to 200° for five hours while being flushed by a slow nitrogen stream, no volatile substances were collected in dry ice-cooled traps.

2. Reaction and Analysis Procedure

The reaction apparatus consisted of a three-necked flask equipped with a magnetic stirring bar, a serum cap, and gas entrance and exit tubes. The exit tube was connected to two dry ice-isopropanol traps in series by tygon tubing. The cold traps were in turn connected to a tared, ascarite filled "U" tube which was equipped with ground glass valves. A gas flow detector terminated the exit stream.

The entrance tube to the round-bottom flask was connected to a source of dry, CO_2 free, nitrogen. This consisted of a tank of purified nitrogen, a drying tower filled with ascarite, a scrubber unit filled with concentrated H_2SO_4 , and another drying tower filled with alternating layers of KOH and indicating Drierite.

Most of the phenyl ether was added to the reaction flask which was then lowered into a preheated oil bath. The system was purged with nitrogen and then connected to the weighed ascarite tube. The perester was dissolved in the remainder of phenyl ether and rapidly introduced into the flask by injection through a serum cap.

After several hours reaction time, the oil bath was removed and the reaction vessel was immersed in a dry ice-isopropanol bath to quench the pyrolysis. After warming to ambient temperature, the reaction mixture was then analyzed for unreacted perester by the method of Silbert and Swern (29). In this procedure an aliquot of the pyrolysis solution was dissolved in chloroform, saturated sodium iodide solution was added along with 0.002% FeCl₃·6H₂O in glacial acetic acid, and the mixture was kept in the dark for ten minutes. Water was then added to the flask and the mixture was titrated to a starch endpoint using standard thiosulfate solution. Magnetic stirring was necessary in this titration.

The carbon dioxide evolved during the perester pyrolysis was determined by weighing the ascarite trap.

Volatile materials condensed in the dry ice traps were weighed and analyzed by vapor phase chromatography, 20% SE-30, six foot column. Most of the acetone and t-butyl alcohol formed in the reaction were found here.

Fractional distillation of the pyrolysis mixture at reduced pressure (ca. lmm) using a spinning band column was continued until most of the solvent had distilled. The first two fractions (ca. 3ml) contained additional volatile reaction products (v.p.c. analysis), but the remaining fractions were greater than 99% pure phenyl ether. These volatile products were identified by comparing their retention times with those of known compounds and from the ir, nmr, and mass spectra of samples trapped by vapor phase chromatography.

The residue from the distillation was examined by vapor phase chromatography and partition chromatography on silica gel. The major components other than phenyl ether proved to be substituted phenyl ether. These were collected and examined by spectroscopic methods.

B. In Triglyme

1. Purification of Triglyme

Triglyme was dried over magnesium sulfate and distilled from lithium aluminum hydride. The first fraction contained glyme and diglyme and was discarded; however, the higher fractions were greater than 99% pure by v.p.c. analysis. When the purified triglyme was heated to 150° for several hours in a nitrogen stream, only a trace of volatile material was collected in a dry ice-cooled trap.

2. Analysis and Reaction Procedure

The reaction apparatus and procedure was the same as that for phenyl ether.

C. In Sealed Ampoules

A benzene solution containing 1.5 equivalents triphenyltin hydride, 1.0 equivalents 4-halo-3,3-dimethyl-2-butanone, and 3-5 mole percent di-t-butylperoxide was placed in an ampoule made by drawing out a four inch Pyrex test tube. The ampoule was attached to a vacuum system and degassed as follows: (1) The ampoule was slowly inserted into a liquid nitrogen bath. (2) The cooled ampoule was evacuated. (3) The ampoule was allowed to warm to ambient temperature. This process was repeated three times following which the ampoule was sealed while under vacuum. An oil bath was preheated to 130° and the sealed ampoule was suspended in the oil bath for thirty-six to forty-eight hours. At the end of this time the ampoule was removed and cooled. After the cooled ampoule was opened, the contents were analyzed by v.p.c The v.p.c. column was disconnected from the detector immediately after being used, steam washed several times at 150°, and left overnight with gas flowing through the column. If this procedure was not followed, the detector became contaminated.
IV. Identification of Reaction Products

A. Identification of 2-Butanone-<u>d</u>5

The 2-butanone- \underline{d}_5 separated from the t-butylperlevulinate- \underline{d}_5 pyrolysis products by v.p.c. was collected as a CCl₄ solution in an nmr tube. This solution was compared with a CCl₄ solution of synthetically prepared 2-butanone- \underline{d}_5 by nmr spectroscopy and parent ions at m/e 74 (1.55%), 75 (7.22%), 76 (23.71%), 77 (45.36%), 78 (18.04%), and 79 (4.12%) were present in the mass spectrum.

B. Identification of 3,3-Dimethy1-2-butanone

The major product from the reaction of 4-bromo-3,3-dimethyl-2butanone with triphenyltin hydride was analyzed by nmr and ir spectroscopy. These spectra were identical with those from authentic 3,3-dimethyl-2butanone.

C. Identification of 4-Methyl-2-pentanone

The volatile products from thermal decomposition of t-butyl-3,3dimethylperlevulinate were separated by v.p.c. on a 20% SE-30 column. The major product, with a retention time identical to 4-methyl-2pentanone, was passed into a 2,4-dinitrophenylhydrazine solution, and the solid derivative was isolated and purified. A mixed melting point with the 2,4-dinitrophenylhydrazone of authentic 4-methyl-2-pentanone (mp 93-94°) was not depressed.

D. Identification of 4-t-Butoxy-3,3dimethyl-2-butanone (XXIV)

The largest concentration of this compound was found in the first fraction from the spinning band distillation. This fraction was separated by v.p.c. on a 20% SE-30 column and the very volatile keto ether was collected by passing into CCl_4 or a 2,4-dinitrophenylhydrazine solution. The properties of this substance--ir (Figure 2) 2960, 1710, 1365, 1195, 1080, and 980cm⁻¹; nmr (CCl_4) (Figure 3) γ 6.75 (s, 2H), 7.95 (s, 3H), 8.84 (s, 9H), and γ 8.91 (s, 6H); and its 2,4-dinitrophenylhydrazone derivative, mp 115-116°, parent ion at m/e 352 in the mass spectrum--are consistent with the assigned structure.

Anal. Calcd. for $C_{16}H_{24}N_4O_5$: C, 54.54; H, 6.90; N, 15.90 Found: c, 54.74; H, 6.97; N, 16.06.

An nmr comparison (Table IV) of 4-t-butoxy-2-butanone (XXV) and 4-t-butoxy-3-phenyl-3-methyl-2-butanone (18) supports the assignment of resonance signals made in this case.

	TABLE IV		
NMR Chemical Shifts (7) of CH ₃ -CO-CR ₁ R ₂ -CH ₂ -OC(CH ₃) ₃			
(a) (b) (c) (d)			
Position	$R_1 = R_2 = H$	$R_1 = R_2 = CH_3$	$R_1 = CH_3, R_2 = \emptyset$
(a)	7.92	7.95	8.10
(b)	7.50	8.91	8.53 2.77
(c)	6.44	6.75	6.25
(d)	8.85	8.84	8.87

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