

# A Lead User of Instruments in Science

## John D. Roberts and the Adaptation of Nuclear Magnetic Resonance to Organic Chemistry, 1955–1975

*By Carsten Reinhardt\**

### ABSTRACT

During the 1960s organic chemistry underwent a spectacular transformation as a result of the introduction of high-tech instruments. In this process, nuclear magnetic resonance (NMR) became an important analytical technique in organic chemistry. The theme of this essay is the relationship of Varian Associates of Palo Alto, California, the major manufacturer of NMR spectrometers up to the 1970s, with one early and crucial user, the organic chemist John D. Roberts, who was based at the California Institute of Technology in Pasadena. Roberts's research and teaching contributed to the fast and smooth acceptance of NMR in organic chemistry. He embraced the role of mediator between the instrument manufacturer, which had expertise mainly in physics and electrical engineering, and the customers, who were mostly organic chemists. This essay focuses on the tactics used by Roberts and James N. Shoolery at Varian Associates to implement novel types of instrumentation and on the modes of cooperation between instrument manufacturer and academic scientist.

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I N 1953, the authors of a National Science Foundation (NSF) report on the status of chemistry in the United States regarded the pursuit of fundamental ideas as “one of the greatest present needs.” By way of explanation, they referred to the recent history of their discipline. In the past, they observed, many research problems had been conceived in European countries. However, because of the unsettled situation in Europe after World War II, the flow of ideas to the United States had been interrupted. American chemists believed that an important goal of NSF policy should be providing conditions for enhanced creative work. At that time, the overall budget of the NSF was only around \$2.5 million. Four years later, the chemists’ emphasis (and the foundation’s budget) had radically changed. In 1957 instruments seemed the most urgent need: “Much can still be done with test tubes, slide rule, paper and pencil, but there is now convincing evidence that great scientific discoveries are to be expected through the development and use of the expensive new tools of scientific research.” This process gained such momentum that by 1962 the chairman of the NSF chemistry advisory panel, the organic chemist William von Eggers Doering, called such instruments “pieces of equipment without which no department could pretend to be supporting modern chemical research.”<sup>1</sup> In the rhetoric of grant applications, reports, and official letters, chemists declared high-technology instrumentation the *sine qua non* for competitive research. But their vision embraced more than just a move to raise more money. Sparked by the age of electronics, fueled by increased funding, and assisted by the sales efforts of instrument manufacturers, instrumentation of a novel kind had a deep impact on laboratory practice and the experimental style of chemistry. In the 1950s and 1960s chemistry adopted a distinctly physical mode because most of the new techniques, such as ultraviolet and infrared spectroscopy, mass spectrometry, and nuclear magnetic resonance (NMR), had originated in physical research. In combination with the impact of quantum chemistry and the rise of physical organic chemistry in the 1940s and 1950s, these changes shaped the instrumental, experimental, and theoretical dimensions of chemistry to such an extent that some historians call them, collectively, the “second chemical revolution.”<sup>2</sup>

<sup>1</sup> William von Eggers Doering to Geoffrey Keller, 1 Aug. 1962, National Archives and Records Administration (NARA), College Park, Maryland, Record Group (RG) 307, National Science Foundation (NSF), Office of the Director, General Records, 1949–1963, 1957–1959, box 76, folder “M, P, & E Chemistry Program.” On the situation in 1953 see “Status Report on MPE (Mathematical, Physical, and Engineering) Sciences,” 31 Jan. 1953, NARA, RG 307, NSF, Office of the Director, General Records, 1949–1963, 1951–1956, box 11. For circumstances by 1957 see MPE Divisional Committee, Chairman Thomas K. Sherwood, to Detlev Bronk and Alan T. Waterman, 21 Jan. 1957, NARA, RG 307, NSF, Office of the Director, General Records, 1949–1963, 1960–1961, box 48, folder “Division of M, P, and ES.” The NSF budget for the fiscal year 1957 (Research & Development) was ca. \$30.65 million. See National Science Foundation, Division of Science Resources Statistics, “Federal Funds for Research and Development, Detailed Historical Tables, Fiscal Years 1951–2000, Table B, Federal Obligations for Total Research and Development, by Major Agency,” <http://www.nsf.gov/sbe/srs/nsf01308/htmstart.htm#sum> (accessed 7 Mar. 2005).

