NBS CIRCULAR 575

Bibliography on Nitrogen 15

UNITED STATES DEPARTMENT OF COMMERCE

NATIONAL BUREAU OF STANDARDS

PERIODICALS OF THE NATIONAL BUREAU OF STANDARDS

(Published monthly)

The National Bureau of Standards is engaged in fundamental and applied research in physics, chemistry, mathematics, and engineering. Projects are conducted in fifteen fields: electricity and electronics, optics and metrology, heat and power, atomic and radiation physics, chemistry, mechanics, organic and fibrous materials, metallurgy, mineral products, building technology, applied mathematics, data processing systems, cryogenic engineering, radio propagation, and radio standards. The Bureau has custody of the national standards of measurement and conducts research leading to the improvement of scientific and engineering standards and of techniques and methods of measurement. Testing methods and instruments are developed, physical constants and properties of materials are determined, and technical processes are investigated.

Journal of Research

The Journal presents research papers by authorities in the specialized fields of physics, mathematics, chemistry, and engineering. Complete details of the work are presented, including laboratory data, experimental procedures, and theoretical and mathematical analyses. Annual subscription: domestic, $4.00; $1.25 additional for foreign mailing.

Technical News Bulletin

Summaries of current research at the National Bureau of Standards are published each month in the Technical News Bulletin. The articles are brief, with emphasis on the results of research, chosen on the basis of their scientific or technologic importance. Lists of all Bureau publications during the preceding month are given, including Research Papers, Handbooks, Applied Mathematics Series, Building Materials and Structures Reports, Miscellaneous Publications, and Circulars. Each issue contains 12 or more two-column pages; illustrated. Annual subscription: domestic, $1.00; 35 cents additional for foreign mailing.

Basic Radio Propagation Predictions

The Predictions provide the information necessary for calculating the best frequencies for communication between any two points in the world at any time during the given month. The data are important to all users of long-range radio communications and navigation, including broadcasting, airline, steamship, and wireless services, as well as to investigators of radio propagation and ionosphere. Each issue, covering a period of one month, is released three months in advance and contains 16 large pages, including pertinent charts, drawings, and tables. Annual subscription: domestic, $1.00; 25 cents additional for foreign mailing.

CATALOG OF NBS PUBLICATIONS

National Bureau of Standards Circular 460 and its Supplement list all Bureau publications from 1901 through June 1952, including Applied Mathematics Series, Building Materials and Structures Reports, Circulars, Handbooks, Research Papers, and Miscellaneous Publications. Brief abstracts for the publications issued after January 1, 1942, are also included.

National Bureau of Standards Circular 460, 375 pages, $1.25. Supplement to Circular 460, 223 pages, 75 cents. (A free mimeographed list of publications issued since June 1952 is available on request to the National Bureau of Standards.)

Order all publications from the Superintendent of Documents
U. S. Government Printing Office, Washington 25, D. C.

UNITED STATES DEPARTMENT OF COMMERCE • Sinclair Weeks, *Secretary*
NATIONAL BUREAU OF STANDARDS • A. V. Astin, *Director*

Bibliography on Nitrogen 15

Margaret W. Chapman and Herbert P. Broida

National Bureau of Standards Circular 575

Issued October 1, 1956

For sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.
Price 15 cents

Preface

This literature survey, concerning the nitrogen isotope N^{15}, was made as an aid to a study to extend the optical spectroscopic method of isotope analysis to the measurement of N^{15}/N^{14} ratios. It is not intended to be a complete bibliography of this extensive field. For convenience, the bibliography is grouped according to subjects. Therefore, some references appear in more than one group.

A. V. Astin, *Director.*

Contents

381951—56

Bibliography on Nitrogen 15*

M. W. Chapman and H. P. Broida

References to the literature on nitrogen 15 that has appeared from 1919 to 1952, inclusive, with a few later references, are given. The citations relate to the abundance of N^{15} naturally occurring, its physical properties, methods of concentrating it, methods of N^{15}/N^{14} measurement, and the synthesis and uses of N^{15} compounds.

1. Natural Abundance of N^{15}

Since 1929, when N^{15} was discovered by Naude in the band spectra of NO [1(19)],[1] there have been many measurements of the abundance ratio (N^{14}/N^{15}) of nitrogen isotopes. A summary of values measured for the abundance ratio and of listings in tables of isotopes from 1930 through 1952 is given in table 1. The table was compiled from the bibliography, section 4.1. It shows the date when each value was reported and the reference.

In 1937 the Committee on Atoms of the International Union of Chemistry made its first report [1(2)]. N^{15} was listed as having an abundance of 0.38 percent. Each following report of this committee gave the same value through the sixth report in 1942 [1(3)], which listed only changes to be made in the previous report. This value was still quoted as the standard when Schaffer [1(29)] issued A New Table of Isotopes in 1949. However, the table by Hollander, et al. [1(11)], based on values recorded in the literature or by private communication through approximately December 1952, gives a new value of 0.365 percent as measured by Nier [1(21)] in 1950. This value is the one presently used by the authers.

Apparently plants and animals do not fractionate nitrogen isotopes during anabolism and catabolism as is the case with hydrogen in plants.[2] [3] This is the conclusion that Schoenheimer and

TABLE 1. N^{15} *relative abundance*

Year	Source	Reference	Abundance		Comments
			(N^{14}/N^{15})	$\left(\frac{N^{15}}{N^{15}+N^{14}}\right)\times 100$	
1930	Naude	1(20)	700	0. 143	Estimate.
1930	Herzberg	1(10)	800	. 125	Estimate.
1931	Birge and Menzel	1(8)	320	. 312	Calculation using Mecke's values for oxygen isotopes and bringing the writer's figure for N^{14} mass into agreement with the chemical atomic weight.
1931	Urey and Murphy	1(38)	347	. 288	From ratio of $N^{15}O^{16}$ to $N^{14}O^{18}$ from measurement of absorption bands and assuming Mecke's value of 630 for ratio of O^{16} to O^{18}.
1932	Murphy and Urey	1(18)	346	. 289	Same as above, but more measurements.
1934	Vaughan, Williams, and Tate.	1(39)	265	. 377	Direct measurement of ratio, using mass spectrometer.
1935	Wahl, Huffman, and Hipple.	1(40)	265	. 38	Confirmed measurement of Vaughan, etc.
1937	Aston, et al	1(2)	------	. 38	International table of stable isotopes.
1939	Schoenheimer and Rittenberg.	1(30)	------	. 368	Referred to as the natural abundance.
1949	Schaffer	1(29)	------	. 38	Table of isotopes.
1950	White and Yagoda	1(42)	------	. 371	Refers to Vaughan 0.376 as natural abundance but measured 0.371 for air.
1950	Nier	1(21)	273	. 366	Ratio measurement from room air directly, using mass spectrometer.
1950	Nier	1(21)	274. 5	. 364	Recomputation of data of Urey and Murphy on assumption $O^{16}/O^{18}=500$.
1952	Palmer	1(24)	264	. 379	Not a precision measurement.
1953	Hollander	1(11)	------	. 365	Quotes value by Nier in 1950.

*The work covered by this Circular was sponsored by the U. S. Atomic Energy Commission.

[1] Figures in brackets are the subsection and literature reference numbers in the bibliography, section 4, beginning on page 3.

[2] T. Titani and M. Harada, The concentration of heavy isotopes in carbohydrates, Bul. Chem. Soc. Japan **10**, 205 (1935).

[3] E. W. Washburn and E. R. Smith, The isotopic fractionation of water by physiological processes, Science **79**, 188 (1934).

Rittenberg reached in 1939, based on the evidence of equal distribution of nitrogen isotopes in air and organic compounds [1(30)]. The only exception noted was an increase in N^{15} concentration by more than 50 percent as found by White and Yagoda in 1950 for very old radioactive minerals [1(42)]. They later suggested the explanation [1(45)] that nitrogen may have been a component of the minerals at the time of formation, and that the ratio of N^{15} to N^{14} increased as a result of more rapid diffusion of the lighter isotope. The possibility of such an increase also being true for chemically bound nitrogen in crude oil and coal deposits was investigated in 1951 by Smith and Hudson [1(32)], but no increase over atmospheric nitrogen isotopic content was found.

Isotopic separation takes place in the atmosphere due to settling in the earth's gravitational field, and has been detected above 40 kilometers. This possibility was pointed out by Lindemann and Aston [1(16)] in 1919, and was tested in 1948 and 1950 by McQueen [1(17)] when air samples were collected from the altitude range 40 to 60 kilometers and were analyzed for percent separation using a 60° Nier-type mass spectrometer. The method of analysis compared the ratio of the intensities of the $N^{14}N^{14}$ molecular ion beam (mass No. 28) to that of the $N^{14}N^{15}$ molecular ion beam (mass No. 29) in the sample to that in a standard sample collected at ground level.

2. Methods of Concentrating N^{15}

The usual methods of separating and concentrating isotopes [2(4)] are chemical exchange, gaseous diffusion and mass diffusion, which are more frequently used for large scale production, and gas centrifuge and thermal diffusion, which are more frequently used for small scale production. Among other methods that have been used for separation of nitrogen isotopes are the electric discharge and electrolysis. Two reports giving general descriptions and comparisons of different methods of separating and concentrating isotopes were published in 1947 by Benedict [2(4)] and in 1948 by Vick [2(51)].

The method of obtaining the highest concentration of N^{15} noted in the literature is that of Clusius, who inserted an electric discharge in the gas stream of a thermal diffusion column, thereby dissociating the molecules into atomic nitrogen. In 1947 he and Becker used this method to isolate $N^{14}N^{15}$ to 98.9 percent [2(9)] and in 1950 he used it to produce 99.8 percent pure $N^{15}N^{15}$ [2(7)].

3. Methods of Measurement

Methods of measurement of N^{15} include the mass spectrometer, gas density, crystal suspension, microwave spectroscopy, and optical spectroscopy.

The bibliography listed in section 4.3 includes some articles that give little information about the method of measurement but do state the accuracy obtained or the size of sample required.

No evaluation was made of the different methods of measurement on basis of precision, reproducibility, or accuracy obtained because of the numerous difficulties involved. Seldom are these values given in units that allow comparison with another method of measurement. Also the description of how the data were analyzed to obtain the value or an actual tabulation of the data is seldom complete enough for recalculation. Average deviation, for instance, has no absolute significance as does standard deviation of the mean or coefficient of variation.[4] In general, however, the accuracy of an isotope measurement depends on the isotope concentration of the sample being analyzed and the precision of the instrument. Nier in 1948 [3(46)] points out that absolute ratios are not as important in tracer work as are changes in the ratio as compared to standards. Thus some sources of error are automatically eliminated and a higher degree of accuracy is obtainable.

The mass spectrometer is the instrument most widely used for analyzing N^{15}/N^{14} ratios. It requires that the sample be in gaseous form, usually N_2. This is not the form in which the isotope is introduced into most experiments, nor the form in which it is usually reclaimed. The chemical procedure for changing the sample to gaseous form was outlined by Sprinson and Rittenberg [3(40)] in 1949.

