A Carbon-14 Tracer Study of the Acid-catalyzed Rearrangement of 3,3-Dimethyl-2-butanone-1-C[14] [1]

By Thomas S. Rothrock and Arthur Fry[2]

3,3-Dimethyl-2-butanone-1-C[14] was treated with sulfuric acid under conditions which are known to produce rearrangements of similar aliphatic ketones. The carbon-14 was found to migrate away from the 1-position, presumably by a carbonium ion mechanism, and at sufficiently long times to become equally distributed among the four methyl groups. The rate of this rearrangement was obtained and compared to the reported rates for similar ketones. The recovered ketone was completely degraded, and no carbon-14 was found in the carbonyl carbon or the central carbon of the t-butyl group. No rearrangement of 2,2-dimethyl-3-pentanone took place upon treatment with Lucas reagent under conditions where alcohols, from which somewhat similar carbonium ions can be derived, rearranged extensively. The implications of these findings with respect to carbonium ion stabilities and the reversibility of the pinacol rearrangement are discussed.

Introduction

Acid-catalyzed rearrangements of aromatic carbonyl compounds have been known for many years[3] and considerable work has been done recently on similar rearrangements of aliphatic ketones.[4-8]

All of the mechanisms which have been proposed for these rearrangements of aliphatic ketones involve the conjugate acids of the ketones and, in most cases, other carbonium ion intermediates derived from them by alkyl group shifts. In addition, one mechanism[8] involves the shift of the conjugate acid hydroxyl group to an adjacent carbon atom. A second mechanism[7] involves the shift of the carbonyl oxygen to an adjacent carbon atom through the protonated oxide. A third mechanism[9] involves only alkyl group shifts.

In order to distinguish between mechanisms which involve migration of the carbonyl oxygen and those which do not, Barton and Porter[6] treated 2,2,4,4-tetramethyl-3-pentanone-3-C[14] with concentrated sulfuric acid and obtained 3,3,4,4-tetramethyl-2-pentanone-2-C[14]. Therefore, the main path for the rearrangement of this compound did not involve carbonyl oxygen migration.[10,11] However, on the basis of the reported data, it is not possible to exclude a small fraction of reaction by some other path.

Application of the above mechanisms to 3,3-dimethyl-2-butanone (methyl t-butyl ketone) leads

to the prediction that the methyl group in the 1-position would exchange with the methyl groups of the t-butyl group. In order to check this point, 3,3-dimethyl-2-butanone-1-C[14] was treated with sulfuric acid and the recovered ketone was degraded to determine the distribution of carbon-14 among the methyl groups. In view of the fact that extensive skeletal rearrangements are known to occur in carbonium ion reactions under certain conditions,[12,13] it seemed possible that some of the carbon-14 would be found in the carbonyl carbon or the central carbon of the t-butyl group. Accordingly, the recovered ketone was subjected to a complete stepwise degradation.

The synthetic and degradative procedures used are outlined.

$$C^{14}H_3I \xrightarrow{Mg} C^{14}H_3MgI \xrightarrow{CdCl_2}$$

$$(C^{14}H_3)_2Cd \xrightarrow[(CH_3)_3CCOCl]{} (CH_3)_3CCOC^{14}H_3$$

$$(CH_3)_3CCOC^{14}H_3 \xrightarrow{H_2SO_4} \begin{array}{c} C^{14}H_3C(CH_3)_2COCH_3 \\ + \\ (CH_3)_3CCOC^{14}H_3 \end{array} \xrightarrow{NaOBr}$$

$$C^{14}Br_4 + C^{14}H_3C(CH_3)_2COOH \xrightarrow{HN_3}$$

$$CO_2 + C^{14}H_3C(CH_3)_2NH_2 \xrightarrow[2, Ag_2O]{1, excess CH_3I}$$

$$C^{14}H_3C(CH_3)_2N^+(CH_3)_3OH^- \xrightarrow{heat} (CH_3)_3N +$$

$$\begin{array}{cc} CH_2=C(CH_3)C^{14}H_3 \\ CH_2=C(CH_3)C^{14}H_3 \\ + & HCO_3H \\ C^{14}H_2=C(CH_3)_2 \end{array} \xrightarrow{} \begin{array}{c} OH\ OH \\ | \ \ | \\ CH_2C(CH_3)C^{14}H_3 \\ + \\ C^{14}H_2C(CH_3)_2 \\ | \ \ | \\ OH\ OH \end{array} \xrightarrow{NaIO_4}$$

$$C^{14}H_2O + C^{14}H_3COCH_3 \xrightarrow{NaOI} C^{14}HI_3 + C^{14}H_3COOH$$

The specific rate constants for the sulfuric acid-catalyzed rearrangements of the three ketones in which the hydrogens of the methyl group of t-butyl methyl ketone have been progressively replaced with methyl groups, have been measured by Zook, Smith and Greene.[5] When it was found that carbon-14 rearrangement in 3,3-dimethyl-2-butanone-1-C[14] (t-butyl methyl ketone) did take place, the specific rate constant for the reaction was

(1) This work was abstracted from the Ph.D. thesis of Thomas S. Rothrock. University of Arkansas, 1958, and was supported by the Atomic Energy Commission.

