When oximation of the protio ketones was carried out in the absence of primary amines, *N*-methylmorpholine buffers were used over the pH range 6.2–8.6, trimethylamine buffers over the range 8.8–10.2, and triethylamine buffers over the range 10.5–11.2. *N*-Ethylmorpholine buffers were used in all the 3-pentanone-d_4 runs and in the cyclopentanone-d_4 runs from pH 6.2 to 8.7. From pH 8.9 to 10.8 (2-hydroxyethyl)diisopropylamine buffers were used for cyclopentanone-d_4. Total buffer concentrations were 0.10 M except for the three runs where 0.05 M buffer was used to test for general catalysis. Fourteen runs were made on 3-pentanone-d_4, and more than 20 were made on each of the other three ketones.

In the absence of primary amines, second-order rate constants (k_2) for oximation were obtained from eq 7, in which c is defined

$$A_t = \frac{c(A_0 - A_\infty)}{[\mathrm{Hx}]_{t_0} \exp(ck_2t) - [\mathrm{K}]_0} + A_\infty \quad (7)$$

in eq 8. All values of the absorbance at time t (A_t) were weighted

$$c = [\mathrm{Hx}]_{t_0} - [\mathrm{K}]_0 \quad (8)$$

equally in the nonlinear least-squares treatment,[10] which gave initial and infinite absorbance values (A_0 and A_∞) as well as the rate constant. The molar absorbances of the ketone and oxime (ϵ_K and ϵ_{Ox}) and the initial total concentration of hydroxylamine in both states of protonation ($[\mathrm{Hx}]_{t_0}$) were taken as knowns. Equations 9 and 10 were assumed for the absorbances, with Δ

$$A_0 = \epsilon_K[\mathrm{K}]_0 + \Delta \quad (9)$$

$$A_\infty = \epsilon_{Ox}[\mathrm{K}]_0 + \Delta \quad (10)$$

being a factor to allow for imperfectly matched cells, machine drift, etc. In the first iteration of the nonlinear least-squares treatment Δ was set equal to zero and $[\mathrm{K}]_0$ treated as a known. In subsequent iterations a value of Δ was calculated from the A_∞ value obtained with eq 10, and then a $[\mathrm{K}]_0$ value was calculated from eq 9. A value of c was then obtained from eq 8. The observed rate constant k_2 was transformed to k_{Ox}, the second-order rate constant for the reaction of the ketone with free hydroxylamine, by use of eq 11. To obtain values of k_H, k_h, and k_w, we transformed eq

$$k_{Ox} = k_2[\mathrm{Hx}]_t/[\mathrm{Hx}] \quad (11)$$

3 to the logarithmic form (eq 12) and each log k_{Ox} value was weighted equally in the least-squares treatment.[10]

$$\log k_{Ox} = \log (k_H[\mathrm{H}^+] + k_h[\mathrm{OH}^-] + k_w) \quad (12)$$

For primary-amine-catalyzed oximation, eq 13 was used, with

$$A_t = \frac{(k_1 + k_2c)(A_0 - A_\infty)}{(k_1 + k_2[\mathrm{Hx}]_{t_0}) \exp[(k_1 + k_2c)t] - k_2[\mathrm{K}]_0} + \epsilon_{Ox}[\mathrm{K}]_0 + \Delta \quad (13)$$

k_1 as defined in eq 14. From the values of k_H, k_h, and k_w obtained

$$k_1 = k_{lm}[\mathrm{Am}]_t \quad (14)$$

in the absence of primary amines, k_{Ox} and then k_2 were calculated. The nonlinear least-squares treatment[10] gave values for Δ, $[\mathrm{K}]_0$, and k_1. From these values, improved values of $A_0 - A_\infty$ were calculated iteratively. The average value of Δ obtained was about 0.015, and no value was larger than 0.08. The standard deviations of the calculated from the experimental absorbance values averaged about 0.001 and never exceeded 0.005.

Registry No. 3-Pentanone, 96-22-0; cyclopentanone, 120-92-3; butylamine, 109-73-9; *endo*-2-norbonylamine, 31002-73-0; *N,N*,2,2-tetramethyl-1,3-propanediamine, 53369-71-4; *N,N*-dimethyl-1,3-propanediamine, 109-55-7; 3-methoxy-1-propanamine, 5332-73-0; *N,N*-dimethylethanediamine, 108-00-9; 2-methoxyethanamine, 109-85-3; protonated *N,N*-dimethyl-1,3-propanediamine, 61507-91-3; protonated *N,N*,2,2-tetramethyl-1,3-propanediamine, 71171-48-7; protonated *N,N*-dimethyl-1,2-ethanediamine, 51380-72-4; hydroxylamine, 7803-49-8; *N*-ethylmorpholinium, 57133-80-9; *N*-(2-hydroxyethyl)-*N,N*-diisopropylammonium ion, 71171-49-8; (2-methoxyethyl)ammonium ion, 54005-66-2; (3-methoxypropyl)ammonium ion, 54005-67-3.

Carbon-13 Study of Oxygen Function Rearrangement in the Acid-Catalyzed Rearrangement of 2,2,4-Trimethyl-3-pentanone-3-^{13}C to 3,3,4-Trimethyl-2-pentanone-3-^{13}C[1a]

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The acid-catalyzed rearrangement of 2,2,4-trimethyl-3-pentanone-3-^{13}C, **1b**, affords, as predicted, rearranged 3,3,4-trimethyl-2-pentanone-2-^{13}C, **2b**, and, in lesser amounts, its isotopic isomer 3,3,4-trimethyl-2-pentanone-3-^{13}C, **2c**. In addition, an isotopic isomer of **1b**, 2,2,4-trimethyl-3-pentanone-2-^{13}C, **1c**, is formed in small amounts. Measurements of the amount of this oxygen function rearrangement were carried out by using ^{1}H NMR ^{13}C satellite and direct ^{13}C NMR techniques, and the utility of these techniques compared to carbon-14 methods is discussed. The mechanisms of these rearrangements are discussed in terms of competing alkyl shifts and oxygen function rearrangements in the ketone conjugate acids and carbocations derived from them.