Winter [3(47)] published in 1948 a description of the operation and history of the mass spectrometer. He states that for an abundance ratio of 1 percent or greater, an accuracy of 1 percent can be obtained with practice and, using extreme care and expert personnel, an accuracy of 0.3 percent can be obtained. The time of measurement is about 45 min per sample, which could be reduced somewhat by using an automatic recorder. Brown in 1951 [3(4)], reporting on his work with adenine, states that the size of N_2 sample preferred was about a milligram. Rittenberg [3(30)], 1942, found that the mass spectrometer he used could detect 1 part in 10,000 of 50 atom percent N^{15} diluted with normal urea, and it was felt that results with the mass spectrometer were not affected by the purity of the sample. Later it was realized, however, that CO and NO present either in the sample or in the decomposition products of the ion beam can cause errors difficult to detect [3(14)].

Roberts [3(33)] published in 1948 a report on the gas density, liquid density, and thermal conductivity methods of isotope analysis. He points out that the mass spectrometer is expensive and requires a high degree of operational skill and that the alternate methods of analysis that he describes, although they may be incapable of the accuracy of the mass spectrometer and may demand exceptional care in the chemical purification of samples, are nevertheless relatively cheap to initiate and involve techniques well within the

[4] W. J. Youden, Statistical methods for chemists (John Wiley & Sons, Inc., New York, N. Y., 1951).

range of the chemist. The measurement of isotope ratios by atomic weights is time-consuming, requires large samples, and is not sensitive to small variations in concentration.

Research on the development of the microwave spectrograph for analysis of nitrogen 15 in ammonia was reported in 1950 by Southern, et al. [3(39)]. N^{15} could be determined to approximately 3 percent of its concentration in the range 0.38 percent to 4.5 percent. The minimum sample size was 0.00015 mole of gas, which was mostly recoverable. A standard curve was used for calibration. Each total analysis required 2.5 hr, including 20 to 30 minutes for the analysis itself and 2 hr between samples.

The optical spectroscopic method of N^{15} analysis is the one in which this laboratory is primarily interested. Following is a brief résumé of the work done on it as noted in the literature.

In the discovery of N^{15} and measurement of its abundance ratio, Naude [3(23,24)] and Urey and Murphy [3(44)] in 1929 and 1931 used the continuous spectrum from a hydrogen lamp, passed the light through NO in a variable pressure tube, and photographed the isotopic separation with a Hilger E1 quartz spectrograph. In 1939 Kruger [3(19)], in order to follow the progress of his work on concentrating N^{15}, excited N bands with an electrodeless discharge and used the isotope separation of band heads as a guide. Only rough accuracy was needed. In 1947 Clusius and Becker [3(7)], also following the progress of isotope concentration, excited N_2 in a hollow cathode tube and observed the (2,0) band of the 2d positive system of N_2 at 2977.5 A. In 1948 Holmes [3(15)], in measuring atomic nitrogen isotope shifts, obtained high intensity and eliminated most background N_2 bands by exciting a mixture of N_2 in He with an electrodeless discharge of about 30 mc. In order to get the lines sharp enough to resolve the isotope structure, the cross section of the tube was made a thin rectangle and the discharge was immersed in liquid nitrogen. The lines were then observed with a Hilger E478 spectrograph in series with a Fabry-Perot interferometer. In 1950 Hoch and Weisser [3(14)] excited N_2 gas in an electrodeless discharge tube of pyrex at 3 to 5 mm pressure. They were developing a method insensitive to most impurities, particularly those undesirable for the mass spectrometer, as well as one that works with a much smaller sample. They observed the (1,0 and 0,1) violet emission bands of the 2d positive system of nitrogen with a Hilger spectrograph. From the plates obtained, intensities were measured with a Moll microphotometer and the relative accuracy obtained was 2 to 3 percent. In 1952 Dieke [3(8)] obtained a patent for a method in which the nitrogen is incorporated into cesium uranyl nitrate to enhance the spectral line separation and a fluorescence spectrum is produced with an arc light. This is observed with a light-sensitive tube to obtain an electric current as indication of the relative amount of N^{15} present.

4. Bibliography

4.1. Natural Abundance and Physical Properties

(1) F. W. Aston, Mass spectra and isotopes, p. 130 (Longmans, Green & Co., New York, N. Y., 1942).

(2) F. W. Aston, N. Bohr, O. Hahn, W. D. Harkins, and G. Urbain, First report of the Committee on Atoms of the International Union of Chemistry, J. Chem. Soc., (London) 1910 (1937).

(3) F. W. Aston, International table of stable isotopes. Nature **150,** 515 (1942).

(4) L. Aujeszky, Isotopes in the atmosphere, Idöjárás (in Hungarian) **53,** 289 (1949) [also Nuclear Sci. Abstracts **4,** 382 (1950)].

(5) K. T. Bainbridge and E. B. Jordan, Atomic masses of hydrogen, helium, carbon and nitrogen isotopes, Phys. Rev. **51,** 384 (1937).

(6) H. Bethe, Masses of light atoms from transmutation data, Phys. Rev. **47,** 633 (1935).

(7) J. Bigeleisen and L. Friedman, The infra-red spectra of $N^{15}N^{14}O^{16}$ and $N^{14}N^{15}O^{16}$. Some thermodynamic properties of the isotopic N_2O molecules, J. Chem. Phys. **18,** 1656 (1950).

(8) R. T. Birge and D. H. Menzel, The relative abundance of the oxygen isotopes and the basis of the atomic weight system, Phys. Rev. **37,** 1669 (1931).

(9) R. W. Cole, Exchange magnetic moments of nuclei with almost closed shells of nucleons, Phys. Rev. **89,** 883 (1953).

(10) G. Herzberg, The nitrogen isotope of mass 15, Z. Physik. Chem. (in German) **B9,** 43 (1930).

(11) J. M. Hollander, I. Perlman and G. T. Seaborg, Table of isotopes, Revs. Mod. Phys. **25,** 469 (1953).

(12) E. Ingerson, Nonradiogenic isotopes in geology: a review, Bul. Geol. Soc. Am. **64,** 301 (1953).

(13) I. Kirshenbaum, The vapor pressure and heat of vaporization of N^{15}, J. Chem. Phys. **9,** 660 (1941).

(14) H. Krüger, Enrichment of N^{15} isotope and spectroscopic study of N^{15}, Naturwissenschaften (in German) **26,** 445 (1938).

(15) H. Krüger, The enriching of the N^{15} isotope and some spectroscopic investigations on N^{15}, Z. Physik **111,** 467 (1939).

(16) F. A. Lindemann and F. W. Aston, The possibility of separating isotopes, Phil. Mag. **37,** 523 (1919).

(17) J. H. McQueen, Isotopic separation due to settling in the atmosphere, Phys. Rev. **80,** 100 (1950).

(18) G. M. Murphy and H. C. Urey, The relative abundance of the nitrogen and oxygen isotopes, Phys. Rev. **41,** 141 (1932).

(19) S. M. Naudé, An isotope of nitrogen, mass 15, Phys. Rev. **34,** 1498 (1929).

(20) S. M. Naudé, The isotopes of nitrogen, mass 15, and oxygen, mass 18 and 17, and their abundances, Phys. Rev. **36,** 333 (1930).

(21) A. O. Nier, A redetermination of the relative abundances of the isotopes of carbon, nitrogen, oxygen, argon, and potassium, Phys. Rev. **77,** 789 (1950).

(22) K. Ogata and H. Matsuda, Masses of light atoms, Phys. Rev. **89,** 27 (1953).

(23) K. Ogata and H. Matsuda, Substandards of atomic mass, Natl. Bur. Standards Circ. 522, 59 (1953).

(24) G. H. Palmer, Isotope abundance measurements, Mass Spectrometry, 108 (1952).

(25) W. G. Proctor, F. C. Yu, On the nuclear magnetic moments of several stable isotopes, Phys. Rev. **81,** 20 (1951).

(26) W. G. Proctor and F. C. Yu, The magnetic moments of Mn^{55}, Co^{59}, Cl^{37}, N^{15} and N^{14}, Phys. Rev. **77,** 716 (1950).

(27) D. Rittenberg, A. S. Keston, F. Rosebury, and R. Schoenheimer, Studies in protein metabolism. II. The determination of nitrogen isotopes in organic compounds, J. Biol. Chem. **127,** 291 (1939).

(28) U. Sborgi, Presence of krypton and xenon, besides other inert gases, in the fumaroles of hot borax-bearing Tuscan springs. Geochemical aspects of the composition of the fumaroles, Mem. Accad. Italia, Classe Sci. Fis., Mat. Nat. **8,** 533 (1937).
(29) J. J. Schaffer, A new table of isotopes, Bol. Fac. Ing. Montevideo (in Spanish) **3,** 355 (1949).
(30) R. Schoenheimer and D. Rittenberg, Studies in protein metabolism. I. General considerations in the application of isotopes to the study of protein metabolism. The normal abundance of nitrogen isotopes in amino acids, J. Biol. Chem. **127,** 285 (1939).
(31) G. T. Seaborg, Table of isotopes, Revs. Mod. Phys. **16,** 1 (1944).
(32) P. V. Smith, Jr. and B. E. Hudson, Jr., Abundance of N^{15} in the nitrogen present in crude oil and coal, Science **113,** 577 (1951).
(33) H. G. Thode, The vapor pressures, heats of vaporization and melting points of N^{14} and N^{15} ammonias, J. Am. Chem. Soc. **62,** 581 (1940).
(34) H. G. Thode, Variations in abundances of isotopes in nature, Research (London) **2,** 154 (1949).
(35) H. von Ubisch, The mass spectrometer and its use II, Fra Fysik Verden No. **4,** 229 (1949).
(36) H. C. Urey, The thermodynamic properties of isotopic substances, J. Chem. Soc. (London), 562 (1947).
(37) H. C. Urey and L. J. Greiff, Isotopic exchange equilibria, J. Am. Chem. Soc. **57,** 321 (1935).
(38) H. C. Urey and G. M. Murphy, The relative abundance of N^{14} and N^{15}, Phys. Rev. **38,** 575 (1931).
(39) A. L. Vaughan, J. H. Williams, and J. T. Tate, Isotopic abundance ratios of C, N, A, Ne, and He, Phys. Rev. **46,** 327 (1934).
(40) M. H. Wahl, J. F. Huffman, and J. A. Hipple, Jr., An attempted concentration of the heavy nitrogen isotope, J. Chem. Phys. **3,** 434 (1935).
(41) K. Way, L. Fano, M. R. Scott, and K. Thew, Nuclear data. A collection of experimental values of half lives, radiation energies, relative isotopic abundances, nuclear moments and cross sections, Natl. Bur. Standards Circ. 499, 12 (1950).
(42) W. C. White and H. Yagoda, Abundance of N^{15} in in the N occluded in radioactive minerals, Science **111,** 307 (1950).
(43) D. W. Wilson, A. O. C. Nier, and S. P. Reimann, Preparation and measurement of isotopic tracers (J. W. Edwards, Ann Arbor, Michigan, 1948).
(44) R. W. Wood and G. H. Dieke, The nuclear spin of N^{15}, J. Chem. Phys. **6,** 908 (1938).
(45) H. Yagoda and W. C. White, Ratio of N^{15}/N^{14} in gases occluded in radioactive minerals, Phys. Rev. **78,** 330 (1950).