(2) To whom correspondence concerning this paper should be sent.

(3) For a recent review see S. N. Danilov, Reaktsii i Metody Issledovan, Org. Soedineni, 4, 159 (1956).

(4) M. Stiles and R. P. Mayer, Chemistry & Industry, 1357 (1957).

(5) H. D. Zook, W. E. Smith and J. L. Greene, This Journal, 79, 4436 (1957).

(6) S. Barton and C. R. Porter, J. Chem. Soc., 2483 (1956).

(7) H. Zook and S. C. Paviak, This Journal, 77, 2501 (1955).

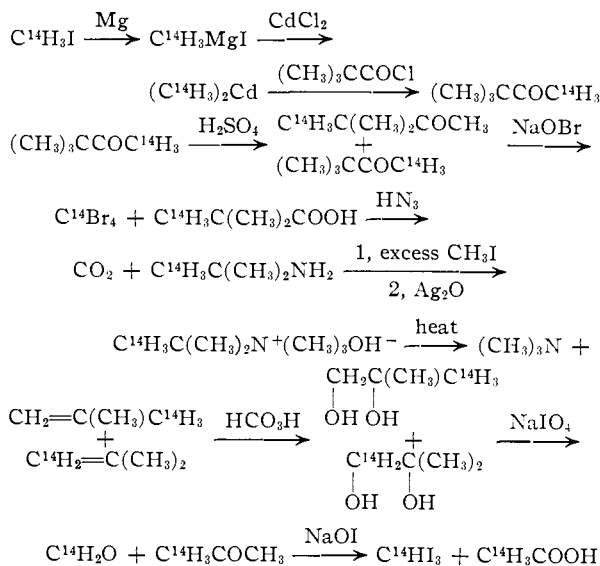(8) S. Barton, F. Morton and C. R. Porter, Nature, 169, 373 (1952).

(9) T. E. Zalesskaya, Zhur. obshchei Khim., 18, 1168 (1948).

(10) Our work on ketone rearrangements was started before the publication of Barton and Porter's paper and our original intention was to carry out a study similar to their using 2,2-dimethyl-3-pentanone-3-C[14]. Upon publication of their work the emphasis of our work was shifted to the present study.

(11) Zook, Smith and Greene[5] point out that formation of the protonated oxide from 2,2,4,4-tetramethyl-3-pentanone might be followed by rearrangement of the t-butyl group rather than a methyl group. This would lead to 3,3,4,4-tetramethyl-2-pentanone without migration of the carbonyl oxygen (the oxide ring would reopen in the same way in which it originally formed). Thus the protonated oxide mechanism cannot be ruled out by the work of Barton and Porter. nor can it be excluded by the results presented here.

(12) J. D. Roberts, R. E. McMahon and J. S. Hine, This Journal. 72, 4237 (1950).

(13) R. L. Burwell, Jr., R. B. Scott, L. G. Maury and A. S. Hussey, ibid., 76, 5822 (1954).

determined, since this ketone is another member of the above series. As a check of our work against that of Zook, Smith and Greene, the specific rate constant for the rearrangement of t-butyl ethyl ketone was measured, using vapor phase chromatography to analyze the ketone mixtures produced.

The action of Lucas reagent as a rearrangement catalyst for t-butyl ethyl ketone also was investigated.

Experimental

Preparation of 3,3-Dimethyl-2-butanone-1-C[14].—3,3-Dimethyl-2-butanone-1-C[14] was prepared from trimethylacetyl chloride and dimethyl-C[14]-cadmium by conventional procedures.[14] In the final purification step, a benzene solution of the ketone was fractionated using a 90 cm. by 5 mm. closed center monel spiral column at a 20/1 reflux ratio. The fraction boiling at 104° (730 mm.) was diluted to the desired activity level with unlabeled ketone which had been purified in a similar manner. The reported[15] boiling point of t-butyl methyl ketone is 104–105° (730 mm.).