<sup>2</sup> Although the very definition of the chemical sciences rests on laboratory methods, historians have largely neglected the issue of instrumentation until recently. For new work see Peter J. T. Morris, ed., *From Classical to Modern Chemistry: The Instrumental Revolution* (Cambridge: Royal Society of Chemistry, 2002); Ursula Klein, ed., *Tools and Modes of Representation in the Laboratory Sciences* (Dordrecht: Kluwer, 2001); and Frederic L. Holmes and Trevor H. Levere, eds., *Instruments and Experimentation in the History of Chemistry* (Cambridge, Mass.: MIT Press, 2000). See also Yakov Rabkin, “Uses and Images of Instruments in Chemistry,” in *Chemical Sciences in the Modern World*, ed. Seymour H. Mauskopf (Philadelphia: Univ. Pennsylvania Press, 1993), pp. 25–42; Davis Baird, “Analytical Chemistry and the ‘Big’ Scientific Instrumentation Revolution,” *Annals of Science*, 1993, 50:267–290; Leo Slater, “Instruments and Rules: R. B. Woodward and the Tools of Twentieth-Century Organic Chemistry,” *Studies in History and Philosophy of Science*, 2002, 33:1–33; and Jeffrey K. Stine, “Scientific Instrumentation as an Element of U.S. Science Policy: National Science Foundation Support

In reconstructing this revolution, historians of science and technology have singled out the war-related needs of the chemical and petroleum industries and the subsequent efforts of instrument manufacturers to spread the techniques in the scientific and industrial spheres.<sup>3</sup> Thus much historical work considers the uses of instruments in routine analytical chemistry. Neglected, so far, are the roles of the scientists themselves in this process and the impact of instruments on chemical research. Chemists were not just passive users of the new techniques; some were prolific innovators. One of the most important techniques in this respect, NMR, had its theoretical underpinnings in quantum physics and was rooted in high-technology fields such as magnet design and electronics.<sup>4</sup> Though these characteristics made it difficult for the average chemist to contribute to the development of innovative hardware, certain users became critically important for the development of new applications and for the active adaptation of the technique more generally.

This essay analyzes the actions and motivations of John D. Roberts, one of the first users of NMR in organic chemistry, at the California Institute of Technology from 1955 to the 1970s. Roberts (b. 1918), a physical organic chemist by training, recognized the potential of NMR for the development of this subfield of organic chemistry very early on. In the early 1950s only one company manufactured and sold NMR spectrometers: Varian Associates of Palo Alto, California. A symbiotic relationship emerged between Roberts and Varian Associates, which in those first years was represented by the chemist James N. Shoolery (b. 1925). Although Roberts's research was originally in the core areas of physical organic chemistry, he rapidly moved into the realm of NMR. First he emphasized conformational studies of small organic compounds (1956 to the mid 1960s); he then moved on to the development of the special techniques of carbon-13 NMR (1966 to the mid 1970s) and nitrogen-15 NMR (1974 to the mid 1980s). During these years, Roberts's primary aim was to develop novel kinds of instrumentation in cooperation with an instrument manufacturer; he avoided doing the construction work on his own. Reliance on advanced instrumentation and the symbiotic relationship of industrial and academic research were key aspects of Roberts's and Shoolery's work; I approach them here by means of the concept of the scientific lead user.

