liquor permitted the recovery of 5 g. of L-mannonic lactone. The over-all yields thus represent the production of 49.6% L-gluconic and 14.9% of L-mannonic acid by the use of sodium cyanide.

Obviously the procedure can be used advantageously for the preparation of D-gluconic acid and D-glucose labeled at carbon atom 1 from D-arabinose and labeled sodium cyanide.

NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND C. S. HUDSON

RECEIVED AUGUST 6, 1951

MECHANISM OF THE LOW TEMPERATURE CHLORINATION OF ISOBUTYLENE

Sir:

Chlorine reacts practically instantaneously with excess isobutylene at 0° to form the unsaturated monohalide, methallyl chloride, in 83% yield, based on the chlorine consumed.[1] We have studied the reaction of chlorine with 1-C^{14}-2-methyl-1-propene to determine whether the mechanism of this reaction involves an attack by an electrophilic chlorine atom on the terminal unsaturated carbon atom with a subsequent elimination of a proton from the carbonium ion thus formed or, alternatively, a direct attack by chlorine on one of the methyl groups without the double bond entering into the reaction.

1-C^{14}-2-Methylpropionic acid was prepared by the carbonation of isopropylmagnesium bromide[2]; this was esterified, reduced to isobutyl alcohol, converted to the iodide with phosphorus and iodine, and dehydrohalogenated to isobutylene with potassium hydroxide. A sample of this was shown to have all the C^{14} in the one position by ozonolysis and the examination of the formaldehyde and the acetone thus formed. The dimedone derivative of the formaldehyde gave 1400 counts per minute; the 2,4-dinitrophenylhydrazone derivative of the acetone was inactive. The reaction with chlorine involved mixing 30% excess isobutylene with the chlorine in a 0.8-mm. glass capillary flow system immersed in an ice-bath. The methallyl chloride (4.2 g., 60% yield based on the total isobutylene) was purified by distillation, b.p. 72 to 74° (760 mm.). It probably contained 1 to 3% of isocrotyl chloride ($(CH_3)_2C{=}CHCl$) which boils at 68.1°.[1] The methallyl chloride was ozonized, and the ozonide decomposed in the presence of an excess of platinized zinc to convert the chloroacetone to acetone. The formaldehyde and acetone were examined as their dimedone and 2,4-dinitrophenylhydrazone derivatives, respectively. The former had little activity (50 counts/min.) possibly due to the isocrotyl chloride ozonide giving formaldehyde under our experimental conditions. The acetone derivative had an estimated 97% of the radioactive carbon (1760 counts/min.).

The above clearly shows that the chlorination of isobutylene near 0° involves as the first step an attack by an electrophilic chlorine atom at the number one carbon atom. This is followed by the loss of a proton to form the methallyl chloride, the double bond now being in a new position. It is thus apparent that the first step in the chlorination of isobutylene is much like that in the case of ethylene. Unlike the case of ethylene, however, the intermediate postulated loses a proton before the usual final step can occur, namely, the addition of a nucleophilic chlorine atom at the positive center.

The procedure for preparing the isobutyl alcohol was worked out by Mrs. Claudia Sebeste Prickett. Dr. Carl Rollinson's apparatus was used in making the counts.

DEPARTMENT OF CHEMISTRY WILKINS REEVE
UNIVERSITY OF MARYLAND D. HARRY CHAMBERS
COLLEGE PARK, MARYLAND

RECEIVED JULY 23, 1951

AN UNUSUAL ISOTOPE EFFECT

Sir:

We have observed an unusual isotope effect in connection with a study of the hydrolysis of triphenylsilane in moist piperidine.[1] The reaction is first order in silane, half order in water, and has a positive value of ρ in the Hammett equation, leading to the conclusion that one of the two following mechanisms is operative.

$$C_5H_{10}NH + H_2O \rightleftharpoons C_5H_{10}NH_2^{\oplus} + OH^{\ominus}$$

Mechanism A:

$$OH^{\ominus} + Ph_3SiH \longrightarrow \left[Ph_3Si\begin{matrix}OH\\H\end{matrix}\right]^{\ominus}$$

$$\left[Ph_3Si\begin{matrix}OH\\H\end{matrix}\right]^{\ominus} + C_5H_{10}NH \longrightarrow Ph_3SiOH + H_2 + C_5H_{10}N^{\ominus}$$