Radiochemical Purity of the 3,3-Dimethyl-2-butanone-1-C[14].—The radiochemical purity of the labeled ketone was established by the determination of the activities of several derivatives. It was shown by analysis by vapor phase chromatography on a 25 ft. by $1/4$ in. Tide column that the labeled ketone contained about 1.5% of an impurity (see Fig. 1). The labeled ketone as initially prepared was diluted with 20 to 25 parts of unlabeled ketone. A vapor phase chromatograph of the unlabeled ketone was indis-
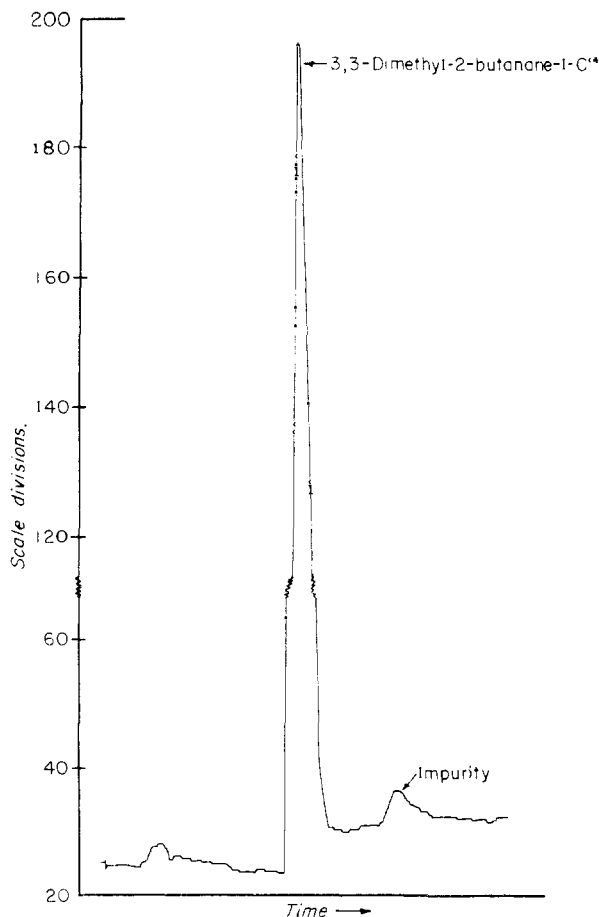
tinguishable from Fig. 1, showing that at least most of the impurity came from the unlabeled material. The results of the activity determinations on the ketone and its derivatives are given in Table I. The deviations given in Table I and the following tables are the average deviations of duplicate determinations. The molar activity of the ketone itself was 3 to 5% lower than that of its derivatives. This was assumed to be largely due to the impurity that had been shown to be present in the inactive ketone used to dilute the labeled ketone. This impurity presumably was removed in the preparation and purification of the derivatives.

TABLE I

MOLAR ACTIVITIES FOR 3,3-DIMETHYL-2-BUTANONE-1-C[14] AND ITS DERIVATIVES

Compound	Activity in μc./mmole
3,3-Dimethyl-2-butanone-1-C[14]	0.1319 ± 0.0004
2,4-Dinitrophenylhydrazone of ketone recrystd. once from ethanol–water[a]	.1368 ± .0002
2,4-Dinitrophenylhydrazone of ketone recrystd. twice from ethanol–water[a]	.1366 ± .0002
2,4-Dinitrophenylhydrazone of ketone recrystd. once from petroleum ether[a]	.1376 ± .0013
Oxime of ketone recrystd. once from ethanol–water[b]	.1369
Semicarbazone of ketone recrystd. once from ethanol[c]	.1352 ± .0009
Carbon-14 tetrabromide[d,f]	.1357 ± .0016
Trimethylacetic acid[e,f]	.00

[a] M.p. 126–127°, reported[15] m.p. 126–127°. [b] M.p. 78–79°, reported[15] m.p. 78.5–79.5°. [c] M.p. 156–157°, reported[16] m.p. 156–157°. [d] M.p. 94–95°, reported[17] m.p. 94.3°. [e] B.p. 160–162°, reported[18] b.p. 163–164°. [f] The carbon-14 tetrabromide and trimethylacetic acid were obtained from the sodium hypobromite cleavage of 3,3-dimethyl-2-butanone-1-C[14].

Attempted Detection of Isomeric Products Formed by the Treatment of 3,3-Dimethyl-2-butanone with Concentrated Sulfuric Acid.—Ten grams of t-butyl methyl ketone was mixed, with cooling, with 20 ml. of concentrated sulfuric acid. The resulting mixture was stirred for 72 hours at $50 \pm 3°$ while protected from moisture with a drying tube filled with calcium chloride. The reaction mixture was poured on cracked ice and extracted with ether. The ether layer was washed with water until neutral, dried over anhydrous sodium sulfate and distilled with a short Vigreux column. A fraction boiling from 80–104° was collected. The contents of the distillation flask distilled to dryness at this point.

Analysis of the 80–104° fraction by vapor-phase chromatography on a 20 ft. by $1/4$ in. column containing polypropylene glycol supported on fire brick showed only the original ketone plus a small amount of a higher boiling impurity to be present. This impurity was assumed to be derived from the impurity present in the starting ketone since they were present in about the same amount.

Isomerization of 3,3-Dimethyl-2-butanone-1-C[14].—Twenty-one grams of 3,3-dimethyl-2-butanone-1-C[14] was placed in a 250-ml. three-necked flask equipped with a Trubore stirrer, reflux condenser and a dropping funnel. The system was protected from moisture by a drying tube filled with calcium chloride.

The ketone was cooled in an ice-bath and 40 ml. of 95.7% sulfuric acid was added slowly with stirring. After completion of the addition of the acid the reaction mixture was heated to $40 \pm 2°$ and stirred at this temperature for 72 hours. The reaction mixture was then poured on cracked ice and extracted with ether. The ether was washed with water until neutral and dried over anhydrous sodium sulfate. Fourteen grams of 3,3-dimethyl-2-butanone-X-C[14] was recovered by distillation. Several similar experiments were carried out and the reaction times, reaction tempera-

Fig. 1.—A chromatogram of 3,3-dimethyl-2-butanone-1-C[14].

(14) J. Cason, Chem. Revs., 40, 15 (1947).

(15) I. Heilbron, "Dictionary of Organic Compounds," 2nd ed. Oxford University Press, New York, N. Y., 1953, Vol. IV, p. 210.

(16) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," Thomas Y. Crowell Co., New York, N. Y., 1947, p. 396.