In economics and innovation studies, Eric von Hippel's concept of the lead user refers to those who "face needs that will be general in a marketplace, but they face them months or years before the bulk of that marketplace encounters them, and . . . are positioned to benefit significantly by obtaining a solution to those needs." Von Hippel distinguishes the

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of Chemistry Instrumentation," in *Invisible Connections: Instruments, Institutions, and Science*, ed. Robert Bud and Susan E. Cozzens (Bellingham, Wash.: SPIE Optical Engineering Press, 1992), pp. 238–263. For a contemporary description of the impact of physical instrumentation on 1960s U.S. chemistry see National Academy of Sciences, National Research Council, *Chemistry: Opportunities and Needs: A Report on Basic Research in U.S. Chemistry by the Committee for the Survey of Chemistry* (Washington, D.C., 1965), pp. 86–102.

<sup>3</sup> Yakov M. Rabkin, "Technological Innovation in Science: The Adoption of Infrared Spectroscopy by Chemists," *Isis*, 1987, 78:31–54; and Timothy Lenoir and Christophe Lécuyer, "Instrument Makers and Discipline Builders: The Case of Nuclear Magnetic Resonance," *Perspectives on Science*, 1995, 3:276–345.

<sup>4</sup> For a general history of NMR see Edwin D. Becker, Cherie Fisk, and C. L. Khetrpal, "The Development of NMR," in *Encyclopedia of Nuclear Magnetic Resonance*, 8 vols., ed. David M. Grant and Robin K. Harris, Vol. 1: *Historical Perspectives* (Chichester: Wiley, 1996), pp. 1–158. For a history from a philosophical perspective see Henk Zandvoort, *Models of Scientific Development and the Case of Nuclear Magnetic Resonance* (Dordrecht: Reidel, 1986); and Zandvoort, "Nuclear Magnetic Resonance and the Acceptability of Guiding Assumptions," in *Scrutinizing Science: Empirical Studies of Scientific Change*, ed. Arthur Donovan *et al.* (Dordrecht: Kluwer, 1988), pp. 337–358. For its early history see John S. Rigden, "Quantum States and Precession: The Two Discoveries of NMR," *Reviews of Modern Physics*, 1986, 58:433–448; and Mark Gerstein, "Purcell's Role in the Discovery of Nuclear Magnetic Resonance: Contingency versus Inevitability," *American Journal of Physics*, 1994, 62:596–601.

notion of the lead user from another concept he has advanced, that of user-dominated innovation. The latter affords important insights into the roles academic scientists have played in the development of new instruments, among other products. The concept of the lead user, in contrast, describes the effects such users had on the later stages of innovation and on the marketing of high technology.<sup>5</sup> Expanding on von Hippel's concept, I argue that the development and the dissemination of new research methods are at the center of scientific lead users' activities. With regard to scientific instruments, such methods link the technological and marketing-related parts of the innovation process, and methods-oriented scientists are ideally suited to act as mediators between instrument manufacturers and their customers in academic chemistry. Furthermore, in my view the concept of the lead user is not necessarily restricted to academic scientists such as Roberts. Lead users' functions could be fulfilled by industrial scientists—as was the case with Shoolery of Varian Associates.

The background for the story presented in this essay is a crucial moment in the history of NMR: the period when it ceased to be a problem-generating technique in physics and physical chemistry and started to become a question-answering method in general chemistry and, especially, organic chemistry. In the 1950s, organic chemistry represented the greatest part of American chemistry. Some organic chemists found it worthwhile to join forces with instrument manufacturers in order to obtain access to one-of-a-kind instruments; in return, they supplied manufacturers with design ideas and used grant money for instrument development. At the same time, manufacturers were eager to tap the huge market in organic chemistry, and for that reason Varian Associates engaged—to a limited extent—in in-house organic chemical research. While Shoolery of Varian Associates began to publish his work in chemical research—even using advertisements as a way to promote his research—Roberts at Caltech helped to boost the company's sales and marketing efforts through lectures, research articles, and textbooks. I illustrate this partial overlap of industrial and academic functions by describing Roberts and Shoolery's cooperation in the late 1950s, Roberts's innovative design contributions during the 1960s and 1970s, and Roberts's teaching and textbook-writing efforts.