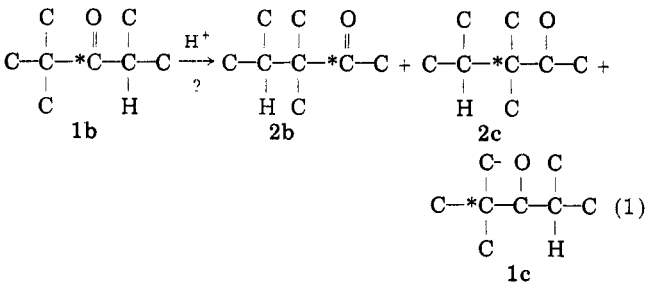
Acid-catalyzed ketone rearrangements[2] sometimes involve oxygen function rearrangements[3] (OFR) such as would be required in the formation of **2c**, 3,3,4-trimethyl-2-pentanone-3-^{13}C, and **1c**, 2,2,4-trimethyl-3-pentanone-2-^{13}C, from **1b**, 2,2,4-trimethyl-3-pentanone-3-^{13}C (the natural-abundance molecules are designated **1a**, **2a**, etc., and labeled isotopic isomers are designated **1b**, **1c**, etc.; *C = ^{13}C):

(1) (a) Taken from the Ph.D. dissertation of M.O., University of Arkansas, 1973; presented in part at the 2nd Rocky Mountain Regional Meeting of the American Chemical Society, Albuquerque, N.M., July 8–9, 1974. A brief summary of this work appears in ref 5. (b) Address correspondence to this author at California State Polytechnic University, Pomona, Calif. 91768.

(2) For a review, see A. Fry, *Mech. Mol. Migr.*, 4, 113 (1971).

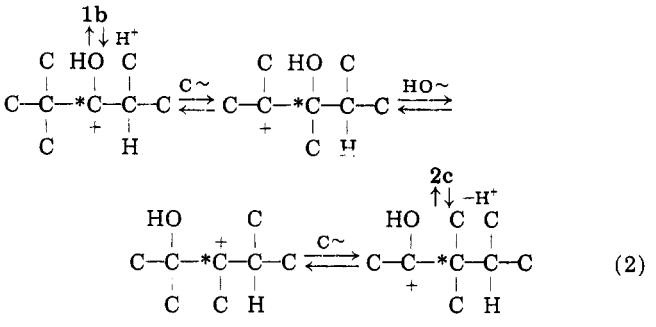
(3) A. Fry, W. Carrick, and C. Adams, *J. Am. Chem. Soc.*, 80, 4743 (1958), and other research cited in ref 2.

0022-3263/79/1944-3545$01.00/0



(1)

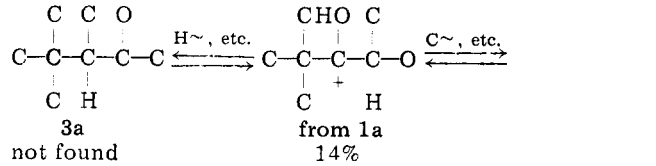
Several mechanisms have been suggested for these oxygen function rearrangements,[2] the simplest involving sequential alkyl, hydroxyl, alkyl shifts in the ketone conjugate acids:

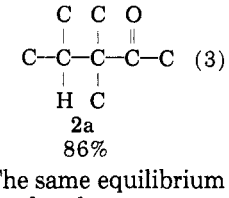


(2)

In evaluating the scope of the oxygen function rearrangement, it was predicted[2,4] that all α-disubstituted ketones should show it, and the case studied here, **1b** $\xrightarrow{?}$ **2c** + **1c**, is a test of that prediction. All previous OFR studies[2] have used carbon-14 as the tracer atom, in which the position of the labeled atom in the product could be determined only by laborious and time-consuming degradative procedures. Our research demonstrates the utility of ^{13}C NMR and ^{1}H NMR ^{13}C satellite spectroscopy[5] for such tracer studies.

Rearrangement of Unlabeled 2,2,4-Trimethyl-3-pentanone. Preliminary experiments on the rearrangement of unlabeled 2,2,4-trimethyl-3-pentanone, **1a** (concentrated sulfuric acid, 2 h, 70 °C, GLC analysis and separation, ^{1}H NMR analysis), showed the presence of only starting material (14%) and 3,3,4-trimethyl-2-pentanone, **2a** (86%), and no 3,4,4-trimethyl-2-pentanone, **3a** (esti-





(3)

mated detection limit 0.1%) (eq 3). The same equilibrium mixture of **1a** and **2a** was obtained under the same conditions starting with **2a**. This preferential initial migration of methyl over hydrogen is in accord with earlier studies by Barton and Porter[6] and Zook, Smith, and Green[7] and with the conclusions reached by Brouwer and Van Doorn[8] from their kinetic studies on related compounds.