(17) Reference 15, Vol. I, p. 428.

(18) Reference 15, Vol. IV, p. 224.

tures, ketone–acid ratios and percentages of the carbon-14 remaining in the 1-position are given in Table II. (Additional data of this type were obtained in the kinetic experiments and are given in Table IV.)

TABLE II

REACTION TIMES, REACTION TEMPERATURES, KETONE-ACID RATIOS AND PERCENTAGES OF THE CARBON-14 REMAINING IN THE NUMBER ONE POSITION OF 3,3-DIMETHYL-2-BUTANONE-X-C[14]

Rearrangement[a]	Reaction temp., °C.	Reaction time	Ketone/acid ratio in g./cc.	Carbon-14, %, in 1-position[b]
1	40 ± 2	72 hr.	0.525	41.3
2	40 ± 2	24 hr.	.50	78.0
3	40 ± 2	120 hr.	.50	35.3
4	40 ± 0.2	18 days	.50	25.3
5	30 ± 0.05	52 hr.	.02	55.3

[a] With the exception of rearrangement 5 the concentration of the sulfuric acid used was 95.7%. In rearrangement 5 it was 92.9%. [b] See Table III for the activities used to determine these percentages.

sodium hydroxide and collected as barium carbonate according to standard procedures. The residual solution was extracted with benzene to remove hydrazoic acid and other non-basic materials. The aqueous layer was cooled with an ice-bath, made basic with sodium hydroxide, saturated with potassium carbonate and extracted twice with ether. The ether extracts were combined and washed with a 10% hydrochloric acid solution. The hydrochloric acid solution was evaporated to dryness and the solid residue of 1,1-dimethylethylamine-X-C[14] hydrochloride was recrystallized from ethanol–ethyl acetate to give a product of m.p. 270–272°, reported[21] m.p. 270–280°. The phenylthiourea derivative, recrystallized from ethanol–water, m.p. 119–120°, reported[22] m.p. 119–120°, was used for activity determinations.

Hofmann Degradation of 1,1-Dimethylethylamine-X-C[14]. —1,1-Dimethylethyl-X-C[14]-trimethylammonium hydroxide was prepared by exhaustive methylation of 1,1-dimethylethylamine-X-C[14] followed by treatment with silver oxide in the usual manner.[23] The quaternary ammonium hydroxide was decomposed by heating in a distillation apparatus the output of which led through an absorption train consisting of two gas wash bottles cooled in an ice-bath and containing a saturated succinic acid solution, a cold trap

TABLE III

MOLAR ACTIVITIES IN μC./MMOLE OF 3,3-DIMETHYL-2-BUTANONE-1-C[14], 3,3-DIMETHYL-2-BUTANONE-X-C[14] AND COMPOUNDS OBTAINED IN THE DEGRADATION OF 3,3-DIMETHYL-2-BUTANONE-X-C[14]

Compound	1	2	Rearrangement 3	4	5
2,4-Dinitrophenylhydrazone of starting ketone	0.1366 ±0.0002	0.1366 ±0.0002	0.1366 ±0.0002	0.1366 ±0.0002	0.1017 ±0.0005
2,4-Dinitrophenylhydrazone of recovd. ketone	0.1375 ±0.0003	0.1368 ±0.0001	0.1383 ±0.0008	0.1379 ±0.0018	0.09966 ±0.00134
Carbon-14 tetrabromide	0.05636 ±0.00012	0.1065 ±0.0008	0.04823 ±0.00008	0.03459 ±0.00007	0.05625 ±0.00001
p-Phenylphenacyl ester of 2,2-dimethylpropionic acid-X-C[14]	0.08045[a] ±0.00006	0.03027 ±0.00006	0.08771 ±0.00153	0.1043 ±0.0007	0.04546 ±0.00107
Barium carbonate	....	....	0.00	0.00	....
1,1-Dimethylethylamine-X-C[14] hydrochloride	....	....	0.08906 ±0.00131	0.1021 ±0.0007	....
Phenylthiourea of 1,1-dimethylethylamine-X-C[14]	....	....	0.08933 ±0.00078	....	....
Dimedon derivative of formaldehyde-C[14]	....	....	0.02992 ±0.00014	....	....
2,4-Dinitrophenylhydrazone of acetone-X-C[14]	....	....	0.05981 ±0.00059	....	....
Iodoform-C[14]	....	....	0.02998 ±0.00027	....	....

[a] The molar activity of 2,2-dimethylpropionic acid-X-C[14] from rearrangement 1 was 0.0779 ± 0.00019 μc./mmole.

Sodium Hypobromite Cleavage of 3,3-Dimethyl-2-butanone-X-C[14].—3,3-Dimethyl-2-butanone-X-C[14] was converted to carbon-14 tetrabromide and 2,2-dimethylpropionic acid-X-C[14] following the procedure of Roberts and Yancey.[19] A sample of the carbon-14 tetrabromide was purified for activity determinations by two sublimations, m.p. 94–95°, reported[17] m.p. 94.3°. The ether solution of the 2,2-dimethylpropionic acid-X-C[14] was fractionated and the fraction boiling at 160–162° was used for further degradative work. The reported[18] b.p. for 2,2-dimethylpropionic acid is 163–164°. The p-phenylphenacyl ester of the acid was prepared and recrystallized once from an ethanol–water mixture, m.p. 112.5–113.5°, reported[18] m.p. 113.1–114°. This purified ester was used for activity determinations.