4.2. Methods of Concentrating

(1) J. W. Beams and F. B. Haynes, The separation of isotopes by centrifuging, Phys. Rev. **50,** 491 (1936).
(2) E. W. Becker and H. Baumgärtel, Concentration of N^{15} by means of the chemical exchange method, Angew. Chem. (in German) [A] **59,** 88 (1947).
(3) E. W. Becker and H. Baumgärtel, The enrichment of N^{15} with a two-fold exchange arrangement, Z. Naturforsch. (in German) **1,** 514 (1946).
(4) M. Benedict, Multistage separation processes, Trans. Am. Inst. Chem. Engrs. **43,** 41 (1947).
(5) H. Brown, Thermal separation ratios calculated from viscosity data, Phys. Rev. **57,** 242 (1940).
(6) K. Clusius, Separation of isotopes by thermal diffusion, Review of Programme, IUPAC Plenary Lectures, Stockholm and Uppsala (in German), 53 (1953).
(7) K. Clusius, Separation tube. IX. Preparation of pure heavy nitrogen N^{15}, Helv. Chim. Acta (in German) **33,** 2134 (1950).
(8) K. Clusius and E. Becker, Atomic-weight determination of N^{15}-rich nitrogen by means of the gas-density balance, Z. anorg. u. allgem. Chem. **251,** 92 (1943).
(9) K. Clusius and E. W. Becker, The separation tube. VI. Isolation of the mixed molecule $N^{14}N^{15}$, Z. Naturforsch. (in German) [A] **2,** 154 (1947).
(10) K. Clusius, E. Becker, and H. Lauckner, Enrichment of N^{15} by exchange, Sitzber. Math. Naturw. Abt. Bayer Akad. Wiss. Munchen 145 (1941).
(11) K. Clusius and G. Dickel, New Process for separation of gas mixtures and isotopes, Naturwissenschaften (in German) **26,** 546 (1938).
(12) K. Clusius and G. Dickel, The separation tube. I. Principles of a new method of gas and isotope separation by thermal diffusion, Z. physik. Chem. [B] **44,** 397 (1939).
(13) K. Clusius, G. Dickel, and E. Becker, Pure oxygen isotope O_2^{18} and nitrogen isotope $N^{14}N^{15}$, Naturwissenschaften (in German) **31,** 210 (1943).
(14) A. N. Davenport and E. R. S. Winter, Diffusion properties of gases. V. Thermal diffusion of carbon monoxide, nitrogen and methane, Trans. Faraday Soc. **47,** 1160 (1951).
(15) E. David, Separation of isotopes with continuously working separation tubes, Z. Physik (in German) **134,** 377 (1953).
(16) H. Eyring and A. Sherman, Theoretical considerations concerning the separation of isotopes, J. Chem. Phys. **1,** 345 (1933).
(17) I. G. Farbenind. A.-G. (Alvin Krauss, inventor), Isotopes of oxygen and nitrogen, German Patent No. 632,071 (July 2, 1936).
(18) R. Fleischmann, Concentration of N^{15} by the separating-tube process of Clusius and Dickel, Physik. Z. (in German) **41,** 14 (1940).
(19) W. Groth and P. Harteck, Separation of isotopes by gaseous diffusion, Z. Physik. Chem. (in German) **199,** 114 (1952).
(20) G. Hertz, A method of separating isotope mixtures by diffusion through streaming mercury vapor, Z. Physik (in German) **91,** 810 (1934)
(21) D. A. Hutchison, Efficiency of the electrolytic separation of N isotopes, Phys. Rev. **75,** 1303 (1949).
(22) D. A. Hutchison, Efficiency of the electrolytic separation of potassium isotopes, J. Chem. Phys. **14,** 401 (1946).
(23) R. C. Jones and W. H. Furry, Calculation of the thermal diffusion constant from viscosity data, Phys. Rev. **57,** 547 (1940).
(24) R. C. Jones and W. H. Furry, The separation of isotopes by thermal diffusion, Revs. Mod. Phys. **18,** 151 (1946).
(25) I. Kirshenbaum, J. S. Smith, T. Crowell, J. Graff, and R. McKee, Separation of the nitrogen isotopes by the exchange reaction between ammonia and solutions of ammonium nitrate, J. Chem. Phys. **15,** 440 (1947).
(26) H. Krüger, Enrichment of N^{15} isotope and spectroscopic study of N^{15}, Naturwissenschaften (in German) **26,** 445 (1938).
(27) H. Krüger, The enriching of the N^{15} isotope and some spectroscopic investigations on N^{15}, Z. Physik **111,** 467 (1939)
(28) A. N. Murin, Thermodiffusion method for the separation of isotopes, Uspekhi Khim. **10,** 671 (1941).
(29) R. Nakane, Concentration of heavy nitrogen isotope (supplement), Repts. Sci. Research Inst. (Japan) **28,** 413 (1952)
(30) R. Nakane, Concentration of heavy nitrogen isotope—concentrating efficiency of the packed column and its liquid hold-up determined by radioactive cobalt, Repts. Sci. Research Inst. (Japan) **28,** 276 (1952).
(31) E. Ogawa, Mechanism of isotopic exchange reactions, Bul. Chem. Soc. Japan **11,** 425 (1936).

(32) E. Ogawa, The isotopic separation of oxygen, chlorine bromine and nitrogen by chemical methods, Bul. Chem. Soc. Japan **11,** 428 (1936).
(33) E. H. Riesenfeld, Experiments on the separation of isotopes, Arkiv. Kemi, Mineral. Geol. [A] **13,** No. 16, 11 pp. (1939).
(34) I. Roberts, H. G. Thode, and H. C. Urey, The concentration of C^{13} by chemical exchange, J. Chem. Phys. **7,** 137 (1939).
(35) W. Spindel, The concentration of nitrogen^{15} by countercurrent gaseous exchange, Univ. Microfilms, Ann Arbor, Mich., Publ. No. 4616, [also Dissertation abstracts **13,** 18 (1953)].
(36) T. Sugimoto, Concentration and application of N^{15}, Kagaku (Science) Japan (in Japanese) **19,** 245 (1949).
(37) A. Sugimoto, R. Nakane, R. Shibata, T. Watanabe, S. Motonaga, and S. Isomura, Concentration of the heavy nitrogen isotope, I, Repts. Sci. Research Inst. (Japan) **26,** 1 (1950).
(38) A. Sugimoto, R. Nakane, and T. Watanabe, Concentration of N^{15} by chemical exchange reaction method, Bul. Chem. Soc. Japan (in English) **24,** 153 (1951).
(39) A. Sugimoto, R. Nakane, T. Watanabe, T. Matsuo, S. Isomura, and M. Morishita, Concentration of heavy nitrogen, II, Repts. Sci. Research Inst. (Japan) **27,** 19 (1951).
(40) T. I. Taylor and W. Spindel, Concentration of N^{15} in a gaseous exchange column, J. Chem. Phys. **16,** 635 (1948).
(41) T. I. Taylor and H. C. Urey, Fractionation of the lithium and potassium isotopes by chemical exchange with zeolites, J. Chem. Phys. **6,** 429 (1938)
(42) T. I. Taylor and H. C. Urey, The electrolytic and chemical exchange methods for the separation of the lithium isotopes, J. Chem. Phys. **5,** 597 (1937).
(43) H. G. Thode, Preparation of stable tracers, Proc. Conf. on Nuclear Chem., Chem. Inst. Canada (Ottawa), p. 127 (1947).
(44) H. G. Thode, Separation of stable isotopes by chemical methods, Natl. Research Council, Can., Atomic Energy Project, Div. of Research, NRC No. 1681, 16 pp. (1947).
(45) H. G. Thode, J. E. Gorham, and H. C. Urey, The concentration of N^{15} and S^{34}, J. Chem. Phys. **6,** 296 (1938).
(46) H. G. Thode and H. C. Urey, The further concentration of N^{15}, J. Chem. Phys. **7,** 34 (1939).
(47) H. C. Urey, Separation of Isotopes, Repts. Prog. in Phys. **6,** 48 (1940).
(48) H. C. Urey and A. H. W. Aten, Jr., Chemical differences between nitrogen isotopes, Phys. Rev. **50,** 575 (1936).
(49) H. C. Urey, M. Fox, J. R. Huffman, and H. G. Thode, Concentration of N^{15} by a chemical exchange reaction, J. Am. Chem. Soc. **59,** 1407 (1937).
(50) H. C. Urey, J. R. Huffman, H. G. Thode, and M. Fox, Concentration of N^{15} by chemical methods, J. Chem. Phys. **5,** 856 (1937).
(51) F. A. Vick, Recent work with stable isotopes and mass spectrographs, Science Progr. **36,** 78 (1948).
(52) M. H. Wahl, J. R. Huffman, and J. A. Hipple, Jr., An attempted concentration of the heavy nitrogen isotope, J. Chem. Phys. **3,** 434 (1935).
(53) L. Waldmann, The theory of isotope separation by exchange reactions, Naturwissenschaften (in German) **31,** 205 (1943).
(54) D. W. Wilson, A. O. C., Nier and S. P. Reimann, Preparation and measurement of isotopic tracers (J. W. Edwards, Ann Arbor, Michigan, 1948).
(55) D. E. Wooldridge and F. A. Jenkins, Enrichment of nitrogen in the isotope N^{15}, Phys. Rev. **49,** 704 (1936).
(56) D. E. Wooldridge and W. R. Smythe, The separation of gaseous isotopes by diffusion, Phys. Rev. **50,** 233 (1936).