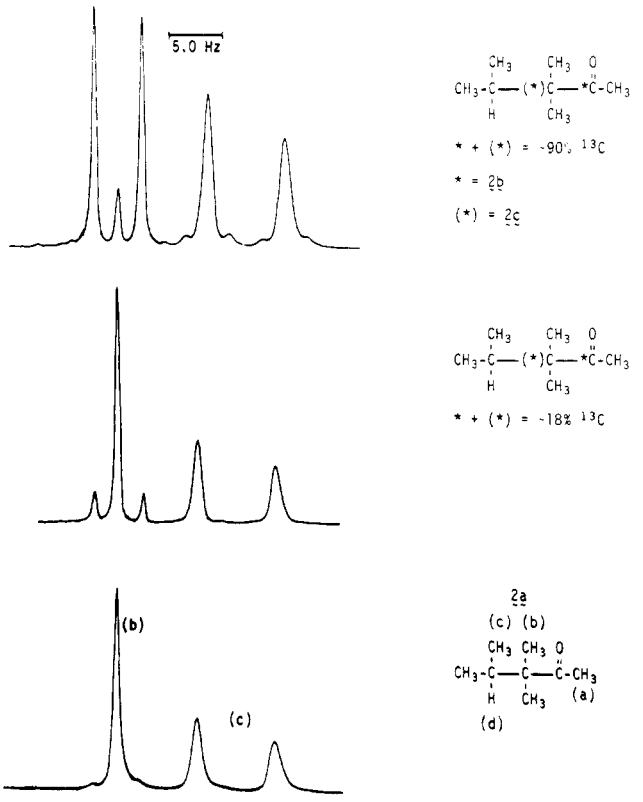


Figure 1. ^{1}H NMR spectra of upfield signals of unlabeled 3,3,4-trimethyl-2-pentanone and of ~18% ^{13}C and ~90% ^{13}C enriched 3,3,4-trimethyl-2-pentanone-x-^{13}C.

Rearrangements of Labeled Compounds. Two rearrangement experiments were carried out with 2,2,4-trimethyl-3-pentanone-3-^{13}C, **1b** (mixed with **1a**), the first at the 18% carbon-13 enrichment level and the second at the 90% enrichment level. Samples of the rearranged ketone mixture (**2a** + **2b** + **2c**) were isolated by preparative GLC for ^{1}H NMR ^{13}C satellite spectral analysis, but the mixture of starting (and rearranged starting) ketone (**1a** + **1b** + **1c**), 14.8%, with rearranged ketone (**2a** + **2b** + **2c**), 85.2%, was used directly for ^{13}C NMR analysis.

^{1}H NMR ^{13}C Satellite Spectral Analysis. Figure 1 shows the upfield ^{1}H NMR spectrum (hydrogens b and c in Figure 1) of unlabeled 3,3,4-trimethyl-2-pentanone (**2a**) together with the corresponding spectra for the enriched ketones (**2a** + **2b** + **2c**) recovered from the rearrangement reactions. In the spectrum from the ~18% enriched material the coupling of the carbon-13 at the carbonyl carbon with the b methyl hydrogens is obvious [$J(^{13}C\text{-}(C{=}O)\text{-}C\text{-}C\text{-}H_b)$ = 4.5 Hz], but (as expected) there is no corresponding splitting of the c methyl hydrogens, so $J(^{13}C(C{=}O)C\text{-}C\text{-}C\text{-}H_c)$ must be ≈0 (any satellites from this coupling should be obvious, since they would comprise ~18% of the total signal). Therefore, in the spectrum from the 90% enriched material, the obvious satellites flanking the main c methyl hydrogen signals must come from isomer **2c** [$J(^{13}C\text{-}C\text{-}C\text{-}H_c)$ = 4.0 Hz], thus confirming that oxygen function rearrangement takes place.[9] The relative amounts of the two isotopic isomers **2b** and **2c**

(4) M. Oka, Ph.D. Dissertation, University of Arkansas, Fayetteville, Ark., 1973.
(5) For a recent review on these techniques, see J. Hinton, M. Oka, and A. Fry, in "Carbon-13 in Organic Chemistry", E. Buncel and C. C. Lee, Eds., Elsevier, Amsterdam, The Netherlands, 1977, Chapter 2, p 41.
(6) S. Barton and C. Porter, *J. Chem. Soc.*, 2483 (1956).
(7) H. Zook, W. Smith, and J. Greene, *J. Am. Chem. Soc.*, **79**, 4436 (1957).
(8) D. M. Brouwer and J. A. Van Doorn, *Recl. Trav. Chim. Pays-Bas*, **90**, 1010 (1971).
(9) Hydrogens a cannot be used to confirm the presence of **2c** since their coupling constants to the carbon-13 at the carbonyl carbon of **2b** [$J(^{13}C(C{=}O)\text{-}C\text{-}H_a)$ = 6.0 Hz] and to the carbon-13 at the other α carbon in **2c** [$J(^{13}C\text{-}C(C{=}O)\text{-}C\text{-}H_a)$ = 4 Hz (estimated)] are so close together that the satellite peaks are not resolved. Hydrogen d suffers from the same type of disadvantage and, in addition, is a low-intensity septet.

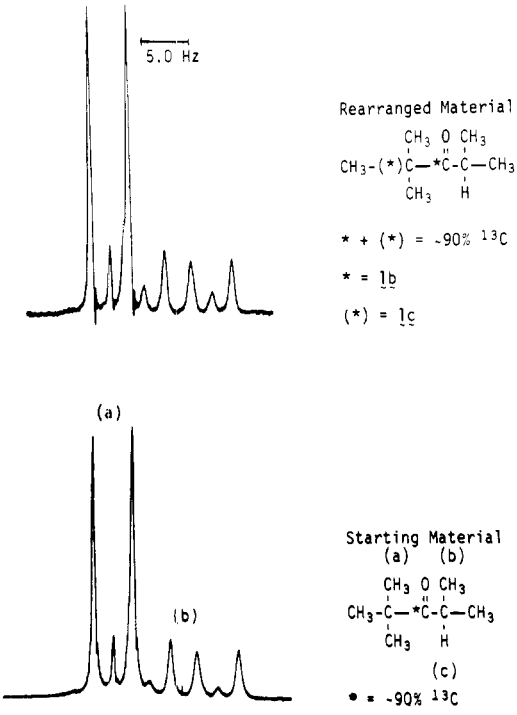
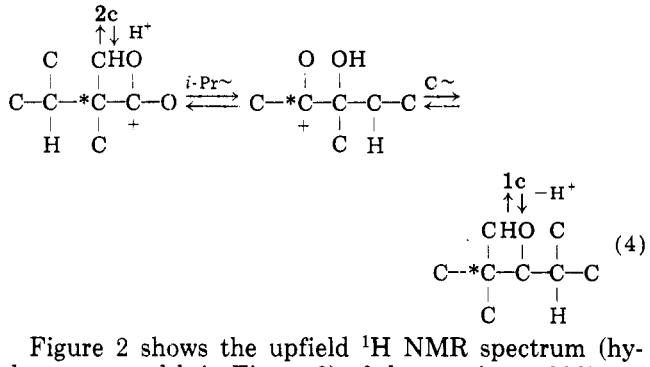