Degradation of 2,2-Dimethylpropionic Acid-X-C[14] by the Schmidt Reaction.—2,2-Dimethylpropionic acid-X-C[14] was converted to carbon-14 dioxide and 1,1-dimethylethylamine-X-C[14] by treatment with hydrazoic acid in the usual manner.[20] The reaction was carried out in a sweep system. The carbon-14 dioxide evolved was absorbed in a solution of

cooled in an ice–salt-bath, and a cold trap cooled with a Dry Ice–isopropyl alcohol mixture. A nitrogen source was connected to the distillation apparatus and, after the decomposition was complete, the whole system was swept with nitrogen for six hours. The 2-methylpropene-X-C[14] collected in the Dry Ice–isopropyl alcohol cooled trap.

Degradation of 2-Methylpropene-X-C[14].—The degradation of 2-methylpropene-X-C[14] followed the reaction sequence used by Roberts, McMahon and Hine.[12] The 2-methyl-1,2-propanediol-X-C[14] obtained boiled at 96–97° (35 mm.), reported[12] b.p. 96–97° (30 mm.). Because of the difficulty in working with the small amount of diol available, this material was degraded to acetone and formaldehyde without further purification. The formaldehyde was isolated as the dimedon derivative, m.p. 190–191°, reported[12] m.p. 190–191°, after recrystallization from ethanol–water. The acetone was isolated as the 2,4-dinitrophenylhydrazone, m.p. 125–126°, reported[24] m.p. 126° after recrystallization from ethanol–water. A portion of the ace-

(19) J. D. Roberts and J. A. Yancey, THIS JOURNAL, 77, 5558 (1955).

(20) H. Wolff, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 307.

(21) Reference 15, Vol. I, p. 289.

(22) B. W. Howk, E. L. Little, S. L. Scott and G. M. Whitman, THIS JOURNAL, 76, 1899 (1954).

(23) G. Norcross and H. T. Openshaw, J. Chem. Soc., 1174 (1949).

(24) Reference 15, Vol. I, p. 13.

tone was degraded to iodoform, m.p. 119–120°, reported[26] m.p. 119°.

Activity Determinations.—All compounds were converted to carbon dioxide by a Van Slyke–Folch wet combustion method.[26] The carbon dioxide obtained was transferred to an ionization chamber by the method of Neville.[27] The activity of the carbon dioxide was determined by the use of a vibrating reed electrometer connected to a Brown recorder. A uranium oxide standard was used as a control to eliminate errors due to instrumental variations and suitable background corrections were applied. Almost all of the reported activities are the averages of two determinations. The average error in the activity determinations is from 0.5 to 1.0%.

The molar activities of the ketone, both before and after rearrangement, and the various compounds obtained from the degradation of the rearranged ketone are given in Table III.

Preparation of 2,2-Dimethyl-3-pentanone.—2,2-Dimethyl-3-pentanone was prepared in 30% yield (based on t-butyl bromide) from t-butylmagnesium bromide and propionyl chloride following the general procedure of Percival, Wagner and Cook.[28] The ferric chloride catalyst appeared to have little if any effect. The final purification was carried out by fractionation using a 90 cm. by 5 mm. closed center monel spiral column at a 10/1 reflux ratio. The material used for further work had a boiling point of 124–125° (725 mm.), reported[29] b.p. 123–124° (755 mm.). This material gave a 2,4-dinitrophenylhydrazone of m.p. 143–144°, reported[30] m.p. 143.5–144°.

Attempted Rearrangement of 2,2-Dimethyl-3-pentanone Using Lucas Reagent.—Following the procedure of Roberts and Yancey,[19] 4 g. of t-butyl ethyl ketone, 10 ml. of methylene chloride and 50 ml. of Lucas reagent (1.6 g. of zinc chloride/ml. of concentrated hydrochloric acid) were shaken at 30° for 3 hours. The layers were separated and the methylene chloride layer was washed with water and dried over anhydrous sodium sulfate. Most of the solvent was evaporated and analysis of the remaining material by vapor phase chromatography using a 25 ft. by $1/4$ in. Tide column showed that no detectable amount of t-amyl methyl ketone was present.

Kinetic Experiments.—Specific rate constants for the rearrangement of 2,2-dimethyl-3-pentanone and of the carbon-14 in 3,3-dimethyl-2-butanone-1-C^{14} were determined following the procedure of Zook, Smith and Greene.[5] For the 3,3-dimethyl-2-butanone-1-C^{14}, the amount of rearrangement was determined by measurement of the activity of the carbon-14 tetrabromide obtained from degradation of the ketone recovered after various reaction times. For the 2,2-dimethyl-3-pentanone, the amount of rearrangement was determined by quantitative vapor phase chromatography. The results of these experiments are given in Table IV. Since pure 3,3-dimethyl-2-pentanone, the product of the rearrangement of 2,2-dimethyl-3-pentanone, was not available, known mixtures of the two compounds could not be prepared to use as a check on the method of analysis and therefore the accuracy of the chromatographic analysis may be subject to some question.