4.3. Methods of Measurement

(1) V. Allfrey and A. E. Mirsky, Incorporation of N^{15}-glycine by avian erythrocytes and reticulocytes in vivo, J. Gen. Physiol. **35,** 841 (1952).
(2) F. W. Aston, Mass Spectra and isotopes, p. 130 (Longmans, Green & Co., New York, N. Y., 1942).
(3) R. Bentley, The use of stable isotopes in biological chemistry, Mass Spectrometry, pp. 117–26 (1950).
(4) G. B. Brown, Precursors of nucleic acids, J. Cellular Comp. Physiol. **38** supp., 121 (1951).
(5) R. H. Burris, F. J. Eppling, H. B. Wahlin, and P. W. Wilson, Detection of nitrogen fixation with isotopic nitrogen, J. Biol. Chem. **148,** 349 (1943).
(6) K. Clusius and E. Becker, Atomic-weight determination of N^{15}-rich nitrogen by means of the gas-density balance, Z. anorg. u. allgem. Chem. **251,** 92 (1943).
(7) K. Clusius and E. W. Becker, The separation tube. VI. Isolation of the mixed molecule $N^{14}N^{15}$, Z. Naturforsch. (in German) [A] **2,** 154 (1947).
(8) G. H. Dieke, Method of isotope analysis, U. S. Patent No. 2,585,901 (Feb. 1952).
(9) R. A. Friedel, A. G. Sharkey, Jr., J. L. Shultz, and C. R. Humbert, Mass spectrometric analysis of mixtures containing nitrogen dioxide, Anal. Chem. **25,** 1314 (1953).
(10) J. George, Decrease of nitrogen^{15}/nitrogen^{14} ratio measurement as a function of pump-out time—for Nier-type isotope-ratio mass spectrometer, Anal. Chem. **24,** 1662 (1952).
(11) A. V. Grosse, S. G. Hindin, and A. D. Kirshenbaum, Elementary isotopic analysis. Determination of oxygen, carbon and nitrogen in organic compounds, Anal. Chem. **21,** 386 (1949).
(12) G. Herzberg, Nitrogen isotope of mass 15, Z. Physik. Chem. (in German) [B] **9,** 43 (1930).
(13) S. G. Hindin and A. V. Grosse, Determination of nitrogen in organic materials, Application of the mass spectrometer, Anal. Chem. **20,** 1019 (1948).
(14) M. Hoch and H-R Weisser, Reactions with N^{15}. II. A spectroscopic micromethod for determination of N^{15}, Helv. Chim. Acta (in German) **33,** 2128 (1950).
(15) J. R. Holmes, Isotope shifts in some previously unexplored lines of nitrogen, Phys. Rev. **73,** 539 (1948).
(16) J. A. Hunter, R. W. Stacy, and F. A. Hitchcock, Mass spectrometer for continuous gas analysis, Rev. Sci. Instr. **20,** 333 (1949).
(17) D. A. Hutchison, Efficiency of the electrolytic separation of potassium isotopes, J. Chem. Phys. **14,** 401 (1946).
(18) A. D. Kirshenbaum, S. G. Hindin and A. V. Grosse, Elementary isotopic analysis: Determination of nitrogen, Nature **160,** 187 (1947).
(19) H. Kruger, The enriching of the N^{15} isotope and some spectroscopic investigations on N^{15}, Z. Physik **111,** 467 (1939).
(20) J. Mattauch, Double focusing mass spectrograph and the masses of N^{15} and O^{18}, Phys. Rev. **50,** 617 (1936).
(21) J. Mattauch, Stable isotopes, their measurement and application, Angew. Chem. (in German) [A] **59,** 37 (1947).
(22) E. Moles, The precision obtainable with the method of limiting densities, Arch. sci. phys. et nat. **20,** 59 (1938).
(23) S. M. Naudé, An isotope of nitrogen, mass 15, Phys. Rev. **34,** 1498 (1929).
(24) S. M. Naudé, The isotopes of nitrogen, mass 15, and oxygen, mass 18 and 17, and their abundances, Phys. Rev. **36,** 333 (1930).
(25) A. O. Nier, A mass spectrometer for isotope and gas analysis, Rev. Sci. Instr. **18,** 398 (1947).
(26) A. O. Nier, A mass spectrometer for routine isotope abundance measurements, Rev. Sci. Instr. **11,** 212 (1940).

(27) G. H. Palmer, Isotope abundance measurements, Mass Spectrometry, 108 (1952).
(28) W. Paul, Mass spectrometer for determination of isotope ratios, Z. Physik (in German) **124,** 244 (1948).
(29) Process and Instruments Company, Mass spectrometer, Rev. Sci. Instr. **19,** 124 (1948).
(30) D. Rittenberg, Some applications of mass spectrometric analysis to chemistry, J. Appl. Phys. **13,** 561 (1942).
(31) D. Rittenberg and G. L. Foster, A new procedure for quantitative analysis by isotope dilution, with application to the determination of amino acids and fatty acids, J. Biol. Chem. **133,** 737 (1940).
(32) D. Rittenberg, A. S. Keston, F. Rosebury, and R. Schoenheimer, Studies in protein metabolism. II. The determination of nitrogen isotopes in organic compounds, J. Biol. Chem. **127,** 291 (1939).
(33) E. R. Roberts, The measurement of stable isotope abundance ratios, Analyst **73,** 657 (1948).
(34) M. A. Rothenberg, D. B. Sprinson, and D. Nachmansohn, Site of action of acetylcholine, J. Neurophysiol. **11,** 111 (1948).
(35) R. Schoenheimer and D. Rittenberg, Studies in protein metabolism. I. General consideration in the application of isotopes to the study of protein metabolism. The normal abundance of nitrogen isotopes in amino acids, J. Biol. Chem. **127,** 285 (1939).
(36) R. Schoenheimer, D. Rittenberg, G. L. Foster, A. S. Keston, and S. Ratner, Application of the nitrogen isotope N^{15} for the study of protein metabolism, Science **88,** 599 (1938).
(37) E. Schumacher, H. Mollet, and K. Clusius, Gas-density measurements with the suspension balance, Helv. Chim. Acta (in German) **33,** 2117 (1950).
(38) S. Soloway, Reference standard for mass spectrometric analysis of nitrogen, Anal. Chem. **23,** 386 (1951).
(39) A. L. Southern, H. W. Morgan, G. W. Keilholtz, and W. V. Smith, Isotopic determination of nitrogen and carbon by means of a microwave spectrograph, Anal. Chem. **23,** 1000 (1951) [also Phys. Rev. **78,** 639 (1950)].
(40) D. B. Sprinson and D. Rittenberg, The rate of utilization of ammonia for protein synthesis, J. Biol. Chem. **180,** 707 (1949).
(41) R. C. Taylor, R. A. Brown, W. S. Young, and C. E. Headington, The mass spectrometer in organic chemical analysis, Anal. Chem. **20,** 396 (1948).
(42) H. G. Thode, R. L. Graham, and J. A. Ziegler, A mass spectrometer and the measurement of isotope exchange factors, Can. J. Research [B] **23,** 40 (1945).
(43) H. von Ubisch, The mass spectrometer and its use. I. Fra Fysik. Verden **3,** 170 (1949).
(44) H. C. Urey and G. M. Murphy, The relative abundance of N^{14} and N^{15}, Phys. Rev. **38,** 575 (1931).
(45) F. A. Vick, Recent work with stable isotopes and mass spectrographs, Science Progr. **36,** 78 (1948).
(46) D. W. Wilson, A. O. C. Nier, and S. P. Reiman, Preparation and measurement of isotopic tracers, (J. W. Edwards, Ann Arbor, Michigan, 1948).
(47) E. R. S. Winter, Measurement of abundance ratios of non-radioactive isotopes, Analyst **73,** 653 (1948).

4.4. Use

(1) R. Abrams, E. Hammarsten, P. Reichard, and E. Sperber, Tracer studies of N assimilation in yeast, J. Gen. Physiol. **32,** 271 (1949).
(2) R. Abrams, E. Hammarsten, and D. Shemin, Glycine as a precursor of purines in yeast, J. Biol. Chem. **173,** 429 (1948).
(3) C. F. H. Allen and C. V. Wilson, Use of N^{15} as a tracer element in chemical reactions. The mechanism of the Fischer indole synthesis, J. Am. Chem Soc. **65,** 611 (1943).
(4) V. Allfrey and A. E. Mirsky, Incorporation of N^{15}-glycine by avian erythrocytes and reticulocytes in vivo, J. Gen. Physiol. **35.** 841 (1952).
(5) A. R. Amell and F. Daniels, Kinetics of the exchange of nitrogen^{15} between $N^{15}O_2$ and N_2O_5, J. Am. Chem. Soc. **74,** 6209 (1952).
(6) E. P. Anderson and S. E. G. Aqvist, A double precursor study of nucleic acid turnover in normal and regenerating liver, J. Biol. Chem. **202,** 513 (1953).
(7) T. F. Andreeva and E. G. Plyshevskaya, Formation of protein in the process of photosynthesis with application of nitrogen^{15} (in Russian), Doklady Akad. Nauk S. S. S. R. **87,** 301 (1952).
(8) M. H. Aprison and R. H. Burris, Time course of fixation of N by excised soybean nodules, Science **115,** 264 (1952).
(9) M. H. Aprison, W. E. Magee, and R. H. Burris, Nitrogen fixation by excised soy bean root nodules, J. Biol. Chem. **208,** 29 (1954).
(10) S. E. G. Aqvist, Amino acid interrelationships during growth, studied with N^{15}-labeled glycine in regenerating rat liver, Acta Chem. Scand. **5,** 1065 (1951).
(11) S. E. G. Aqvist, Metabolic interrelationships among amino acids studied with isotopic N, Acta Chem. Scand. **5,** 1046 (1951).
(12) H. R. V. Arnstein and A. Neuberger, Hippuric acid synthesis in the rat, Biochem. J. (London) **50,** 154 (1951).
(13) H. Arvidson, N. A. Eliasson, E. Hammarsten, P. Reichard, H. von Ubisch, and S. Bergström, Orotic acid as a precursor of pyrimidines in the rat, J. Biol. Chem. **179.** 169 (1949).
(14) H. S. Bailey and J. E. Christian, The distribution of nitrogen^{15} in rat tissues following the intraperitoneal administration of nitrogen-labeled urethan, J. Am. Pharm. Assoc. **41,** 517 (1952).
(15) W. V. Bartholomew, L. B. Nelson, and C. H. Werkman, The use of the nitrogen isotope N^{15} in field studies with oats, Agron. J. **42,** 100 (1950).
(16) P. D. Bartlett, O. H. Gaebler, and B. Cady, The mechanism of N storage VI. Rate of protein synthesis and size of the N pool, J. Biol. Chem. **196,** 1 (1952).
(17) A. Bendich, S. S. Furst, and G. B. Brown, On the role of the 2,6-diaminopurine in the biosynthesis of nucleic acid guanine, J. Biol. Chem. **185,** 423 (1950).
(18) A. Bendich, W. D. Geren, and G. B. Brown, Study of the metabolism of 2,4-diaminopyrimidine, J. Biol. Chem. **185,** 435 (1950).
(19) J. D. Benedict, P. H. Forsham, and D. Stetten, Jr., Metabolism of uric acid in the normal and gouty human studied with the aid of isotopic uric acid, J. Biol. Chem. **181,** 183 (1949).
(20) J. D. Benedict, M. Roche, T. F. Yu, E. J. Bien, A. B. Gutman, and D. Stetten, Jr., Incorporation of glycine N into uric acid in normal and gouty man, Metabolism **1,** 3 (1952).
(21) J. D. Benedict, T. F. Yü, E. J. Bien, A. B. Gutman, and D. Stetten, Jr., A further study of the utilization of dietary glycine nitrogen for uric acid synthesis in gout, J. Clin. Invest. **32,** 775 (1953).
(22) M. Berenbom and J. White, Metabolism of N^{15}-labeled *p*-dimethylamino-azobenzene in rats, J. Natl. Cancer Inst. **12,** 583 (1951).
(23) M. Berenbom and J. White, The metabolism of intravenously administered ammonium glutamate and glutamine, J. Biol. Chem. **182,** 5 (1950).
(24) E. J. Bien, T. F. Yü, J. D. Benedict, A. B. Gutman, and D. Stetten, Jr., The relation of dietary nitrogen consumption of the rate of uric acid synthesis in normal and gouty man, J. Clin. Invest. **32,** 778 (1953).
(25) J. Bigeleisen, The effects of isotopic substitution on the rates of chemical reactions, J. Phys. Chem. **56,** 823 (1952).