Figure 2. ^1H NMR ^{13}C satellite spectra of ~90% ^{13}C enriched 2,2,4-trimethyl-3-pentanone-3-^{13}C and ~90% ^{13}C enriched 2,-2,4-trimethyl-3-pentanone-x-^{13}C.

were measured (by weighing cut out peaks) to be 93.3 ± ~0.5% and 6.7 ± ~0.5% (**2a**:**2b**:**2c** = 10:84:6) from either the upfield or downfield satellites, assuming no contribution from any carbon-13 natural-abundance satellites. Thus, **1b** rearranges to ~93% **2b** (without OFR) and ~7% **2c** (with OFR).

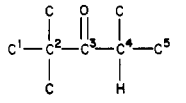
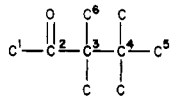
If the oxygen function rearrangement is reversible as shown in eq 2, isomer **1c** should be formed from **2c**:



(4)

Figure 2 shows the upfield ^1H NMR spectrum (hydrogens a and b in Figure 2) of the starting ~90% enriched 2,2,4-trimethyl-3-pentanone-3-^{13}C (**1a** + **1b**), together with that of the 2,2,4-trimethyl-3-pentanone mixture (**1a** + **1b** + **1c**) recovered from the rearrangement experiment. In the starting material, the coupling of the carbon-13 at the carbonyl carbon with both the a [J(^{13}C(C=O)-C-C-H_a) = 4.2 Hz] and b [J(^{13}C(C=O)-C-C-C-H_b) = 4.2 Hz] hydrogens is obvious (the left-hand leg of the b hydrogens doublet of doublets is under the right-hand leg of the a doublet). For isotopic isomer **1c**, by analogy to **2c** and other compounds, it may be assumed that J(^{13}C-C-H_a) ≃ 5 Hz, and J(^{13}C-C(C=O)-C-C-H_b) ≃ 0 Hz. This will make it impossible to resolve the a methyl hydrogens satellite peaks from **1b** and **1c** in the ketone mixture recovered from the rearrangement experiment. However, for the b methyl hydrogens, the presence of **1c** [for which J(^{13}C-C(C=O)-C-C-H_b) ≃ 0 Hz in the recovered ketone mixture] should show up as a *decrease* in the intensity of the satellite peaks due to **1b** relative to the (unchanged from the starting material) intensity of the (central) b hydrogen peaks from **1a**. A casual inspection of Figure 1 shows this to be true. By weighing cut out peaks we determined that the relative amounts of **1b** and **1c** present were 95.5 and 4.5%.

Table I. Carbon-13 Chemical Shifts of 2,2,4-Trimethyl-3-pentanone (1a) and 3,3,4-Trimethyl-2-pentanone (2a)

	chem shift from Me_4Si, ppm					
	C^1	C^2	C^3	C^4	C^5	C^6
 **1a**	24.9 25.1[b]	43.4 43.5[b]	*a* 217.4[b]	32.5	19.0	
 **2a**	23.5	210.0	49.4	32.6	16.1	19.1

[a] Not recorded due to instrumental limitations. [b] Reference 11; original data converted, using $\delta^{Me_4Si} = 192.8 - \delta^{CS_2}$.