Plots of $\ln (A_0 - A_e)/(A - A_e)$ versus time are shown in Fig. 2; the terminology is that of Zook, Smith and Greene.[5] The values for the specific rate constants were obtained from least squares calculations and are presented in Table VI.

Discussion of Experimental Procedures

The molar activity of the carbon-14 tetrabromide (see Table I) obtained from the cleavage of the unrearranged ketone was the same as that of the starting ketone, and the trimethylacetic acid obtained was inactive. Therefore, no rearrangement occurred during the synthesis of the 3,3-dimethyl-2-

(25) Reference 15, Vol. III, p. 29.

(26) A. Fry, B. M. Tolbert and M. Calvin, *Trans. Faraday Soc.*, **49**, 1444 (1953).

(27) O. K. Neville, THIS JOURNAL, **70**, 3499 (1948).

(28) W. C. Percival, R. B. Wagner and N. C. Cook, *ibid.*, **75**, 3731 (1953).

(29) Reference 15, Vol. II, p. 495.

(30) F. C. Whitmore, C. I. Noll and V. C. Meunier, THIS JOURNAL, **61**, 683 (1939).

KINETIC DATA FOR REARRANGEMENTS OF 3,3-DIMETHYL-2-BUTANONE-1-C^{14} AND 2,2-DIMETHYL-3-PENTANONE

3,3-Dimethyl-2-butanone-1-C^{14}			2,2-Dimethyl-3-pentanone	
Time, sec. $\times 10^{-4}$	$C^{14}Br_4$ activity,[a] $\mu c./$mmole $\times 10^2$	% C^{14} in 1-position	Time, sec. $\times 10^{-4}$	% 2,2-dimethyl-3-pentanone remaining
2.16	9.40 ± 0.02	92.4	1.08	88.7
4.32	8.55 ± .07	84.1	2.16	77.8
9.64	7.53 ± .09	74.1	3.24	68.6
17.28	5.76 ± .06	56.6	4.32	57.9
25.92	4.65 ± .02	45.7	8.64	33.9

[a] The activity of the ketone before rearrangement was 0.1017 ± 0.0005 and after rearrangement 0.1014 ± 0.0008 $\mu c./$mmole.

butanone-1-C^{14}. These results also show that no rearrangement occurred during the sodium hypobromite cleavage of the ketone. This fact is in accord with the assumption of Roberts and Yancey.[16]

The fact that all of the derivatives of 3,3-dimethyl-2-butanone-1-C^{14} had the same molar activity within experimental error shows conclusively that no radioactive impurities are present and, hence, that any subsequent changes in radioactivity distribution must be due to reactions of the ketone. The fact that no isomeric products could be found upon treatment of 3,3-dimethyl-2-butanone with concentrated sulfuric acid shows that the radiochemical results are results on this ketone and not on an isomeric product or mixture of products.

There has been some question[31,32] concerning rearrangement within the migrating alkyl group in the Schmidt reaction. Since no appreciable carbon-14 was found in the central carbon of the t-butylamine, no appreciable rearrangement of the t-butyl group occurred in this reaction. These results are in agreement with the results of Lee, Slater and Spinks[33] on 3-phenylpropionic acid-2-C^{14} and Roberts and Halmann[34] on propionic acid-1-C^{14}.

The absence of any appreciable carbon-14 in the central carbon of the t-butyl group also shows that the Hoffman exhaustive methylation procedure may be used to degrade t-butylamine to isobutylene without rearrangement of the carbon skeleton.

Discussion of Results

Upon treatment with concentrated sulfuric acid the carbon-14 of 3,3-dimethyl-2-butanone-1-C^{14} was found to migrate away from the one position and at sufficiently long reaction times, rearrangement 4, to become equally distributed among the four methyl groups. Within experimental error all of the carbon-14 was present in the four methyl groups of the rearranged ketone. The carbon-14 distribution among the carbons of the ketone as calculated from the molar activities in Table III is given in Table V (see Introduction for the degradative scheme). It should be noted that good

(31) E. F. Phares, *Arch. Biochem. and Biophys.*, **33**, 173 (1951).

(32) C. Schuerch, Jr., and E. H. Huntress, THIS JOURNAL, **71**, 2233, 2238 (1949).

(33) C. C. Lee, G. P. Slater and J. W. T. Spinks, *Can. J. Chem.*, **35**, 276 (1957).

(34) J. D. Roberts and M. Halmann, THIS JOURNAL, **75**, 5759 (1953).