(26) K. Bloch, The synthesis of glutathione in isolated liver, J. Biol. Chem. **179,** 1245 (1949).
(27) K. Bloch and R. Schoenheimer, Protein metabolism. XI. The metabolic relation of creatine and creatinine studied with isotopic nitrogen, J. Biol. Chem. **131,** 111 (1939).
(28) K. Bloch and R. Schoenheimer, The biological formation of creatine, J. Biol. Chem. **133,** 633 (1940).
(29) K. Bloch and R. Schoenheimer, The biological precursors of creatine, J. Biol. Chem. **138,** 167 (1941).
(30) K. Bloch, R. Schoenheimer, and D. Rittenberg, Rate of formation and disappearance of body creatine in normal animals, J. Biol. Chem. **138,** 155 (1941).
(31) D. M. Bonner and E. Wasserman, The conversion of N^{15}-containing indole to niacin by niacin-requiring strain 39401 of neurospora, J. Biol. Chem. **185,** 69 (1950).
(32) A. A. Bothner-By and L. Friedman, A nitrogen^{15} tracer study of organic azide reactions. I. The Curtis rearrangement of 3,5-dinitrobenzazide-N^{15}, J. Am. Chem. Soc. **73,** 5391 (1951).
(33) G. B. Brown, Precursors of nucleic acids, J. Cellular Comp. Physiol. **38,** supp. 121 (1951).
(34) G. B. Brown, M. L. Petermann, and S. S. Furst, The incorporation of adenine into pentose and desoxypentose nucleic acids, J. Biol. Chem. **174,** 1043 (1948).
(35) G. B. Brown, P. M. Roll, and L. F. Cavalieri, The in vivo oxidation of uric acid, J. Biol. Chem. **171,** 835 (1947).
(36) G. B. Brown, P. M. Roll, A. A. Plentl, and L. F. Cavalieri, Utilization of adenine for nucleic acid synthesis and as a precursor of guanine, J. Biol. Chem. **172,** 469 (1948).
(37) V. C. E. Burnop, D. E. Richards, W. M. Watkins, and A. Wormall, Combination of nitrogen^{15}-labeled nitrogen mustard with proteins, Nature **168,** 251 (1951).
(38) R. H. Burris, Distribution of isotopic N in Azotobacter vinelandii, J. Biol. Chem. **143,** 509 (1942).
(39) R. H. Burris, F. J. Eppling, H. B. Wahlin, and P. W. Wilson, Detection of nitrogen fixation with isotopic nitrogen, J. Biol. Chem. **148,** 349 (1943).
(40) R. H. Burris, F. J. Eppling, H. B. Wahlin, and P. W. Wilson, Studies of biological nitrogen fixation with isotopic nitrogen, Soil Sci. Soc. Amer., Proc. **7,** 258 (1943).
(41) R. H. Burris and C. E. Miller, Application of N^{15} to the study of biological nitrogen fixation, Science **93,** 114 (1941).
(42) G. C. Butler, Tracers in biology, Proc. Conf. Nuclear Chem., Chem. Inst. Canada (Ottawa) **1947,** 159–166.
(43) R. Caren and M. E. Morton, Pyrimidine metabolism in normal man studied with N^{15}-labeled uracil, J. Clin. Endocrinol. and Metabolism **13,** 1201 (1953).
(44) L. F. Cavaliere, J. F. Tinker, and G. B. Brown, Degradations in the purine series studied with isotopes of nitrogen and carbon, J. Am. Chem. Soc. **71,** 3973 (1949).
(45) Fu-Chuan Chao, C. C. Delwiche, and D. M. Greenberg, Biological precursors of glycine, Biochim. et Biophys. Acta **10,** 103 (1953).
(46) E. Chargaff, M. Ziff, and D. Rittenberg, Determination of the bases of phospholipides by the isotope dilution method, J. Biol. Chem. **138,** 439 (1941).
(47) E. Chargaff, M. Ziff, and D. Rittenberg, Study of the nitrogenous constituents of tissue phosphatides, J. Biol. Chem. **144,** 343 (1942).
(48) K. Clusius and H. Hurzeler, Reactions with N^{15}. X. Reduction and oxidation of hydrazoic acid, Helv. Chim. Acta (in German) **36,** 1326 (1953).
(49) K. Clusius and H. R. Weisser, Reactions with N^{15}. III. Mechanism of the Fischer indole synthesis, Helv. Chim. Acta (in German) **35,** 400 (1952).
(50) K. Clusius and H. R. Weisser, Reactions with nitrogen^{15}. V. Mechanism of the rearrangement of diazoaminobenzine to p-aminoazobenzine, Helv. Chim. Acta (in German) **35,** 1524 (1952).
(51) K. Clusius and H. R. Weisser, Reactions with N^{15}. VI. Structure of Phenylazide, Helv. Chim. Acta (in German) **35,** 1548 (1952).
(52) K. Clusius and M. Vecchi, Reactions with N^{15}. VII. Proof of the nitrate ion in liquid nitrogen tetroxide, Helv. Chim. Acta (in German) **36,** 930 (1953).
(53) K. Clusius and M. Vecchi, Reactions with N^{15}. VIII. Cracking mechanism of N,N-diphenylhydrazine, Helv. Chim. Acta (in German) **36,** 933 (1953).
(54) K. Clusius and M. Vecchi, Reactions with N^{15}. IX. The mechanism of uric acid synthesis by Traube, Helv. Chim. Acta (in German) **36,** 1324 (1953).
(56) C. C. Delwiche, The assimilation of ammonium and nitrate ions by tobacco plants, J. Biol. Chem. **189,** 167 (1951).
(57) C. C. Delwiche, W. D. Loomis, and P. K. Stumpf, Amide metabolism in higher plants II. The exchange of isotopic ammonia by glutamyl transphorase, Arch. Biochem. and Biophys. **33,** 333 (1951).
(58) F. J. DiCarlo, A. S. Schultz, P. M. Roll, and G. B. Brown, Isotopically labeled nucleic acid from yeast, J. Biol. Chem. **180,** 329 (1949).
(59) G. H. Dieke and A. B. F. Duncan, Spectroscopic properties of uranium compounds (McGraw-Hill Book Co. Inc., New York, N. Y., 1949).
(60) V. DuVigneaud, Migration of the methyl group in the body, Proc. Am. Phil. Soc. **92,** 127 (1948).
(61) V. DuVigneaud, M. Cohn, G. B. Brown, O. J. Irish, R. Schoenheimer, and D. Rittenberg, A study of the inversion of d-phenylaminobutyric acid and the acetylation of l-phenylaminobutyric acid by means of the isotopes of nitrogen and hydrogen, J. Biol. Chem. **131,** 273 (1939).
(62) R. R. Edwards, Isotopic tracers in chemical systems, Ann. Rev. of Nuclear Sci. **1,** 301 (1952).
(63) N. A. Eliasson, E. Hammarsten, P. Reichard, S. Aqvist, B. Thorell, and G. Ehrensvärd, Turnover rates during formation of proteins and polynucleotides in regenerating tissues, Acta Chem. Scand. (in English) **5,** 431 (1951).
(64) D. Elwyn and D. B. Sprinson, Certain interrelationships in the metabolism of glycine and serine, J. Biol. Chem. **207,** 459 (1954).
(65) D. Elwyn and D. B. Sprinson, Reaction of folic acid to the metabolism of serine, J. Biol. Chem. **184,** 475 (1950).
(66) D. Elwyn and D. B. Sprinson, Role of serine and acetate in uric acid formation, J. Biol. Chem. **184,** 465 (1950).
(67) D. Elwyn and D. B. Sprinson, The synthesis of thymine and purines from serine and glycine in the rat, J. Biol. Chem. **207,** 467 (1954).
(68) G. L. Foster, Some amino acid analyses of hemoglobin and β-loctoglobulin, J. Biol. Chem. **159,** 431 (1945).
(69) G. L. Foster, R. Schoenheimer and D. Rittenberg, Protein Metabolism. V. The utilization of ammonia for amino acid and creatine formation in animals, J. Biol. Chem. **127,** 319 (1939).
(70) L. Friedman and J. Bigeleisen, Oxygen and nitrogen isotope effects in the decomposition of ammonium nitrate, J. Chem. Phys. **18,** 1325 (1950).
(71) J. S. Fruton, The role of proteolytic enzymes in the biosynthesis of peptide bonds, Yale J. Biol. and Med. **22,** 263 (1950).
(72) J. S. Fruton, R. B. Johnston, and M. Fried, Elongation of peptide chains in enzyme-catalyzed transamidation reactions, J. Biol. Chem. **190,** 39 (1951).