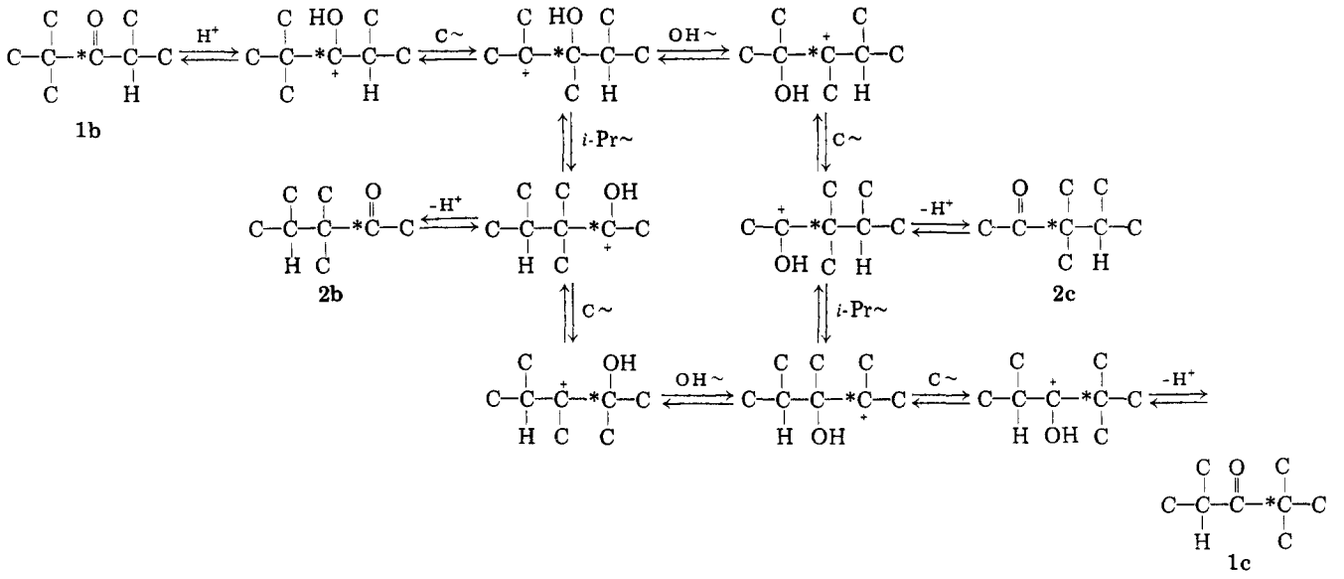
^{13}C NMR Spectral Analysis. Although the major conclusion that OFR does take place in a reversible fashion is clear from the ^1H NMR ^{13}C satellite analyses, the accuracy and precision of the data leave much to be desired compared to those for carbon-14 experiments. Direct ^{13}C NMR measurements on these relatively simple compounds offer the advantage that there is little likelihood of serious overlapping of peaks. This not only makes degradation unnecessary to locate the position of a carbon in a molecule, but also, in many cases, makes it possible to analyze for carbon-13 in a particular position without even separating products and recovered reactants. This is a distinct advantage in the case at hand since the reactant and product ketones have very similar properties and are hard to separate, even by GLC.

The carbon-13 NMR chemical shift assignments for compounds **1a** and **2a**, as given in Table I, are based on selective proton-decoupling experiments and are in agreement with values for analogous ketones[10] and, for some carbons in **1a**, with the reported values.[11]

In the 18% carbon-13 enriched experiment starting with **1a** + **1b**, a sample of the rearranged product ketone (**2a** + **2b** + **2c**) was separated by preparative GLC from the reaction mixture. The carbon-13 NMR spectrum of this sample was compared to the natural-abundance spectrum of the same compound. Most of the ~18% enrichment showed up in a massive increase in the size of the C^2 peak (carbonyl carbon peak—for numbering see formula **2a**, Table I), confirming isomer **2b** as the major product from **1b** (rearrangement without OFR). The presence of isomer **2c** was confirmed by the approximate doubling of the size of the C^3 peak, thus confirming oxygen function rearrangement as a minor path in the conversion of **1** to **2**. From the peak height ratios of C^3/C^1, C^3/C^4, C^3/C^5, and C^3/C^6 of the natural-abundance and ~18% enriched sample spectra, the excess carbon-13 in C^3 was calculated to be 1.6, 1.0, 1.4, and 1.3% (average 1.3%).[12] This

(10) L. F. Johnson and W. C. Jankowski, "Carbon-13 NMR Spectra", Wiley, New York, N.Y., 1972.
(11) L. M. Jackman and D. P. Kelly, *J. Chem. Soc. B*, 102 (1970).
(12) Since only peak height ratios are used in these analysis, it is not necessary to take into account the different Overhauser enhancements for the different carbons, providing these and other instrumental parameters remain constant as the natural-abundance and enriched samples are run in immediate succession.

Scheme I



corresponds to 7.2% rearrangement by the OFR path, which compares well with the 6.7% value calculated above from the ^{1}H NMR carbon-13 satellite data. The quantity of the recovered starting material (now presumably a mixture of **1a**, **1b**, and **1c**) was so small that its ^{13}C NMR spectrum could not be obtained.

In the ~90% carbon-13 enriched experiment starting with **1a** + **1b**, the recovered ketone mixture (**1a** + **1b** + **1c** + **2a** + **2b** + **2c**) was not separated but was analyzed directly by ^{13}C NMR spectroscopy. Figure 3 shows the upfield portion of this spectrum (lower trace), together with the corresponding spectrum (upper trace) of the recovered ketone mixture (**1a** + **2a**) from an identical experiment carried out on natural-abundance material. From Table I it is seen that the chemical shifts of the various carbons in each compound are all different but that C^4 of **1a** and C^4 of **2a** overlap, as do C^5 of **1a** and C^6 of **2a**. Fortunately, the key peaks for detection of OFR, C^2 of **1a** and C^3 of **2a**, are well separated. The spectrum of the labeled material in Figure 3 shows a greatly enhanced signal at C^3 of compound **2**, confirming the presence of the OFR product **2c**, and at C^2 of compound **1**, confirming the presence of isomer **1c** and demonstrating the reversibility of the OFR reaction. (Due to the low concentration, 15%, of **1a** in the natural-abundance material, the C^2 peak of **1a** is lost in the noise.) The same type of peak height analysis as that described above led to a value of 8.5% rearrangement by the OFR path. This value was determined by assuming that the total carbon-13 enrichment is 90% and that the total C^3 signal intensity is made up of the central C^3 peak plus its satellites. These satellites arise from the C^3 signal of isomer **2b**. Since the carbon-13 enrichment at C^2 of **2b** is ~82%, most of the 1.1% natural-abundance carbon-13 atoms at C^3 will be adjacent to carbon-13 atoms at C^2, and the signal due to these C^3 carbon-13 atoms will be split into a satellite doublet, $J(^{13}C\text{–}^{13}C(C{=}O)$ = 40.0 Hz. In a similar way the signal due to the C^1 natural-abundance carbon-13 atoms of **2b** is split into a satellite doublet, $J(^{13}C\text{–}^{13}C(C{=}O)$ = 40.0 Hz. This serves to confirm the high concentration of isomer **2b** and also removes any possible doubt about the assignment of the δ = 23.5 peak to C^1.