TABLE V

PERCENTAGE DISTRIBUTION OF CARBON-14 IN 3,3-DIMETHYL-2-BUTANONE-X-C^{14} FROM TREATMENT OF 3,3-DIMETHYL-2-BUTANONE-1-C^{14} WITH CONCENTRATED SULFURIC ACID

Position[a]	Rearrangement 1	2	3	4	5	Compounds used to determine percentage
1	41.3	48.0	35.3	25.3	55.4	Carbon-14 tetrabromide
2,3,4,5,6	58.9	22.2	64.2	76.3	44.7	2,2-Dimethylpropionic acid-X-C^{14}
2	..	..	0.0	0.0	..	Barium carbonate
3,4,5,6	..	..	65.2	74.7	..	1,1-Dimethylethylamine-X-C^{14}
3	..	..	-0.3	..	..	1,1-Dimethylethylamine-X-C^{14} and formaldehyde-C^{14}
3	..	..	0.0	..	..	Formaldehyde-C^{14} and acetone-X-C^{14}
3	..	..	-0.1	..	..	Acetone-X-C^{14} and iodoform-C^{14}
4,5,6	..	..	65.7	..	..	Formaldehyde-C^{14}
4,5,6	..	..	65.8	..	..	Iodoform-C^{14}

[a] $\overset{O}{\overset{\|}{CH_3CC(CH_3)_3}}$. 1 2 3 4,5,6
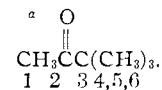
activity balances were obtained in all the steps of the degradation.

The absence of any appreciable amount of carbon-14 in either the carbonyl carbon or the central carbon of the t-butyl group was not surprising. Any rearrangement that would be extensive enough to place carbon-14 in either of these two carbons should also lead to the production of additional isomeric products. It was shown by analysis of the rearranged ketone by vapor phase chromatography that no new products were obtained in the rearrangement. Analysis of the products obtained in the rearrangements of t-butyl ethyl ketone also showed no extensive rearrangements since only the original ketone and t-amyl methyl ketone were found to be present.

Stiles and Mayer[4] have found that the rearrangement of di-t-butyl ketone is first order in the conjugate acid of the ketone, although the activity coefficient ratio for the ketone and its conjugate acid does not vary in the same way with acid concentration as the corresponding ratio for the indicators used in determining the acidity function. In view of this information and the work of Barton and Porter,[6] the results of this work are presented in terms of the reaction sequence
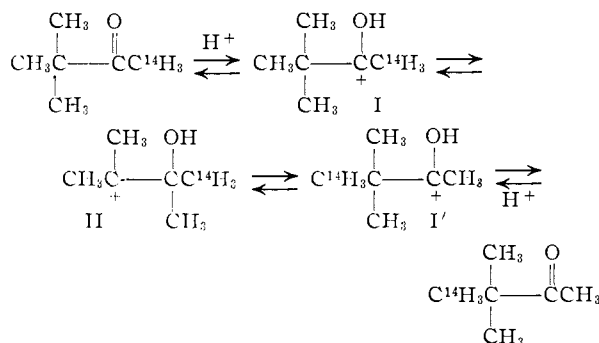
The absence of isomeric products formed by extensive skeletal rearrangements may be understood readily on the basis of relative stabilities of the carbonium ions involved. The usual mechanism for such a rearrangement would involve the formation of primary carbonium ions from I or II (or of primary and/or secondary carbonium ions in the rearrangement of homologous ketones). In the reactions of 2- and 3-methylhexanes with sulfuric acid,[13] products (dimethylpentanes) have been obtained which involve secondary carbonium ions (or the equivalent). However, formation of such
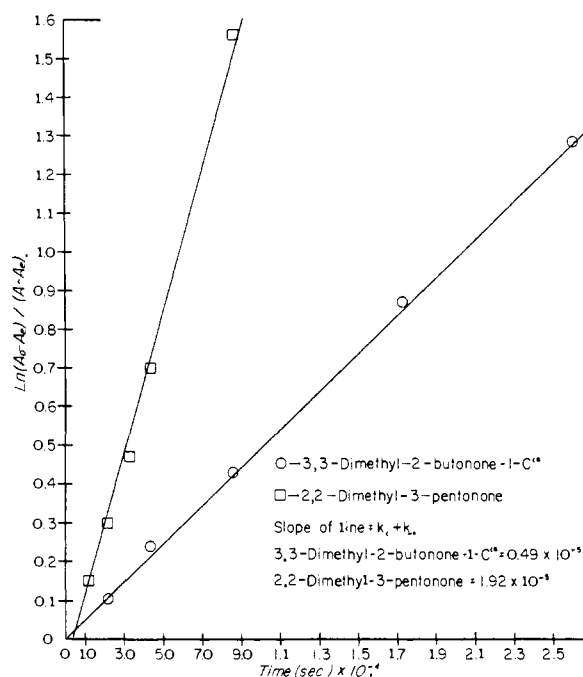

Fig. 2.—A plot of ln $(A_0 - A_e)/(A - A_e)$ versus time for the rearrangements of 3,3-dimethyl-2-butanone-1-C^{14} and of 2,2-dimethyl-3-pentanone.

a primary (or in other cases, secondary) carbonium ion would appear to be much less likely in the present system due to the delocalization of the positive charge in I by resonance interaction between the hydroxyl group and the positively charged carbonyl carbon and in both ions I and II by increased solvation due to the presence of the highly polar hydroxyl group. The fact that diisopropyl ketone does not rearrange[5] makes it seem unlikely that conjugate acid I would rearrange to a primary carbonium ion. The initial step of the rearrangement of diisopropyl ketone would be the rearrangement of its conjugate acid to a secondary carbonium ion.

