The Isotope Effect in the Rearrangement of 2,2,4,4-Tetramethyl-3-pentanone-1-^{14}C

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When 2,2,4,4-tetramethyl-3-pentanone is treated with concentrated sulfuric acid at room temperature it rearranges to 3,3,4,4-tetramethyl-2-pentanone. Mechanisms for this type of rearrangement have been proposed by Barton et al. (1959), Zook and Pavlak (1955), and Zalesskaya (1948). Barton and Porter (1956) showed by carbon-14 tracer experiments that the reaction does not involve migration of the oxygen atom which some investigators had postulated. The mechanism proposed by Zalesskaya (1948) has four steps: (1) protonation of the oxygen atom, (2) migration of a methyl group to the positively charged carbon atom, (3) migration of the *tert*-butyl group to the new positively charged carbon atom, and (4) deprotonation of the oxygen atom. The purpose of this investigation was to determine by means of the carbon-14 isotope effect whether migration of the methyl group was the rate-controlling step of the reaction.

Preparation of the desired ketone was by the following reactions: methyl-^{14}C-magnesium iodide with acetone gave *tert*-butyl alcohol; the latter with concentrated hydrochloric acid gave *tert*-butyl chloride; and the Grignard reagent of the latter with pivaloyl chloride gave 2,2,4,4-tetramethyl-3-pentanone-1-^{14}C. Preparative gas chromatography was used to separate the ketone in pure form from the final reaction mixture, which is known to contain small amounts of *tert*-butyl pivalate and neopentyl alcohol (Cook and Percival, 1949). The 2,2,4,4-tetramethyl-3-pentanone-1-^{14}C was shaken in 81.3% aqueous sulfuric acid at 23 C for 12 hr in order to effect approximately 80% rearrangement to the methyl ketone. The unreacted ketone was recovered and purified by preparative gas chromatography. Samples of the starting ketone and the recovered ketone were oxidized to carbon dioxide and the radioactivity of this gas was determined by means of a vibrating-reed electrometer.

RESULTS AND DISCUSSION

Results of the radioassays of the initial and recovered 2,2,4,4-tetramethyl-3-pentanone-1-^{14}C are shown in Table I, together with values of the isotope effect calculated by the following equation (Downes and Harris, 1952):

$$k^*/k = 1 + [\log (N/N_o)/\log (1-f)]$$

where k^*/k is the intermolecular isotope effect and N and N_o are molar radioactivities of the ketone after an extent of reaction f and at the start of the reaction, respectively.

Since the value of k^*/k for the reaction is 0.999 with a probable error of 0.0075, the deviation from 1.000 is small (0.001) but the probable error is still 0.0075. Since only one methyl group of the six possible in each molecule was labeled with carbon-14, the overall isotope effect in the reaction has only one-sixth of the value that it would have had if all the methyl groups had been labeled. Therefore the isotope effect for each methyl group is 0.6% with a probable error of 4.5%. This large uncertainty does not result from poor experimental work, but comes from the chemical system itself.

This large probable error in the isotope effect renders the value useless in the interpretation of the mechanism of the reaction. On the basis of these results one cannot determine whether methyl migration occurs in the slow step of the reaction. Further experimental evidence is needed to

TABLE I. REARRANGEMENT OF 2,2,4,4-TETRAMETHYL-3-PENTANONE-1-^{14}C.

Run No.	Radioactivity of Ketone mv/sec mg		Fraction Unreacted	Intermolecular Isotope Effect for the Reaction	
		Prob. Error		k^*/k	Prob. Error
1,2,3	1.213	0.0074	1.000	—	—
1	1.209	0.0138	0.174	1.002	0.0170
2	1.218	0.0060	0.139	0.998	0.0100
3	1.216	0.0054	0.209	0.998	0.0111

elucidate the mechanism of the reaction.

EXPERIMENTAL

Preparation of 2-Chloro-2-methylpropane-1-^{14}C.—To a Grignard reagent prepared from 31.23 g (220 mmoles) of methyl iodide containing 1 mc of carbon-14 was added 13.3 g (230 mmoles) of acetone dissolved in ether during 1.5 hr with vigorous stirring. After the reaction mixture was hydrolyzed, the ether layer was washed with water, dried, and fractionally distilled. When most of the ether had been removed the residue containing *tert*-butyl alcohol was shaken with concentrated hydrochloric acid at room temperature for 10 min. The reaction mixture was washed, dried, and distilled. The portion (9.92 g) boiling at 48-52 C was shown by gas chromatography to be 5.1% ether and 94.9% *tert*-butyl chloride; Timmons and Delcourt (1934) report that *tert*-butyl chloride boils at 50.7 C.

Preparation of 2,2,4,4-Tetramethyl-3-pentanone-1-^{14}C.—The Grignard reagent prepared from the radioactive *tert*-butyl chloride by the method of Whitmore and Badertscher (1933) was added to a stirred mixture of 24.1 g (200 mmoles) of pivaloyl chloride, 10 g of a cuprous chloride catalyst (Cook and Percival, 1949), and 200 ml of anhydrous ether. After 1 hr the reaction mixture was decomposed on ice, and the ether layer was washed, dried, and distilled. The labeled ketone was collected at 148-154 C and was purified by preparative gas chromatography. The radioactivity yield from methyl-^{14}C iodide was 3.3%.

Rearrangement of 2,2,4,4-Tetramethyl-3-pentanone-1-^{14}C.—The ketone was rearranged by the procedure of Zook et al. (1957). A 3-g sample was dissolved in 150 ml of 81.3% sulfuric acid in a 250-ml Erlenmeyer flask. The mixture was shaken for 12 hr at 23 C, then poured on 250 ml of ice. The organic compounds were extracted with carbon tetrachloride; this layer was dried and most of the carbon tetrachloride was distilled at atmospheric pressure. The residue was vacuum distilled, and then subjected to preparative gas chromatography in order to obtain the pure unreacted ketone. The extent of reaction was determined by measuring the ratio of 2,2,4,4-tetramethyl-3-pentanone and 3,3,4,4-tetramethyl-2-pentanone by gas chromatography. The purified 2,2,4,4-tetramethyl-3-pentanone was assayed by oxidation of weighed samples to carbon dioxide; this gas was placed in an ionization chamber and the ion current was measured with an Applied Physics Model 30 vibrating-reed electrometer. The rearrangement was performed three times and the product of each run was assayed at least four times with the results shown in Table I.

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