#### AN INSTRUMENTAL REVOLUTION

Since the mid-nineteenth century, the most important aims of organic chemists had been the structural elucidation and synthesis of chemical compounds. Analysis and synthesis were tightly interwoven: without structural knowledge, a chemist's attempt at synthesis was a blind shot; without synthesis, a postulated structural formula did not count as a proven fact.<sup>6</sup> Before the 1950s, chemists routinely determined the structures of organic chemical compounds by chemical means—so-called wet methods—and by combustion analysis. Elemental analysis of a compound by combustion and the subsequent weighing

<sup>5</sup> Eric von Hippel, *The Sources of Innovation* (New York: Oxford Univ. Press, 1995), pp. 107 (quotation), 11–27, 133–163. In the section on user-dominated innovation, von Hippel's book presents innovation histories of gas chromatography, ultraviolet spectroscopy, NMR, and electron microscopy. The borderline between user-innovators and lead users is fluid. Because my focus here is on the development of methods, their illustrative use, and their subsequent diffusion in science, the term "lead user" seems to be adequate. The concept became widely known in economics through von Hippel's efforts (in part with the companies 3M and Business Genetics) to establish it as a development and marketing tool. This even led to the founding of a company called Lead User Concepts, Inc. (LUCI). See "About lead user concepts," <http://www.leaduser.com> (accessed 30 Sept. 2003); and "Lead user research," [http://www.businessgenetics.com/web\\_pdfs/LeadUbrch.pdf](http://www.businessgenetics.com/web_pdfs/LeadUbrch.pdf) (accessed 30 Sept. 2003).

<sup>6</sup> Colin A. Russell, "The Changing Role of Synthesis in Organic Chemistry," *Ambix*, 1987, 34:169–180.

or volumetric measurement of the oxidation products yielded the relative amounts of carbon, hydrogen, and oxygen present in the substance and thus established its empirical formula. Chemists derived structural formulas from chemical tests indicating the presence of certain atomic groupings and degradation reactions that led to the carbon skeleton of the compound. The classical era of chemical structural determination lasted from the 1860s to the 1950s; in this period the structures of a multitude of complex natural products, such as dyes and pigments, alkaloids, vitamins, and hormones, were determined, in work by research groups that often spanned decades. Some successful determinations were found worthy of the highest awards, including the Nobel Prize, and gave rise to industrial prospects.<sup>7</sup>

The end of structural determination by means of traditional chemical degradation and synthesis represented the core of the intellectual changes brought about in the 1950s and 1960s by the instrumental revolution. As early as the late nineteenth century, and increasingly in the first half of the twentieth century, organic chemists had been eager to include spectroscopic evidence in their work on structural determination whenever possible. However, spectroscopic evidence with regard to the structures of organic molecules was still hard to come by. The application of spectroscopic methods in organic chemistry received a great boost in the 1940s, with the advent of commercially available ultraviolet and infrared spectrometers. The correlation of spectral peaks with certain molecular groups gave hints for unraveling the structures of molecules. Organic chemists, who previously had relied almost completely on the information obtained by chemical degradation and identification methods, thus added data from new instruments to their reasoning. Soon, NMR, mass spectrometry, gas chromatography, and X-ray crystallography supplemented the array of techniques available to organic chemists. NMR became the main method for the fast and accurate acquisition of structural information, including evidence on the dynamics of molecules that had been unavailable before. With the help of these instruments, chemists began to unravel the three-dimensional structures, configurations, and conformations of molecules, work that had tremendous applications in both science and industry.<sup>8</sup>

As physical instruments pushed aside classical chemical methods, the epistemic meaning of structural formulas changed too.<sup>9</sup> In the old system, structural formulas were guides for predicting what reactions a substance could undergo, mnemonic symbols referring to chemical affinities. In the new, physical mode of chemistry, structural representation itself became the focus of research. Material characterization nearly disappeared in this process. Other problems appeared on the chemist's agenda: the determination of conformational structure, the analysis of minute amounts of samples that could not be isolated in a pure state, and the study of short-lived reaction intermediates. In twentieth-century chemistry, with its layers of theory, experiment, and instrumentation, these new questions and ap-