(73) M. Gajdos-Torok, H. Bénard, J. Coursaget, and A. Gajdos, Use of nitrogen[15] in the study of the synthesis of porphyrins and hemoglobin in vitro. Compt. rend. soc. biol. **146,** 1076 (1952).
(74) B. A. Geller and G. P. Miklukhin, Nitrogen isotopes in chemistry, Uspekhi Khim. **21,** 808 (1952).
(75) D. A. Goldthwait and A. Bendich, Effects of a folic acid antagonist on nucleic acid metabolism, J. Biol. Chem. **196,** 841 (1952).
(76) J. Graff and H. D. Hoberman, Metabolism of β-alanine. J. Biol. Chem. **186,** 369 (1950).
(77) S. Graff, D. Rittenberg, and G. L. Foster, The glutamic acid of malignant tumors, J. Biol. Chem. **133,** 745 (1940).
(78) C. H. Gray, Isotope studies in porphyria, Brit. Med. Bul. **8,** 229 (1952).
(79) C. H. Gray, I. M. H. Muir, and A. Neuberger, Studies in congenital porphyria. 3. The incorporation of ^{15}N into the haem and glycine of haemoglobin, Biochem. J. (London) **47,** 542 (1950).
(80) C. H. Gray and A. Neuberger, Studies in congenital porphyria 1. Incorporation of ^{15}N into coproporphyrin, uroporphyrin and hippuric acid, Biochem. J. (London) **47,** 81 (1950).
(81) C. H. Gray, A. Neuberger, and P. H. A. Sneath, Studies in congenital porphyria. 2. Incorporation of ^{15}N in the stercobilin in the normal and in the porphyric, Biochem. J. (London) **47,** 87 (1950).
(82) M. Grinstein, R. A. Aldrich, V. Hawkinson, and C. J. Watson, Isotopic study of porphyrin and hemoglobin metabolism in a case of porphyria, J. Biol. Chem. **179,** 983 (1949).
(83) M. Grinstein, M. D. Kamen, H. M. Wikoff, and C. V. Moore, Isotopic studies of porphyrin and hemoglobin metabolism. I. Biosynthesis of coproporphyrin I and its relationship to hemoglobin metabolism, J. Biol. Chem. **182,** 715 (1950).
(84) M. Grinstein, H. M. Wikoff, R. Pimenta de Mello, and C. J. Watson, Isotopic studies of porphyrin and hemoglobin metabolism. II. The biosynthesis of coproporphyrin III in experimental lead poisoning, J. Biol. Chem. **182,** 723 (1950).
(85) S. Grisolia, R. H. Burris, and P. P. Cohen, Carbon dioxide and ammonia fixation in the biosynthesis of citrulline, J. Biol. Chem. **191,** 203 (1951).
(86) A. B. Gutman, Some recent advances in the study of uric acid metabolism and gout, Bul. N. Y. Acad. Med. **27,** 144 (1951).
(87) E. Hammarsten, P. Reichard, and E. Saluste, Pyrimidine nucleosides as precursors of pyrimidines in polynucleotides, J. Biol. Chem. **183,** 105 (1950).
(88) E. Hammarsten, P. Reichard, and E. Saluste, Pyrimidine nucleosides as precursors of ribonucleic acid (PNA) pyrimidines, Acta Chem. Scand. (in English) **3,** 432 (1949).
(89) G. Hevesy, K. Linderstrom-Lang, A. S. Keston, and C. Olsen, Exchange of nitrogen atoms in the leaves of the sunflower, Compt. rend. trav. lab. Carlsberg, Sér. chim. **23,** 213 (1940).
(90) W. C. E. Higginson and D. Sutton, Oxidation of hydrazine in aqueous solution. Part II. Use of N^{15} as a tracer in the oxidation of hydrazine, J. Chem. Soc. (London) 1402 (1953).
(91) C. H. W. Hirs and D. Rittenberg, Studies on urea formation in surviving liver slices, J. Biol. Chem. **186,** 429 (1950).
(92) H. D. Hoberman, Measurements of rates of protein degradation and protein loss in fasting animals, J. Biol. Chem. **188,** 797 (1951).
(93) H. D. Hoberman and J. S. Fruton, The metabolic fate of acetyldehydrotyrosine in the rat. J. Biol. Chem. **182,** 127 (1950).
(94) H. D. Hoberman and J. Graff, Effects of fasting and glucose ingestion on the retention of ammonia J. Biol. Chem. **186,** 373 (1950).
(95) H. D. Hoberman and J. Graff, Influence of thyroxine on metabolism of amino acids and proteins during fasting, Yale J. Biol. and Med. **23,** 195 (1950).
(96) H. D. Hoberman, E. A. H. Sims, and J. H. Peters, Creatine and creatinine metabolism in the normal male adult studied with the aid of isotopic nitrogen, J. Biol. Chem. **172,** 45 (1948).
(97) H. D. Hoberman and D. Stone, The metabolism of glycylglycine, J. Biol. Chem. **194,** 383 (1952).
(98) I. Hochberg and K. G. Rosdahl, The influence of orotic acid on the lateral anterior horn cells of the rat, Acta Pathol. Microbiol. Scand. **33,** 36 (1953).
(99) R. C. Hockett, V. Deulofeu, and J. O. Defarrari, Mechanism of the formation of "aldose acetamides" in the reaction of acelylated aldonic acid nitriles with ammonia, J. Am. Chem. Soc. **72,** 1840 (1950).
(100) P. F. Holt and B. I. Bullock, Study of diazo-compounds by use of nitrogen isotopes. Part I. The structure of the diazonium ion. J. Chem. Soc. (London), 2310 (1950).
(101) P. F. Holt and B. I. Hopson-Hill, A study of diazo compounds by use of nitrogen isotopes. The reduction of mixed diazonium salts of anthranilic acid and aniline, J. Chem. Soc. (London) 4251 (1952).
(102) D. W. Hood, C. M. Lyman, and F. A. Tatum, The preparation of glutamine labeled with nitrogen[15], Arch. Biochem. **30,** 351 (1951).
(103) T. Hultin, Incorporation of nitrogen[15]-labeled ammonium chloride into pyrimidines and purines during the early sea urchin development, Arkiv Kemi **5,** 267 (1953) [also Exptl. Cell Research **3,** 494 (1952)].
(104) T. Hultin, The amino acid metabolism of sea-urchin embryos studied by means of N^{15}-labeled ammonium chloride and alanine, Arkiv Kemi **5,** 543 (1953).
(105) T. Hultin, The assimilation of glycine marked with nitrogen[15] into the liver fractions of freshly killed cocks, Exptl. Cell Research **1,** 376 (1950).
(106) R. B. Johnston, M. J. Mycek, and J. S. Fruton, Catalysis of transamidation reactions by proteolytic enzymes, J. Biol. Chem. **185,** 629 (1950).
(107) G. G. Joris, The exchange reaction between gaseous and combined nitrogen, J. Chem. Phys. **9,** 775 (1941).
(108) H. M. Kalckar, The biological synthesis of purine compounds, Symposia Soc. Exptl. Biol., I. Nucleic Acid, 38 (1947).
(109) H. M. Kalckar and D. Rittenberg, Rejuvenation of muscle adenylic acid nitrogen in vivo studied with isotopic nitrogen, J. Biol. Chem. **170,** 455 (1947).
(110) M. D. Kamen and H. Gest, Evidence for a nitrogenase system in the photosynthetic bacterium Rhodospirillum rubrum, Science **109,** 560 (1949).
(111) A. S. Keston, D. Rittenberg, and R. Schoenheimer, Protein Metabolism. IV. The stability of nitrogen in organic compounds, J. Biol. Chem. **127,** 315 (1939).
(112) A. L. Koch, F. W. Putnam, and E. A. Evans, Jr., Biochemical studies of virus reproduction. VIII. Purine metabolism, J. Biol. Chem. **197,** 113 (1952).
(113) A. S. Konikova and M. G. Kritsman, Microbiological applications of tracer atoms, Mikrobiologiya **20,** 58 (1951).
(114) H. L. Kornberg and R. E. Davies, Metabolism of subcutaneously injected [N^{15}] urea in the cat, Biochem. J. (London) **52,** 345 (1952).
(115) L. M. Kozloff, Biochemical studies of virus reproduction. VI. The breakdown of bacteriophage T_6r^+, J. Biol. Chem. **194,** 83 (1952).
(116) L. M. Kozloff, K. Knowlton, F. W. Putnam, and E. A. Evans, Jr., Biochemical studies of virus reproduction. V. The origin of bacteriophage nitrogen, J. Biol. Chem. **188,** 101 (1951).
(117) A. I. Krasna, P. Peyser, and D. B. Sprinson, The utilization of 2-C^{14}-L-threonine for the synthesis of uric acid, J. Biol. Chem. **198,** 421 (1952).

(118) J. T. Kummer and P. H. Emmett, Use of C^{14}, N^{15} and deuterium in studying catalytic reactions and adsorption processes on iron catalysts, U. S. Brookhaven Conf. Rept. BNL–C–8, 1 (1948).
(119) U. Lagerkvist, Incorporation of ammonia into uric acid in pigeons and ribonucleic acid pyrimidines in rats, Arkiv Kemi **5,** 569 (1953).
(120) U. Lagerkvist, P. Reichard, and G. Ehrensvärd, Aspartic acid as a precursor for ribonucleic acid pyrimidines, Acta Chem. Scand. (in English) **5,** 1212 (1951).
(121) J. M. Lee and D. Stetten, Jr., Alloxan metabolism. I. The distribution and excretion of injected alloxan, J. Biol. Chem. **197,** 205 (1952).
(122) E. Leifer, W. H. Langham, J. F. Nyc, and H. K. Mitchell, Use of isotopic nitrogen in a study of the conversion of 3-hydroxyanthranilic acid to nicotinic acid in neurospora, J. Biol. Chem. **184,** 589 (1950).
(123) I. M. London, Conversion of hematin to bile pigment, J. Biol. Chem. **184,** 373 (1950).
(124) I. M. London, D. Shemin, and D. Rittenberg, Synthesis of heme in vitro by the immature nonnucleated mammalian erythrocyte, J. Biol. Chem. **183,** 749 (1950).
(125) I. M. London, D. Shemin, R. West, and D. Rittenberg, Heme synthesis and red blood cell dynamics in normal humans and in subjects with polycythemia vera, sickle cell anemia and pernicious anemia, J. Biol. Chem. **179,** 463 (1949).
(126) I. M. London, D. Shemin, R. West, and D. Rittenberg, The biosynthesis and metabolism of porphyrins and bile pigment, Intern. Congr. Biochem., Abstrs. Communs., 1st Congr. Cambridge, Engl. 357 (1949).
(127) I. M. London, R. West, D. Shemin, and D. Rittenberg, On the origin of bile pigment in normal man, J. Biol. Chem. **184,** 351 (1950).
(128) M. Lounsbury, Stable tracers in chemistry, Proc. Conf. Nuclear Chem., Chem. Inst. Canada (Ottawa), 153 (1947).
(129) P. T. Lowry, V. Hawkinson, and C. J. Watson, An isotopic study of Type III porphyrins and hemoglobin metabolism in an unusual case of "mixed" porphyria, Metabolism **1,** 149 (1952).
(130) H. A. Machata, R. H. Burris, and P. W. Wilson, Fixation of isotopic N by excised nodules, J. Biol. Chem. **171,** 605 (1947).
(131) R. MacVicar and R. H. Burris, Translocation studies in tomato using ammonium sulfate labeled with N^{15}, Am. J. Botany **35,** 567 (1948).
(132) R. MacVicar, W. L. Garman, and R. Wall, Studies on nitrogen fertilizer utilization using N^{15}, Soil Sci. Soc. Amer., Proc. **15,** 265 (1950).
(133) D. H. Marrian, V. L. Spicer, M. E. Balis, and G. B. Brown, Purine incorporation into pentose nucleotides of the rat, J. Biol. Chem. **189,** 533 (1951).
(134) J. Mattauch, Stable isotopes, their measurement and application, Angew. Chem. (in German) [A] **59,** 37 (1947).
(135) E. W. Maynert and H. B. van Dyke, Absence of localization of barbital in divisions of the central nervous system, J. Pharmacol. Exptl. Therap. **98,** 184 (1950).
(136) E. W. Maynert and H. B. van Dyke, Metabolic fate of pentobarbital. Isotope dilution experiments with urine after administration of labeled pentobarbital, J. Pharmacol. Exptl. Therap. **98,** 174 (1950).
(137) E. W. Maynert and H. B. van Dyke, Metabolism of amytal labeled with N^{15} in dogs, J. Pharmacol. Exptl. Therap. **98,** 180 (1950).
(138) A. S. McFarlane, Biochemical applications of stable and radioactive isotopes, Brit. Med. J. **II,** 766 (1947).
(139) A. Meister and S. V. Tice, Transamination from glutamine to α-keto acids, J. Biol. Chem. **187,** 173 (1950).
(140) E. Melin and H. Nilsson, Transfer of labeled nitrogen from glutamic acid to pine seedlings through the mycelium of Boletus variegatus (Sw.) Fr., Nature **171,** 134 (1953).
(141) H. L. Meltzer and D. B. Sprinson, The synthesis of 4–C^{14}, N^{15}–L–threonine and a study of its metabolism, J. Biol. Chem. **197,** 461 (1952).
(142) J. L. Mendel and D. W. Visser, Nitrate reduction in higher plants, Arch. Biochem. and Biophys. **32,** 158 (1951).
(143) S. Mitsui and K. Ota, Utilization of nitrogen^{15} as tracer element in the studies of nitrogen transformation in soil, J. Sci. Soil Manure, Japan **21,** 83 (1950).
(144) H. M. Muir and A. Neuberger, Biogenesis of porphyrins. Distribution of N^{15} in the ring system, Biochem. J. (London) **45,** 163 (1949).
(145) H. M. Muir and A. Neuberger, Biogenesis of porphyrins. 2. Origin of the methyne carbon atoms, Biochem. J. (London) **47,** 97 (1950).
(146) J. A. Muntz and J. Hurwitz, Inability of choline to transfer a methyl group directly to homocysteine for methionine formation, J. Biol. Chem. **182,** 489 (1950).
(147) A. Neuberger, H. M. Muir, and C. H. Gray, Biosynthesis of porphyrins and congenital porphyria, Nature **165,** 948 (1950).
(148) J. W. Newton, P. W. Wilson, and R. H. Burris, Direct demonstration of ammonia as an intermediate in nitrogen fixation by Azotobacter, J. Biol. Chem. **204,** 445 (1953).
(149) A. G. Norman and L. O. Krampitz, The nitrogen nutrition of soybeans. II. Effect of available soil nitrogen on growth and nitrogen fixation, Soil Sci. Soc. Amer., Proc. **10,** 191 (1945).
(150) C. J. Nyman, S.–C. Fung, and H. W. Dodgen, Proton exchange between ammonia and ammonium ion in liquid ammonia, J. Am. Chem. Soc. **72,** 1033 (1950).
(151) R. A. Ogg, Jr., Isotopic nitrogen exchange between nitrogen pentoxide and dioxide, J. Chem. Phys. **15,** 613 (1947).
(152) R. L. Ory, D. W. Hood, and C. M. Lyman, The role of glutamine in the synthesis or arginine by lactobacillus arabinosus, J. Biol. Chem. **207,** 267 (1954).
(153) K. Ozaki and S. Mitsui, Nitrogen metabolism of rice plant. II. Utilization of isotopically labeled ammonium sulfate, J. Sci. Soil Manure, Japan **23,** 169 (1953).
(154) K. Ozaki, M. Moriyama, and S. Mitsui, Nitrogen metabolism of rice plant. II. 4. Utilization of isotopically labeled ammonium sulfate, J. Sci. Soil Manure, Japan **23,** 237 (1953).
(155) W. Parson, K. R. Crispell, and A. Egbert, Jr., Abnormalities of N^{15} excretion rates after ingestion of tagged glycine in Cushings syndrome and following adrenocorticotropic hormone administration, J. Clin. Invest. **31,** 548 (1952).
(156) C. W. H. Partridge, D. M. Bonner, and C. Yanofsky, A quantitative study of the relationship between tryptophan and niacin in neurospora, J. Biol. Chem. **194,** 269 (1952).
(157) F. W. Putnam, D. Miller, L. Palm, and E. A. Evans, Jr., Biochemical studies of virus reproduction. X. Precursors of bacteriophage T_7. J. Biol. Chem. **199,** 177 (1952).
(158) N. S. Radin, D. Rittenberg, and D. Shemin, The role of glycine in the biosynthesis of heme, J. Biol. Chem. **184,** 745 (1950).
(159) P. Reichard, On the nitrogen turnover in purines from polynucleotides determined with glycine N^{15}, J. Biol. Chem. **179,** 773 (1949).
(160) P. Reichard, On the turnover of purines and pyrimidines from polynucleotides in the rat determined with N^{15}, Acta Chem. Scand. (in English) **3,** 422 (1949).