The specific rate constants found for the carbon-14 rearrangement in 3,3-dimethyl-2-butanone-1-C^{14} and for the rearrangement of t-butyl ethyl ketone, along with the values of Zook, Smith and Greene[5] for the rearrangement of di-t-butyl, t-butyl isopropyl and t-butyl ethyl ketones, are given in Table VI. The value of the specific rate constant, k_1, for the carbon-14 rearrangement is consistent with the general trend established by the three

specific rate constants of Zook, Smith and Greene.

While it is not definitely known, it seems probable that the rate-determining step of the reaction is the migration of a methyl group of conjugate acid I to form carbonium ion II. If this is so, it is possible to explain in a qualitative manner the decrease in specific rate constants from di-t-butyl ketone to t-butyl methyl ketone on the basis of the increased delocalization of the positive charge on the carbonyl carbon of the conjugate acid due to hyperconjugation and solvation effects. It should be noted that the above considerations might be expected to lead to a larger difference between the rate constants for t-butyl isopropyl ketone and t-butyl ethyl ketone than is actually observed.

t-Butyl ethyl ketone was found not to rearrange on treatment with Lucas reagent for three hours at 30°. Since 3,3-dimethyl-2-butanone-1-C^{14} rearranges slower that t-butyl ethyl ketone in concentrated sulfuric acid, it was logical to conclude that 3,3-dimethyl-2-butanone-1-C^{14} would not rearrange on treatment with Lucas reagent under the above conditions. The rapid rearrangement of the carbon-14 in 2,3,3-trimethyl-2-butanol-1-C^{14} [19] under the same conditions is thought to proceed through carbonium ions that are similar to I and II. The rapid rearrangement in this case and the probable lack of rearrangement in 3,3-dimethyl-2-butanone-1-C^{14} is not unexpected on the basis of the carbonium ions involved. The rearrangement of the alcohol is thought to proceed by the rapid interconversion of the energetically equal pentamethylethylcarbonium ions, but as has already been pointed out, the presence of the polar hydroxyl group in I and II would be expected to lead to increased solvation and thus greater delocalization of the positive charge, leading to a slower rate of interconversion of ions I and II.

The pinacol rearrangement may be represented by the reaction sequence
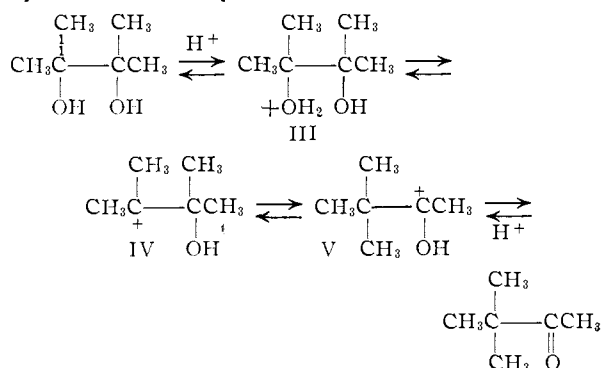
Since IV and V are the same as II and I, respectively, with the exception of the carbon-14 label, the pinacol rearrangement and the rearrangement of 3,3-dimethyl-2-butanone-1-C^{14} apparently proceed through the same intermediate.

It has been reported by Bunton, Hadwick,

Llewellyn and Pocker[35] that pinacol undergoes oxygen exchange under the rearrangement conditions. Therefore it was postulated that formation of carbonium ion IV from conjugate acid III was rapid and reversible and that the rearrangement of IV was the rate-determining step. Since the addition of t-butyl methyl ketone did not affect the rate of reaction it was further said that the formation of V from IV is not reversible. While this last statement probably is true under the acid concentration (1.0 to 3.0 M sulfuric acid) used, the fact that the carbon-14 of 3,3-dimethyl-2-butanone-1-C^{14} rearranges in concentrated sulfuric acid shows that the formation of V from IV is reversible under these conditions.

It was also shown that over the range of acidities used in the oxygen exchange studies with pinacol the relative amounts of exchange and rearrangement were independent of the acidity. If that is still true in the range of sulfuric acid concentration used to catalyze the rearrangement of 3,3-dimethyl-2-butanone-1-C^{14}, then the carbonyl carbon and the central carbon of the t-butyl group should be present, at equilibrium, in equal amounts as the carbonyl carbon of the rearranged ketone. Reversibility of the pinacol rearrangement thus provides an additional mechanism by which the oxygen function may migrate during acid-catalyzed ketone rearrangements (see Introduction).

The work of Barton and Porter[6] shows that the main path for the rearrangement of 2,2,4,4-tetramethyl-3-pentanone-3-C^{14} does not involve carbonyl oxygen migration. However, Carrick[36] found that after treatment of 1,2,2,2-tetraphenyl-1-oxoethane-1-C^{14} (benzopinacol) with concentrated sulfuric acid at 10° for 0.5 hour, approximately 2% of the carbon-14 was present in the 2-position, showing that some mixing of the two central carbons had occurred. Further carbon-14 and oxygen-18 tracer studies on these problems are in progress in this Laboratory.

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(35) C. A. Bunton, T. Hadwick, D. R. Llewellyn and Y. Pocker, *Chemistry & Industry*, 547 (1956); *J. Chem. Soc.*, 403 (1958).

(36) W. L. Carrick, Ph.D. Dissertation, University of Arkansas, 1955.