<sup>7</sup> Leo B. Slater, "Woodward, Robinson, and Strychnine: Chemical Structure and Chemists' Challenge," *Ambix*, 2001, 48:161–189; Peter J. T. Morris and Anthony S. Travis, "The Role of Physical Instrumentation in Structural Organic Chemistry," in *Science in the Twentieth Century*, ed. John Krige and Dominique Pestre (Amsterdam: Harwood, 1997), pp. 715–739, esp. pp. 717–719; and Arthur J. Birch, *To See the Obvious* (Washington, D.C.: American Chemical Society, 1995), pp. 57–59, 67.

<sup>8</sup> See Derek H. R. Barton, "Some Reflections on the Present Status of Organic Chemistry," in *Science and Human Progress: Addresses at the Celebration of the Fiftieth Anniversary of the Mellon Institute* (Pittsburgh: Mellon Institute of Industrial Research, 1964), pp. 85–100.

<sup>9</sup> For a stronger view that connects the changeover in instrumentation to a change in the ontological status of structural formulas see Joachim Schummer, "The Impact of Instrumentation on Chemical Species Identity," in *From Classical to Modern Chemistry*, ed. Morris (cit. n. 2), pp. 188–211; and Leo B. Slater, "Organic Chemistry and Instrumentation: R. B. Woodward and the Reification of Chemical Structures," *ibid.*, pp. 212–228.

proaches arose in connection with one another, and progress on any one front led to progress on the others. A new type of theoretical chemistry, understood as a merger of physical chemistry, physical organic chemistry, and quantum chemistry, came into being from the 1940s on.<sup>10</sup> Major transformations at two levels occurred at the same time, and their co-stabilization became crucial for their successes. On the one hand, theoretical chemistry explained the function of instruments and supplied many of the research questions that could be tackled. On the other hand, the empirical performance of the instruments underwrote the claims of theoretical chemistry.

At first glance, it seems that physical instruments completely changed the experimental practice of chemistry. But as chemical practice changed, chemists altered the physical techniques as well. The transfer of instrumentation from one discipline to the other involved processes of intrusion, promotion, and, most important, active adaptation by users. This adaptation occurred at three levels: in the theoretical background, in the hardware, and in the social organization of the new research technology. It was pushed forward by two groups: first, by the instrument builders (at universities and government agencies as well as in the chemical industry and instrument-building firms), the number of which increased considerably during World War II; and second, by chemists on the users' side in academia and industry, who contributed heavily to the development of new applications, methods, rules, and medium-range theories.

#### ROBERTS, PHYSICAL ORGANIC CHEMISTRY, AND NMR

Together, organic and theoretical chemists reconfigured the complex theory of NMR into a set of rules that could be applied by the nonspecialist chemist.<sup>11</sup> A special subfield of organic chemistry, physical organic chemistry, played the role of catalyst in this process by drawing on existing cultural attributes of chemistry. Its importance was not so much in its contributions to physical instrumentation, but in its concepts of electronic structures of molecules and reaction mechanisms. These prepared the essential ground for the subsequent breakthrough of physical methods. During its development from the 1920s to the 1950s, the field was overshadowed by traditional synthetic organic chemistry. It gained prominence in the 1950s, at least in the United States, Japan, and most Western European countries. As such, it became the new center of gravity of the discipline of organic chemistry, supplying methods and research problems that were seen to merit further exploration. Thus, physical organic chemistry was different from most other subdisciplines and borderline fields of organic chemistry, such as polymer, bioorganic, and organometallic chemistry. While the latter tackled special classes of substances ("special" with respect to either their function or their structure), physical organic chemistry dealt with the whole of organic chemistry from a new vantage point. Moreover, it enjoyed the status of a "scientific" chemistry, distinct from the traditional craft-like "art."<sup>12</sup>

<sup>10</sup> Mary Jo Nye, *From Chemical Philosophy to Theoretical Chemistry: Dynamics of Matter and Dynamics of Disciplines, 1800–1950* (Berkeley: Univ. California Press, 1993), pp. 1–2. Peter Galison differentiated between the layers, or levels, of theory, experimentation, and instrumentation in twentieth-century physics. See Peter Galison, *Image and Logic: A Material Culture of Microphysics* (Chicago: Univ. Chicago Press, 1997), pp. 797–803.