The direct observation of isomer **1c** (greatly enhanced signal at C^2 of **1**) confirms the result obtained from the ^{1}H NMR ^{13}C satellite spectral analysis. However, due to the lack of a usable C^2 signal of compound **1** from the natural-abundance spectrum, it was impossible to caluclate the percent of this isomer present by the method used above. A rough estimate can be made by comparing the peak height of C^3 of **2** to C^2 of **1**, assuming equal Overhauser enhancements, and taking into account the ~85/15 ratio of **2**/**1**. This value is 7.5%.

Table II. Percentages of the Isotopic Isomers 1b and 1c and 2b and 2c Obtained from the Rearrangement of 3,3,4-Trimethyl-3-pentanone-3-^{13}C in Concentrated Sulfuric Acid at 70 ± 1 °C

init 1b ^{13}C enrichment, %	^{1}H NMR ^{13}C satellite spectra				^{13}C NMR spectra			
	1b	1c	2b	2c	1b	1c	2b	2c
~18	*a*	*a*	*b*	*c*	*a*	*a*	92.8	7.2
~90	95.5	4.5	93.3	6.7	92.5	7.5	91.5	8.5

[a] The quantity of recovered 1 was so small that the ^{13}C NMR spectrum could not be obtained. [b] Present. [c] No measurement was possible because of the low ^{13}C enrichment.

Results Summary and Mechanistic Discussion

The predictions[2,4] that **1b** should rearrange by a predominant path to **2b** and by a minor path to **2c** and that reversibility of the oxygen function rearrangement should lead to the presence of isomer **1c** are borne out by the experimental results. These results are summarized in Table II. The results from the direct ^{13}C NMR and the ^{1}H NMR ^{13}C satellite analyses are seen to be in acceptable agreement. The simplest stepwise mechanism for these reactions, as shown in Scheme I, involves the relatively fast rearrangement of **1b** to **2b** through their conjugate acids and a tertiary carbocation, in competition with the slower oxygen function rearrangement of **1b** to **2c** (and eventually to **1c**) via the same tertiary cation and isomeric tertiary cations formed by hydroxyl group migrations. Various concerted versions of this scheme could also be envisioned, and other oxygen function rearrangement mechanisms[2,13,14] than hydroxyl group migration are not ruled out. None of the results of the present experiments bear directly on either of these points.

(13) W. H. Corkern and A. Fry, *J. Am. Chem. Soc.*, **89**, 5888 (1967).
(14) K. Bhatia and A. Fry, *J. Org. Chem.*, **34**, 806 (1969).

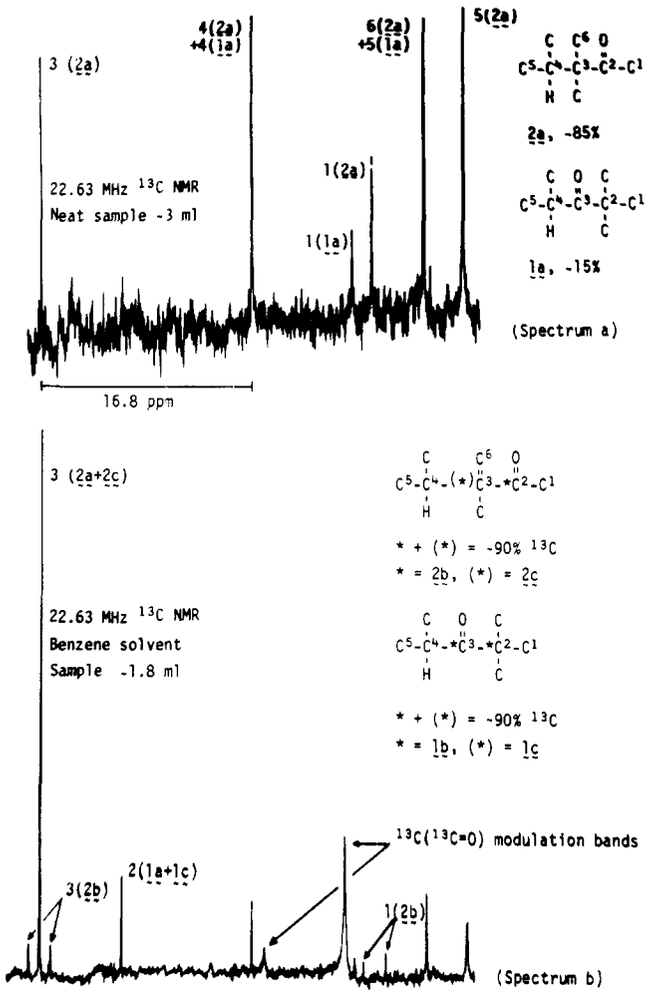


Figure 3. ^{13}C NMR spectra (proton-noise decoupled) of a rearrangement mixture of ~90% ^{13}C enriched 3,3,4-trimethyl-2-pentanone-*x*-^{13}C and 2,2,4-trimethyl-3-pentanone-*x*-^{13}C (spectrum b) and of a similar mixture of the two unenriched ketones (spectrum a).

Equilibration between **1a** and **2a** (equivalent to **1b** and **2b** in Scheme I) has been established in these experiments (14% **1a** and 86% **2a** at equilibrium), but not between **2b** and **2c** or **1b** and **1c** (which would require 50/50 ratios of **2b**/**2c** or **1b**/**1c**, neglecting any isotope effects). This slow OFR compared to alkyl group shifts was demonstrated earlier[14] (about 1:10) in comparative rate studies on 3,3-dimethyl-2-butanone-2-^{14}C and 3,3-dimethyl-2-butanone-1-^{14}C. All other α,α-disubstituted ketones would be expected to show this same behavior, relatively rapid chemical equilibration accompanied by slower OFR.