(161) P. Reichard, Purine and pyrimidine turnover of ribonucleic acid from fractionated rat liver cytoplasm, Acta Chem. Scand. (in English) **4,** 861 (1950).
(162) P. Reichard, The function of orotic acid in the biogenesis of pyrimidines in slices from regenerating liver, J. Biol. Chem. **197,** 391 (1952).
(163) P. Reichard and S. Bergström, Synthesis of polynucleotides in slices from regenerating liver, Acta Chem. Scand. **5,** 190 (1951).
(164) D. Rittenberg, Dynamic aspects of the metabolism of amino acids, Harvey Lectures **44,** 200 (1948).
(165) D. Rittenberg, Use of N^{15} and D for the study of chemical processes in the living cell, Inst. intern. chim. Solvay, 7th Conseil Brussels, 391 (1948).
(166) D. Rittenberg and G. L. Foster, A new procedure for quantitative analysis by isotope dilution with application to the determination of amino acids and fatty acids, J. Biol. Chem. **133,** 737 (1940).
(167) D. Rittenberg and R. Schoenheimer, Protein Metabolism. VI. Hippuric acid formation studied with the aid of the nitrogen isotope, J. Biol. Chem. **127,** 329 (1939).
(168) M. Roche, J. D. Benedict, T. F. Yu, E. J. Bien, and DeWitt Stetten, Jr., Origin of urinary creatine in progressive muscular dystrophy, Metabolism **1,** 13 (1952).
(169) P. M. Roll, G. B. Brown, F. J. DiCarlo, and A. S. Schultz, The metabolism of yeast nucleic acid in the rat, J. Biol. Chem. **180,** 333 (1949).
(170) M. A. Rothenberg, D. B. Sprinson, and D. Nachmansohn, Site of action of acetylcholine, J. Neurophysiol. **11,** 111 (1948).
(171) A. San Pietro, Synthesis of aspartic acid—2,3-C^{14}—N^{15} and its conversion to uric acid in the pigeon, J. Biol. Chem. **198,** 639 (1952).
(172) A. San Pietro and D. Rittenberg, The rate of protein synthesis in humans. I. Measurement of the urea pool and urea space, J. Biol. Chem. **201,** 445 (1953).
(173) A. San Pietro and D. Rittenberg, A study of the rate of protein synthesis in humans. II. Measurement of the metabolic pool and the rate of protein synthesis, J. Biol. Chem. **201,** 457 (1953).
(174) R. W. Schayer, Metabolism of tryptophan labeled with N^{15} in the indole ring, J. Biol. Chem. **187,** 777 (1950).
(175) R. Schoenheimer, S. Ratner, and D. Rittenberg, Protein Metabolism. VII. The metabolism of tyrosine, J. Biol. Chem. **127,** 333 (1939).
(176) R. Schoenheimer, S. Ratner, and D. Rittenberg, Studies in protein metabolism. X. The metabolic activity of body proteins investigated with *l* (−)-leucine containing two isotopes, J. Biol. **130,** 703 (1939).
(177) R. Schoenheimer and D. Rittenberg, Studies in protein metabolism. I. General considerations in the application of isotopes to the study of protein metabolism. The normal abundance of nitrogen isotopes in amino acids, J. Biol. Chem. Chem. **127,** 285 (1939).
(178) R. Schoenheimer, D. Rittenberg, G. L. Foster, A. S. Keston, and S. Ratner, Application of the nitrogen isotope N^{15} for the study of protein metabolism, Science **88,** 599 (1938).
(179) R. Schoenheimer, D. Rittenberg, M. Fox, A. S. Keston, and S. Ratner, Nitrogen isotope (N^{15}) as a tool in the study of the intermediary metabolism of nitrogenous compounds, J. Am. Chem. Soc. **59,** 1768 (1937).
(180) J. F. Schuler, V. M. Diller, and H. J. Kersten, Preferential assimilation of ammonium ion by Chlorella vulgaris, Plant Physiol. **28,** 299 (1953).
(181) D. Shemin, I. M. London, and D. Rittenberg, The relationship of serine to porphyrin synthesis, J. Biol. Chem. **183,** 767 (1950).
(182) D. Shemin, I. M. London, and D. Rittenberg, The synthesis of protoporphyrin in vitro by red blood cells of the duck, J. Biol. Chem. **183,** 757 (1950).
(183) D. Shemin and D. Rittenberg, On the utilization of glycine for uric acid synthesis in man, J. Biol. Chem. **167,** 875 (1947).
(184) D. Shemin and D. Rittenberg, The biological utilization of glycine for the synthesis of the protoporphyrin of hemoglobin, J. Biol. Chem. **166,** 621 (1946).
(185) D. Shemin and D. Rittenberg, The life span of the human red blood cell, J. Biol. Chem. **166,** 627 (1946).
(186) M. S. H. Siddiqi, L. M. Kozloff, F. W. Putnam, and E. A. Evans, Jr., Biochemical studies of virus reproduction. IX. Nature of the host cell contributions, J. Biol. Chem. **199,** 165 (1952).
(187) S. Simmonds, Metabolism of phenylalanine and tyrosine in mutant strains of Escherichia coli, J. Biol. Chem. **185,** 755 (1950).
(188) J. H. Singleton, E. R. Roberts, and E. R. S. Winter, Experiments on the mechanism of the urea-urease reaction, J. Am. Chem. Soc. **73,** 4999 (1951).
(189) R. M. S. Smellie, W. M. McIndoe, and J. N. Davidson, Incorporation of nitrogen^{15}, sulfur^{35} and carbon^{14} into nucleic acids and proteins of rat liver, Biochim. et Biophys. Acta **11,** 559 (1953).
(190) J. C. Sonne, I. Lin, and J. M. Buchanan, The role of N^{15} glycine, glutamine, aspartate and glutamate in hypoxanthine synthesis, J. Am. Chem. Soc. **75,** 1516 (1953).
(191) S. Soloway and D. Stetten, Jr., The metabolism of choline and its conversion to glycine in the rat, J. Biol. Chem. **204,** 207 (1953).
(192) D. B. Sprinson and A. Coulon, The precursors of sphingosine in brain tissue, J. Biol. Chem. **207,** 585 (1954).
(193) D. B. Sprinson and D. Rittenberg, Rate of interaction of the amino acids of the diet with the tissue proteins, J. Biol. Chem. **180,** 715 (1949).
(194) D. B. Sprinson and D. Rittenberg, The metabolic activity of the α-, β- and γ-hydrogen atoms of L-leucine and the α-hydrogen of glycine, J. Biol. Chem. **184,** 405 (1950).
(195) D. B. Sprinson and D. Rittenberg, The rate of utilization of ammonia for protein synthesis, J. Biol. Chem. **180,** 707 (1949).
(196) F. W. Stacey, J. G. Lindsay, and A. N. Bourns, Isotope effects in the thermal deammonation of phthalamide, Can. J. Chem. **30,** 135 (1952).
(197) J. Sterner, Tracer isotopes in industrial toxicology, Occupational Med. **3,** 552 (1947).
(198) D. Stetten, Jr., Biological relationships of choline, ethanolamine and related compounds, J. Biol. Chem. **138,** 437 (1941).
(199) D. Stetten, Jr., The pool of miscible uric acid in normal and gouty man, studied with the aid of isotopic N, J. Mt. Sinai Hosp., N. Y. **17,** 149 (1950).
(200) M. R. Stetten, Aspects of the metabolism of hydroxyproline studied with the aid of isotopic N, J. Biol. Chem. **181,** 31 (1949).
(201) M. R. Stetten, Mechanism of the conversion of ornithine into proline and glutamic acid in vivo, J. Biol. Chem. **189,** 499 (1951).
(202) H. C. Stoerk, H. M. John, and H. N. Eisen, Turnover of serum protein in adrenalectomized rats, Proc. Soc. Exptl. Biol. Med. **66,** 25 (1947).
(203) W. B. Sutton, F. Schlenk, and C. H. Werkman, Glycine as a precursor of bacterial purines, Arch. Biochem. and Biophys. **32,** 85 (1951).
(204) J. H. Talbott, C. Bishop, and W. Garner, Study of labeled uric acid in gouty and non-gouty subjects, Trans. Assoc. Am. Physicians **62,** 201 (1950).
(205) C. Tesar and D. Rittenberg, The metabolism of L-histidine, J. Biol. Chem. **170,** 35 (1947).
(206) B. Thorell, The endocellular formation of some hemoproteins, Intern. Congr. Biochem., Abstrs. Communs., 1st Congr. Cambridge, Engl., 280 (1949).
(207) S. R. Tove, H. F. Niss, and P. W. Wilson, Fixation of N_2^{15} by excised nodules of leguminous plants, J. Biol. Chem. **184,** 77 (1950).