<sup>11</sup> For the importance of rules in the development and applications of instrumentation see Slater, "Instruments and Rules" (cit. n. 2).

<sup>12</sup> Peter J. T. Morris, Anthony S. Travis, and Carsten Reinhardt, "Research Fields and Boundaries in Twentieth-Century Organic Chemistry," in *Chemical Sciences in the Twentieth Century: Bridging Boundaries*, ed. Reinhardt (Weinheim: Wiley-VCH, 2001), pp. 14–42, esp. pp. 14–20; Nye, *From Chemical Philosophy to Theoretical*

Physical organic chemistry became the field of choice for John D. Roberts, and his contributions to this new branch of chemistry embraced its major topics. During his career Roberts combined knowledge of traditional chemistry with new methods and instruments, and—in the words of a chemist of the succeeding generation who had become familiar with NMR already during his education—this helped in the “demystification” of NMR, an achievement “that opened the doors for organic chemists.”<sup>13</sup> In biographical accounts chemists, like other scientists, are often presented as forerunners, pioneers, and leaders; such treatment is part and parcel of the often hagiographical style of this kind of literature. Nonetheless, it is sometimes the case that a scientist’s strategy for opening up a new field through innovation and the dissemination of research methods in fact led to new perspectives and presented fellow-scientists with more and better options for solving problems. Roberts’s standing in the community of acknowledged physical organic chemists and his ability to connect NMR to the accepted paradigm made him a genuine lead user in this regard.

Roberts received his early education in chemistry at the University of California at Los Angeles. When he graduated in 1944 he had a solid training in physical organic chemistry and hands-on experience with the building of laboratory equipment. He received a post-doctoral fellowship stipend from the National Research Council and moved to Harvard University. At nearby MIT, Arthur Cope, one of the most influential American chemists of the time, was in the process of reforming the organic chemistry group.<sup>14</sup> In 1946 Cope offered Roberts a position as an instructor in the Department of Chemistry. Roberts was fortunate to command seemingly unlimited funds, made available through the new MIT Laboratory for Nuclear Science and Engineering. Some of this funding was applied to investigate the use of the radioactive carbon-14 isotope in radiotracer methods for studying reaction mechanisms, work that led to the concept of the nonclassical carbonium ion (carbocation, in modern terminology).<sup>15</sup> With this topic, Roberts embarked on one of the most enduring controversies in organic chemistry; and he installed himself as one of the central figures in the debates that followed. In coining the term “nonclassical carbonium ion,” and especially through his extremely successful investigations in the field, Roberts made his name in the community of physical organic chemists at the age of thirty-three: “That research program on carbocations really went along like a house afire.”<sup>16</sup> The re-

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*Chemistry* (cit. n. 10), pp. 196–223; and William H. Brock, *The Fontana History of Chemistry* (Hammersmith: Fontana, 1992), pp. 506–569. For the coinage of the term “physical organic chemistry” and its description as a truly scientific, quantitative-mathematical enterprise see Louis P. Hammett, *Physical Organic Chemistry: Reaction Rates, Equilibria, and Mechanisms* (New York: McGraw-Hill, 1940).

<sup>13</sup> Peter B. Dervan, “John D. Roberts,” *Aldrichimica Acta*, 1988, 21:71–77, on p. 75. Roberts’s autobiography is John D. Roberts, *The Right Place at the Right Time* (Washington, D.C.: American Chemical Society, 1990) (hereafter cited as **Roberts, Right Place at the Right Time**).