In the only other all aliphatic α,α-diketone case studied, Barton and Porter reported[6] that 2,2,4,4-tetramethyl-3-pentanone-3-^{14}C rearranged to 3,3,4,4-tetramethyl-2-pentanone without oxygen function rearrangement. Their primary conclusion concerning the major path of the reaction must be correct, but there is not a good carbon-14 activity balance in their work between a degradation product and its precursor (a difference of about 10%), so it is questionable as to whether a minor OFR path can be ruled out. Furthermore, in this case, under the reaction conditions the product 3,3,4,4-tetramethyl-2-pentanone undergoes a cleavage reaction to isobutene and 3-methyl-2-butanone, and this may prevent the long-term exposure needed to determine whether OFR is a minor reaction path. Further experiments are in progress in an attempt to clarify these points, as well as to establish the scope of OFR in reactions of mixed aliphatic–aromatic ketones.

This work demonstrates the advantage of carbon-13 over carbon-14 for tracer experiments in that degradation of the product is not needed and in that separation of product from recovered reactant is not required. At this stage of sophistication of ^{13}C NMR and ^{1}H NMR ^{13}C satellite measurement, the accuracy and precision of the measurements are much less than those which can be obtained with carbon-14 techniques.

Experimental Section

2,2,4-Trimethyl-3-pentanone-3-^{13}C (1b). Compound **1b** was prepared by the cuprous chloride catalyzed reaction between isobutyryl chloride-1-^{13}C and *tert*-butylmagnesium chloride. Isobutyric-1-^{13}C acid was prepared at Los Alamos Scientific Laboratory by a standard Grignard carbonation, using ~90% carbon-13 enriched carbon dioxide. For the ~18% enrichment experiment a mixture of 2.0 g of ~90% isobutyric-1-^{13}C acid and 8.0 g of unlabeled isobutyric acid was added to 70 g of benzoyl chloride[15] and isobutyryl-1-^{13}C chloride was distilled in 92.7% yield. Treatment of 10.0 g of the acid chloride, 11.0 g of cuprous chloride, and *tert*-butylmagnesium chloride prepared from 12.03 g of *tert*-butyl chloride and 3.48 g of magnesium in 200 mL of ether gave 8.10 g (67.3% yield) of ~18% enriched 2,2,4-trimethyl-3-pentanone-3-^{13}C. The ketone was shown by GLC and ^{1}H NMR analysis to contain a small amount of unlabeled 2,2,-3,3-tetramethylbutane. An analytical sample of the pure ketone was prepared by preparative GLC, using a 10 ft by $^{3}/_{8}$ in. column of 5% Carbowax 20M on 60/80 mesh firebrick. The GLC and ^{1}H NMR data (except for the carbon-13 satellite bands) were identical with those for an authentic commercial sample. The main fraction of the labeled ketone was used for the rearrangement reaction without purification from the 2,2,3,3-tetramethylbutane, since the hydrocarbon is not labeled and does not react. By the same procedure 10.0 g of ~90% enriched isobutyric-1-^{13}C acid yielded 8.29 g (57.2% yield) of ~90% enriched 2,2,4-trimethyl-3-pentanone-3-^{13}C. Analysis of the ^{1}H NMR ^{13}C satellite spectrum of the ~90% enriched isobutyryl-1-^{13}C chloride gave a total carbon-13 content at C-1 of 90 ± 0.5% and a total carbon-12 content at C-1 of 10 ± 0.5%, based on the integration of the methyl hydrogen signals. Analysis of the ^{1}H NMR spectrum of the ~90% enriched ketone gave ca. 89% carbon-13 and ca. 11% carbon-12 at the carbonyl carbon. The IR carbonyl frequencies of labeled and unlabeled 2,2,4-trimethyl-3-pentanone were 1660 cm^{-1} (ν(^{13}C=O)) and 1770 cm^{-1} (ν(^{12}C=O)) in neat samples.

Rearrangement of 2,2,4-Trimethyl-3-pentanone-3-^{13}C in Concentrated Sulfuric Acid at 70 °C. A mixture of 7.0 mL of 2,2,4-trimethyl-3-pentanone-3-^{13}C (ca. 18% ^{13}C enriched) and 16 mL of concentrated sulfuric acid was placed in a 50-mL flask. The reaction mixture, which contained a small amount of the insoluble impurity 2,2,3,3-tetramethylbutane, was placed in an oil bath at 70 ± 1 °C for 2.0 h. During the rearrangement reaction, the 2,2,3,3-tetramethylbutane sublimed into a drying tube, and the reaction mixture became homogeneous. At the end of the reaction period, the reaction mixture was cooled and treated with ice–water and 8 N sodium hydroxide solution. The ketonic material was extracted into methylene chloride, and the solution was decolorized with charcoal, dried over sodium sulfate, and distilled to give 3.2 g of a mixture of 2,2,4-trimethyl-3-pentanone, **1**, and 3,3,4-trimethyl-2-pentanone, **2**, boiling at ~130 °C. Analysis by GLC showed that the mixture contained 15.8% **1** and 84.2% **2**. Pure ~18% enriched **2** was obtained by preparative GLC for use in the NMR analyses.

In the rearrangement of the ~90% ^{13}C enriched 2,2,4-trimethyl-3-pentanone-3-^{13}C, 8.5 mL of 2,2,4-trimethyl-3-pentanone-3-^{13}C upon treatment with 20 mL of concentrated sulfuric acid at 71 ± 1 °C for 2.0 h afforded 4.36 g (ca. 5.5 mL) of a mixture of the two isomeric ketones containing 14.8% of **1** and 85.2% of **2**. Small amounts of the pure 90% ^{13}C enriched **1** and **2** were isolated by preparative GLC for the ^{1}H NMR ^{13}C satellite studies.