Mechanism B:

$$OH^{\ominus} + Ph_3SiH + C_5H_{10}NH \longrightarrow Ph_3SiOH + H_2 + C_5H_{10}N^{\ominus}$$

In an attempt to learn whether or not the silicon-hydrogen bond is broken in the rate-determining step of the reaction, we prepared triphenyldeuterosilane and compared its rate of hydrolysis with that of the compound having the normal deuterium content. It was anticipated that, if the bond in question were broken in the rate-controlling step, the protium-rich compound would react more rapidly than the deutero compound. This would be in accord with previous work,[2] and with the view that the zero-point vibrational energy of a bond in the process of being broken decreases as the system passes from its resting state to the transition state. Since zero-point energies are always smaller for deuterium compounds than for analogous protium compounds, it would follow that the activation energy for breaking bonds to hydrogen should be decreased by the larger increment. We were, therefore, surprised to find that *the deuterium compound reacted almost six times faster than its protium analog.* Abnormal isotope effects have been both predicted[3]

(1) J. Burgin, W. Engs, H. P. A. Groll and G. Hearne, *Ind. Eng. Chem.*, **31**, 1413 (1939).

(2) The carbon dioxide was prepared from barium carbonate-C^{14} supplied by the Clinton Laboratories on allocation from the U. S. Atomic Energy Commission.

(1) The experimental procedures used are similar to those described by H. Gilman and G. E. Dunn, THIS JOURNAL, **73**, 3404 (1951).

(2) F. H. Westheimer and N. Nicolaides, *ibid.*, **71**, 25 (1949); O. Reitz, *Z. physik. Chem.*, **A184**, 429 (1939); **A179**, 119 (1937); **A176**, 363 (1936).

(3) M. Polanyi, *Nature*, **133**, 26 (1934); B. Topley and H. Eyring, *J. Chem. Phys.*, **2**, 217 (1934).

and observed[4] previously, but this is the first instance in which the difference in rates has been found to be comparable in magnitude to those associated with the normal effect.

A serious consequence of this observation is the introduction of an ambiguity into the interpretation of kinetic studies such as ours. It is entirely conceivable that some reactions which involve breaking bonds to atoms of different masses will not show any considerable isotope effect because of a fortuitous similarity of zero-point energies of the transition and resting states of the reactants.

While the lack of a detailed knowledge of the configuration of the transition state for our reaction does not permit a complete interpretation of the observed results, it seems likely that the abnormal effect should be attributed in large part to the fact that the reaction effectively involves the displacement of a hydride ion. Because of the rather low electron affinity of hydrogen atoms (17 kcal. mole^{-1})[5] we would not expect to observe such a displacement at ordinary temperatures unless the hydrogen is continuously bound to some other atom or atoms throughout the course of the reaction. This means that if the old bond has been largely destroyed in the transition state, the new bond (hydrogen–hydrogen) must have already attained considerable strength. Since the hydrogen–hydrogen bond has a rather large stretching force constant (5.76×10^5 dynes cm.$^{-1}$)[6] the restoring force for vibrational displacement of the hydrogen atom may well be larger in the transition state than in the silane. Reversal of the argument outlined above for the normal isotope effect would then account for the abnormal effect observed here.

CHEMICAL LABORATORY
IOWA STATE COLLEGE
AMES, IOWA

HENRY GILMAN
G. E. DUNN[7]
G. S. HAMMOND

RECEIVED JUNE 20, 1951

(4) S. H. Maron and V. K. LaMer, THIS JOURNAL, **60**, 2588 (1938); P. Gross, H. Steiner and H. Suess, *Trans. Faraday Soc.*, **32**, 883 (1936); P. Gross, H. Steiner and F. Kraus, *ibid.*, **32**, 877 (1936); O. Reitz, *Z. physik. Chem.*, **A177**, 85 (1936); J. C. Hornel and J. A. V. Butler, *J. Chem. Soc.*, 1361 (1936); O. Halpern, *J. Chem. Phys.*, **3**, 456 (1935); W. F. K. Wynne-Jones, *Chem. Rev.*, **17**, 117 (1935); K. Schwarz, *Ans. Akad. Wiss. Wien, Math.-Naturw. Klasse*, **71**, 115 (1934); W. F. K. Wynne-Jones, *J. Chem. Phys.*, **2**, 381 (1934); E. A. Moelwyn-Hughes and K. F. Bonhoeffer, *Naturwissenschaften*, **22**, 174 (1934), *Z. physik. Chem.*, **26B**, 272 (1934). It should be noted that all these cases involve reactions of protium compounds in heavy water. Our reaction is more clearcut than these, in that it concerns only a change of reactants and not of medium.