<sup>14</sup> For the transformation of MIT at large during this period see Christophe Lécuyer, “The Making of a Science-Based Technology University: Karl Compton, James Killian, and the Reform of MIT, 1930–1957,” *Historical Studies in the Physical and Biological Sciences*, 1992, 23:153–180, and the literature cited therein.

<sup>15</sup> For the first year, Roberts obtained the princely sum of \$44,000; in the following years he was given half that amount. See Roberts, *Right Place at the Right Time*, p. 60. For the work that resulted see J. D. Roberts and C. C. Lee, “The Nature of the Intermediate in the Solvolysis of Norbornyl Derivatives,” *Journal of the American Chemical Society*, 1951, 73:5009. See also Paul D. Bartlett, *Nonclassical Ions: Reprints and Commentary* (New York: Benjamin, 1965), p. v; and, for a modern treatment, Jerry March, *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* (New York: Wiley-Interscience, 1992), pp. 312–327.

<sup>16</sup> Rachel Prud’homme, interview with John D. Roberts, Feb.–May 1985, Institute Archives, California Institute of Technology, Pasadena, California, Oral History Collection (hereafter cited as **Prud’homme interview with Roberts**), p. 53. See also Stephen J. Weininger, “‘What’s in a Name?’ From Designation to Denunciation—The Nonclassical Cation Controversy,” *Bulletin for the History of Chemistry*, 2000, 25:123–131.

search leading to this concept exhibited a special feature that also characterized Roberts's later work on NMR: the use of an instrumental technique to establish and investigate novel theoretical ideas.

In 1953, on the basis of Roberts's still-controversial achievements, Linus Pauling, the head of Caltech's chemistry division, offered him a professorship. He was to succeed Howard J. Lucas, who had been one of the early proponents of physical organic chemistry in the United States. In the early 1950s Pauling, whose work dominated the division, had shifted his focus to biological applications of chemistry, and he had just published his alpha-helix model of proteins.<sup>17</sup> Moreover, he worked on the structure of the hereditary material DNA. Thus chemistry and biology at Caltech were strongly interdependent. In addition, Pauling's program focused heavily on the use of physical instrumentation, and he relied on X-ray measurements and electron diffraction methods for his theoretical work in chemistry and biology.

At Caltech, Roberts became the first organic chemist at a university to be fully acquainted with nuclear magnetic resonance spectroscopy. NMR is based on the fact that some atomic nuclei possess spin. This quantum mechanical property can be visualized by thinking of rotation of the nuclei. Because of their electric charge, the spinning of the nuclei generates an internal magnetic field, and a magnetic moment of the nuclei results. If an external magnetic field is applied, those nuclei will tend to line up parallel to the external field; the effect is very similar to that of the earth's magnetic field on compass needles. But in contrast to compass needles, and because of their small size and spin, atomic nuclei do not align but precess around the direction of the external magnetic field. Precession can be visualized if you think of a toy top: as it slows down, the top precesses around its axis. The stronger the magnetic field, the larger the frequency of precession. Under certain conditions, the nuclei may absorb or emit energy at this precession frequency, which usually lies in the radiofrequency region. In experiments using NMR, a sample containing atomic nuclei that possess a magnetic moment is placed inside a strong magnetic field. The magnetic field causes some of the nuclei to precess around the direction of the applied field. Quantum theory predicts the splitting of the energy levels of the nuclei. In the case of hydrogen, for example, the spin one half of the hydrogen nuclei (called protons) could have two values, plus one half and minus one half, and this corresponds to the existence of two energy levels. The value of this energy difference depends on the types of nuclei and the strength of the magnetic field applied. Next, a weaker electromagnetic field is irradiated perpendicular to the direction of the strong magnetic field. If the frequency of the electromagnetic radiation matches the energy difference, absorption or emission of energy occurs: the nuclei are in resonance with the electromagnetic field. Because of some further characteristics, the absorption of energy can be measured. NMR was invented independently in 1945/1946 by two research groups in physics; in the early 1950s it was still a technique used exclusively by physicists and physical chemists, working with self-built instrumentation.<sup>18</sup>