(15) H. C. Brown, *J. Am. Chem. Soc.*, **60**, 1325 (1938).

However, the main fraction of the mixture of the two ~90% ^{13}C labeled ketones was used for the ^{13}C NMR study without separation of the two ketones.

^{1}H and ^{13}C NMR Measurements. ^{1}H NMR ^{13}C satellite spectra were obtained on a Varian Model A-60 instrument on neat samples or on dilute solutions in carbon tetrachloride. The spectral measurements were repeated at least twice. Some ^{1}H–^{13}C long-range coupling constants for the labeled compounds used in this work are listed below. For isobutyric-*1*-^{13}C acid, $J(^{13}C$–C–C–H) = 5.2 Hz (reported[16] 5.4 Hz). For isobutyryl-*1*-^{13}C chloride, $J(^{13}C$–C–C–H) = 7.0 Hz. For 2,2,4-trimethyl-3-pentanone-*3*-^{13}C, $J(^{13}C(C{=}O)$–C–C–H) = 4.2 Hz for the methyl hydrogens of both the isopropyl and the *tert*-butyl groups; compare to $J(^{13}C(C{=}O)C$–C–H) = 3.7 Hz reported[17] for 2,2,-4,4-tetramethyl-3-pentanone-*3*-^{13}C and to $J(^{13}C(C{=}O)C$–C–H) = 5.1 Hz reported[16] for 2,4-dimethyl-3-pentanone-*3*-^{13}C. For 2,2,4-trimethyl-3-pentanone-*2*-^{13}C, $J(^{13}C$–C–H) $\simeq$ 5 Hz (estimated), and $J(^{13}C$–C(C=O)C–C–H) $\simeq$ 0. For 3,3,4-trimethyl-2-pentanone-*2*-^{13}C, $J(^{13}C(C{=}O)$–C–H) = 6.0 Hz, $J(^{13}C(C{=}O)$–C–C–H) = 4.5 Hz, and $J(^{13}C(C{=}O)C$–C–C–H) $\simeq$ 0 Hz. For 3,3,4-trimethyl-2-pentanone-*3*-^{13}C, $J(^{13}C$–C–H) $\simeq$ 5 Hz (estimated), $J(^{13}C$–C–C–H) = 4.0 Hz, and $J(^{13}C$–C(C=O)–C–H) $\simeq$ 4 Hz (estimated).

All carbon-13 spectra were obtained with a Bruker HFX-90 high-resolution NMR spectrometer operating at 22.63 MHz with a ^{19}F lock system. Noise-modulated decoupling of hydrogen-1 resonances was achieved with a Bruker SV-2 decoupler. For carbon-13 NMR analysis, the preliminary measurements were carried out with 13-mm tubes, either neat or in benzene solution with hexafluorobenzene, and the final measurements were with 10-mm tubes. All chemical shifts were measured with respect to Me_4Si.

For preliminary measurements of the ^{13}C chemical shifts of natural-abundance 3,3,4-trimethyl-2-pentanone, **2a**, the ^{13}C NMR spectrum was taken on a 5-mL sample prepared by rearrangement of unlabeled 2,2,4-trimethyl-3-pentanone, **1a**, and isolated by preparative GLC. The ketone was mixed with about 0.5 mL of hexafluorobenzene as an internal standard, and the spectrum was run in a 13-mm NMR tube. For the final measurements, about 3 mL of this mixture of the ketone and hexafluorobenzene was used in a 10-mm NMR tube. In the same manner, the ^{13}C chemical shifts of natural-abundance 2,2,4-trimethyl-3-pentanone, **1a**, were obtained by using the pure commercially available ketone. The carbonyl carbon of **1a** was not recorded because of instrumental limitations. Selective decoupling experiments were carried out to ensure proper assignments of the chemical shifts. The chemical shift data are presented in Table I.

The ^{13}C NMR analysis of ~18% 3,3,4-trimethyl-2-pentanone-*x*-^{13}C was carried out with a mixture of about 2 mL of material isolated by GLC, about 3 mL of benzene, and 0.5 mL of hexafluorobenzene, using a 13-mm NMR tube. About 3 mL of this mixture was used in a 10-mm NMR tube for some of the spectral measurements.

For the ~90% ^{13}C enriched material, about 3.5 mL of the mixture of the two isomeric ketones 3,3,4-trimethyl-2-pentanone-*x*-^{13}C (85.2%) (presumably a mixture of **2a**, **2b**, and **2c**) and 2,2,4-trimethyl-3-pentanone-*x*-^{13}C (14.8%) (presumably a mixture of **1a**, **1b**, and **1c**) obtained from a rearrangement of ~90% ^{13}C enriched 2,2,4-trimethyl-3-pentanone-*3*-^{13}C, **1a** + **1b**, was available for spectral use. For the preliminary ^{13}C NMR measurements the entire 3.5 mL of the mixture was used in a 13-mm NMR tube, and for the final measurements about 2.4 mL of the mixture was used in a 10-mm NMR tube.

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Registry No. **1a**, 5857-36-3; **1b**, 71010-15-6; **1c**, 71010-16-7; **2a**, 5340-47-6; **2b**, 71010-17-8; **2c**, 71010-18-9; isobutyryl-*1*-^{13}C chloride, 71010-19-0; *tert*-butyl chloride, 507-20-0; 2,2,3,3-tetramethylbutane, 594-82-1; isobutyric-*1*-^{13}C acid, 6228-78-0.

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(17) G. J. Karabatsos and C. E. Orzech, Jr., *J. Am. Chem. Soc.*, **87**, 560 (1965).