(5) G. Glockler and S. Lind, "Electrochemistry of Gases and Other Dielectrics," John Wiley and Sons, Inc., New York, N. Y., 1939, pp. 334–335.

(6) G. Herzberg, "Molecular Spectra and Molecular Structure," Prentice-Hall Inc., New York, N. Y., 1939, Vol. I, p. 487.

(7) E. I. du Pont de Nemours and Co. Fellow, Iowa State College, 1950–1951.

THE *IN VIVO* CONVERSION OF GLUTAMIC ACID INTO PROLINE AND ARGININE[1]

Sir:

Several years ago, by the use of compounds "labeled" with isotopes, Schoenheimer and his associates demonstrated conclusively that certain amino acids are converted into each other in the intact mammalian organism. Thus, deuteroörnithine is transformed by the mouse into deuteroarginine,[2] deuteroproline and deuteroglutamic acid[3]; and proline containing both deuterium and N^{15} is converted by the rat into isotopic hydroxyproline, arginine and glutamic acid.[4] These findings provide convincing proof that proline and ornithine (arginine) are mutually interconvertible *in vivo*. However, the authors appear to have made no attempt to determine whether glutamic acid can be transformed into arginine or proline.

In the meantime, investigations in this laboratory[5] showed that albino rats which are deprived of arginine, proline, hydroxyproline and glutamic acid, but receive an otherwise adequate diet, continue to grow but at greatly diminished rates. The addition to the food of either arginine, proline, or glutamic acid improves the rate of gain, though neither of the latter two is so effective as arginine. Under like circumstances, hydroxyproline is without beneficial action. The findings with glutamic acid were interpreted as furnishing "indirect evidence, for the first time, that this amino acid may be transformed *in vivo* into proline or arginine."

The above reaction possesses more than passing interest. Glutamic acid can be formed in the body by the reductive amination of the corresponding α-keto acid. An abundant supply of the latter (α-ketoglutaric acid) arises in carbohydrate metabolism. Therefore, the conversion of glutamic acid into proline or arginine, each of which can be transformed into the other and serve as a precursor of hydroxyproline, would account for the ability of animals to make moderate gains in weight even when deprived of all four of the compounds in question.

In order to obtain *direct* evidence for this relationship, DL-glutamic acid-5-C^{14} has now been synthesized[6] and administered orally to two rats. At the expiration of approximately 27 hours, each animal was sacrificed. From the hydrolyzed carcasses, which were worked up separately, glutamic acid, proline and arginine were isolated in pure condition. Each compound was then oxidized, and the resulting carbon dioxide was tested for radioactivity. The data show that all three of the amino acids were quite active. The order of activity was: proline > arginine > glutamic acid. Probably, the magnitude of the dilution of the radioactive materials by the non-labeled amino acids of the tissues accounts, at least in part, for the differences in C^{14} content of the isolated compounds.

The above findings demonstrate clearly that the reactions whereby proline and arginine are converted into glutamic acid are reversible. The experimental evidence will be presented in full in the near future.

DIVISION OF BIOCHEMISTRY
NOYES LABORATORY OF CHEMISTRY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

H. JAMES SALLACH
ROGER E. KOEPPE
WILLIAM C. ROSE

RECEIVED JULY 25, 1951

(1) Aided by grants from the United States Public Health Service and the Graduate College Research Fund of the University of Illinois.

(2) R. F. Clutton, R. Schoenheimer and D. Rittenberg, *J. Biol. Chem.*, **132**, 227 (1940).

(3) M. Roloff, S. Ratner and R. Schoenheimer, *ibid.*, **136**, 561 (1940).

(4) M. R. Stetten and R. Schoenheimer, *ibid.*, **153**, 113 (1944).

(5) W. Womack and W. C. Rose, *ibid.*, **171**, 37 (1947).

(6) Unpublished work in this laboratory by R. A. Bauman.