(208) W. N. Valentine, M. L. Pearce, R. F. Riley, E. Richter and J. S. Lawrence, Heme synthesis and erythrocyte life span in the cat, Proc. Soc. Exptl. Biol. Med. **77,** 244 (1951).
(209) W. R. Vaughan, D. I. McCane, and G. J. Sloan, Rowe rearrangement, J. Am. Chem. Soc. **73,** 2298 (1951).
(210) B. Vennesland, Nitrogen and carbon isotopes. Their application in vivo to the study of the animal organism, Advances in Biol. and Med. Phys. **1,** 45 (1948).
(211) H. B. Vickery, G. W. Pucher, R. Schoenheimer, and D. Rittenberg, The assimilation of ammonia nitrogen by the tobacco plant: a preliminary study with isotopic nitrogen, J. Biol. Chem. **135,** 531 (1940).
(212) H. B. Vickery, G. W. Pucher, R. Schoenheimer, and D. Rittenberg, The metabolism of nitrogen in the leaves of the buckwheat plant, J. Biol. Chem **129,** 791 (1939).
(213) R. Von Korff and D. Glick, Role of urease in the gastric mucosa. II. In vivo studies with isotopic urea on frog mucosa, Am. J. Physiol. **165,** 688 (1951).
(214) H. Waelsch, P. Owades, E. Borek, N. Grossowicz, and M. Schou, The enzyme-catalyzed exchange of ammonia with the amide group of glutamine and asparagine, Arch. Biochem. **27,** 237 (1950).
(215) C. J. Watson, W. M. Davidson, and J. W. Kennedy, The nutritive value of nitrogeneous compounds for ruminants. II. The formation of body protein from urea labeled with the isotope N^{15}, Sci. Agr. **29,** 185 (1949).
(216) A. Weissbach, D. Elwyn, and D. B. Sprinson, Synthesis of the methyl groups and ethanolamine moiety of choline from serine and glycine in the rat, J. Am. Chem. Soc. **72,** 3316 (1950).
(217) A. Weissbach and D. B. Sprinson, The metabolism of 2-carbon compounds related to glycine, J. Biol. Chem. **203,** 1031 (1953).
(218) N. Weissman and R. Schoenheimer, Protein Metabolism. XV. The relative stability of *l*(+)—lysine in rats studied with deuterium and heavy nitrogen, J. Biol. Chem. **140,** 779)1941).
(219) A. White, H. D. Hoberman, and C. M. Czego, Influence of adrenalectomy and fasting on the incorporation of isotopic N into the tissues of mice, J. Biol. Chem. **174,** 1049 (1948).
(220) P. W. Wilson, The comparative biochemistry of N fixation, Advances in Enzymol. **13,** 345 (1952).
(221) J. Wittenberg and D. Shemin, Location in protoporphyrin of the carbon atoms derived from the α-carbon atom of glycine, J. Biol. Chem. **185,** 103 (1950)
(222) J. Wittenberg and D. Shemin, The utilization of glycine for the biosynthesis of both types of pyrroles in protoporphyrin, J. Biol. Chem **178,** 47 (1949).
(223) H. Wu, Relative concentrations of N^{15} in urinary ammonia nitrogen and urea nitrogen after feeding N^{15}-labeled compounds, J. Gen. Physiol. **34,** 403 (1951).
(224) H. Wu and D. Rittenberg, Metabolism of L-aspartic acid, J. Biol. Chem. **179,** 847 (1949).
(225) H. Wu and S. E. Snyderman, Rate of excretion of N^{15} after feeding N^{15}-labeled L-aspartic acid in man, J. Gen. Physiol. **34,** 339 (1951).
(226) J. B. Wyngaarden and D. Stetten, Jr., Uricolysis in normal man, J. Biol. Chem. **203,** 9 (1953).
(227) I. Zelitch, E. D. Rosenblum, R. H. Burris, and P. W. Wilson, Isolation of the key intermediate in biological N fixation by clostridium, J. Biol. Chem. **191,** 295 (1951).
(228) I. Zelitch, P. W. Wilson, and R. H. Burris, Amino acid composition and distribution of nitrogen^{15} in soybean-root nodules supplied nitrogen^{15}-enriched nitrogen, Plant Physiol. **27,** 1 (1952).
(229) E. A. Zeller and A. Maritz, Enzymic decomposition of monoaminodicarboxylic acids. Experientia (in German) **1,** 30 (1945).

4.5. Synthesis of N^{15} Compounds

(1) S. E. Åqvist, Use of starch chromatography and ion-exchange resin for large scale separations of N^{15}-labeled amino acids, Acta Chem. Scand. (in English) **5,** 1031 (1951).
(2) H. R. V. Arnstein, G. D. Hunter, H. M. Muir, and A. Neuberger, Preparation of optically active lysine labeled with C^{14} and N^{15}, J. Chem. Soc. (London) 1329 (1952).
(3) W. V. Bartholomew, L. B. Nelson and C. H. Werkman, The use of the nitrogen isotope N^{15} in field studies with oats, Agron. J. **42,** 100 (1950).
(4) A. Bendich, J. F. Tinker, and G. B. Brown, Synthesis of isoguanine labeled with isotopic N, J. Am. Chem. Soc. **70,** 3109 (1948).
(5) J. D. Benedict, P. H. Forsham, and D. Stetten, Jr., Metabolism of uric acid in the normal and gouty human studied with the aid of isotopic uric acid, J. Biol. Chem. **181,** 183 (1949).
(6) A. H. Blatt and N. Gross, Synthesis of pentaquine labeled in the side chain with nitrogen 15, J. Am. Chem. Soc. **75,** 1245 (1953).
(7) G. B. Brown, P. M. Roll, A. A. Plentl, and L. F. Cavalieri, Utilization of adenine for nucleic acid synthesis and as a precursor of guanine, J. Biol. Chem. **172,** 469 (1948).
(8) L. F. Cavalieri, V. E. Blair, and G. B. Brown, The synthesis of uric acid containing isotopic nitrogen, J. Am. Chem. Soc. **70,** 1240 (1948).
(9) L. F. Cavalieri, J. F. Tinker, and A. Benedich, Synthesis of adenine. The incorporation of isotopes of N and C, J. Am. Chem. Soc. **71,** 533 (1949).
(10) K. Clusius and E. W. Becker, The separation tube. VI. Isolation of the mixed molecule $N^{14}N^{15}$, Z. Naturforsch. **2a,** 154 (1947).
(11) K. Clusius and M. Hoch, Reactions with N^{15}. I. Decomposition of phenylhydrazine, Helv. Chim. Acta (in German) **33,** 2122 (1950).
(12) K. Clusius and H. Hürzeler, Reactions with heavy nitrogen. IV. Preparation of $NaN^{15}O_2$ and $KN^{15}O_2$ from heavy N, Helv. Chim. Acta (in German) **35,** 1103 (1952).
(13) J. D. Cox, Synthesis of isotopic compounds for use in biological and chemical research, Chemist and Druggist **156,** 627 (1951).
(14) G. H. Dieke and A. B. F. Duncan, Spectroscopic properties of uranium compounds, (McGraw-Hill Book Company, Inc., New York, N. Y. 1949).
(15) R. C. Elderfield, L. L. Smith, and E. Werble, Synthesis of pentaquine labeled in the quinoline ring with nitrogen^{15}, J. Am. Chem. Soc. **75,** 1245 (1953).
(16) W. S. Fones and J. White, Preparation of *p*-dimethylaminoazobenzene containing isotopic nitrogen, Arch. Biochem. **20,** 118 (1949).
(17) E. Hammarsten and P. Reichard, Inability of guanosine to act as a precursor of polynucleotides, Acta Chem. Scand. (in English) **4,** 711 (1950).
(18) E. Hammarsten, P. Reichard, and E. Saluste, Pyrimidine nucleosides as precursors of ribonucleic acid (PNA) pyrimidines, Acta Chem. Scand. (in English) **3,** 432 (1949).
(19) E. L. Hudspeth, C. P. Swann, and N. P. Heydenburg, Deuteron Bombardment of C^{14}, Phys. Rev. **80,** 643 (1950).
(20) G. G. Joris and H. S. Taylor, Exchange reactions of nitrogen isotopes on iron and tungsten surfaces, J. Chem. Phys. **7,** 893 (1939).
(21) J. T. Kummer and P. H. Emmett, Exchange between N_2^{30} and N_2^{28} over iron catalysts, J. Chem. Phys. **19,** 289 (1951).
(22) L. C. Leitch and W. M. Davidson, The nutritive value of nitrogenous compounds for ruminants. III. Synthesis of urea containing N^{15}, Sci. Agr. **29,** 189 (1949).
(23) H. L. Meltzer and D. B. Sprinson, The synthesis of 4-C^{14}, N^{15}-L-threonine and a study of its metabolism. J. Biol. Chem. **197,** 461 (1952).

(24) J. A. Muntz and J. Hurwitz, The inability of choline to transfer a methyl group directly to homocysteine for methionine formation, J. Biol. Chem. **182,** 489 (1950).
(25) A. San Pietro, Synthesis of aspartic acid-2, 3-C^{14}-N^{15} and its conversion to uric acid in the pigeon, J. Biol. Chem. **198,** 639 (1952).
(26) R. W. Schayer, Studies of the metabolism of tryptophan labeled with N^{15} in the indole ring, J. Biol. Chem. **187,** 777 (1950).
(27) R. Schoenheimer and S. Ratner, Studies in Protein metabolism. III. Synthesis of amino acids containing isotopic nitrogen, J. Biol. Chem. **127,** 301 (1939).
(28) R. Schoenheimer, D. Rittenberg, G. L. Foster, A. S. Keston, and S. Ratner, Application of the nitrogen isotope N^{15} for the study of protein metabolism, Science **88,** 599 (1938).
(29) H. Sobotka and F. E. Stynler, Isotopically labeled Nirvanol (5,5-phenylethylhydantoin), J. Mt. Sinai Hosp., N. Y. **19,** 212 (1952).
(30) D. B. Sprinson and D. Rittenberg, The rate of utilization of ammonia for protein synthesis, J. Biol. Chem. **180,** 707 (1949).
(31) M. R. Stetten, Aspects of the metabolism of hydroxyproline, studied with the aid of isotopic nitrogen, J. Biol. Chem. **181,** 31 (1949).
(32) H. S. Taylor, Effect of the heterogeneity of catalysts on chemisorption and chemical kinetics, J. chim. phys. (in French) **47,** 122 (1950).
(33) C. Tesar and D. Rittenberg, The metabolism of L-histidine, J. Biol. Chem. **170,** 35 (1947).
(34) W. R. Vaughan, W. T. Boyd, D. I. McCane, and G. J. Sloan, Procedure for collection of isotopic nitrogen, Anal. Chem. **23,** 508 (1951).
(35) D. W. Wilson, A. O. C. Nier, and S. P. Reimann, Preparation and measurement of isotopic tracers (J. W. Edwards, Ann Arbor, Michigan, 1948).

WASHINGTON, July 22, 1955.

U. S. GOVERNMENT PRINTING OFFICE: 1956


DEPARTMENT OF COMMERCE
UNITED STATES OF AMERICA