<sup>17</sup> Roberts, *Right Place at the Right Time*, p. 141; and Howard J. Lucas, *Organic Chemistry* (New York: American Book, 1935). On Lucas and his succession by Roberts see California Institute of Technology, *Chemistry and Chemical Engineering at the California Institute of Technology, 1952–1953: A Report of the Academic Year and Other Activities of the Division of Chemistry and Chemical Engineering*, pp. 95–99. Pauling's alpha-helix model of proteins was published in Linus C. Pauling and Robert E. Corey, "Atomic Coordinates and Structure Factors for Two Helical Configurations of Polypeptide Chains," *Proceedings of the National Academy of Sciences*, 1951, 37:235–240.

<sup>18</sup> For literature on the history of NMR see note 4, above.



Although Roberts had worked in a laboratory only a short distance from such groups while at MIT, he had missed several opportunities to get involved with the method. Roberts's lack of interest is understandable, because at that time the two most important chemical NMR effects were not widely known and no commercial equipment was available. Clearly, in 1950 NMR still belonged to the physicists and physical chemists. In the next decade this was to change completely, beginning with the finding of the chemical shift and spin-spin coupling in 1949–1951. These effects are based on the molecular surroundings of the atomic nuclei and give rise to a spectrum that can be interpreted in terms of chemical structure. In 1954, while on a consultancy visit at the DuPont chemical firm, Roberts met William D. Phillips, a chemist who introduced him to some early applications of NMR in organic chemistry. In general, DuPont served Roberts as a source of information in many different areas of chemistry and on a huge variety of instruments. Phillips, a student of Richard Lord who had worked on infrared spectroscopy at the MIT Spectroscopy Laboratory, was keenly aware of the rewards of novel spectroscopic techniques when applied to problems in organic chemistry. In 1953 DuPont had bought one of the first commercial NMR spectrometers, manufactured by the Palo Alto-based firm of Varian Associates. A year later, Phillips told Roberts of his successes in the measurement of rotation rates of atomic groups in molecules. Through his consultancy for DuPont Roberts thus gained firsthand knowledge about a development in NMR that was connected to one of the most promising new fields in physical organic chemistry. He had every reason to “hyperventilate with excitement.”<sup>19</sup>

Upon his return to Pasadena, Roberts tried to convince Linus Pauling to provide funds for an NMR spectrometer. Pauling liked the idea, but he opined that any NMR program should be under the auspices of an expert knowledgeable in physics and familiar with electronic equipment. The Caltech chemical physicist Don Yost had initiated an NMR research program in 1950, undertaking investigations in the tradition of molecular spectroscopy. Yost built his own equipment, mainly with funds from the prospecting company Newmont Exploration, Ltd., of New York. There seems to have been little direct contact between Roberts and Yost with regard to NMR, and Yost—though he continued his investigations in the field until his retirement in 1964—soon concentrated his main efforts on a purely mathematical study. Moreover, Yost's involvement with NMR was exactly the opposite of what Roberts had in mind:

I saw the thing differently, because when I was at MIT they had put in a new infrared spectrometer at Harvard, and while they had infrared experts around—Wilson and people like that—it was set up for use by the organic chemists. They could go in and put their samples in; they didn't have to ask Wilson how to do it. They then took the spectra away, and they could talk to people about the spectra as their own thing. I saw NMR in terms like that, not as the kind of thing that you had to have an expert to carry out for you, and then tell you what the results meant, in your context. I wanted results much faster than I knew they could be gotten that way. . . . So I saw NMR as a technique for organic chemists or chemists in general, to use in their own way.<sup>20</sup>

<sup>19</sup> Roberts, *Right Place at the Right Time*, p. 152; and Carsten Reinhardt, interview with John D. Roberts, 28 Jan. 1999.

<sup>20</sup> Prud'homme interview with Roberts, p. 101. On the chemical physicist E. Bright Wilson see Carsten Reinhardt, “Chemistry in a Physical Mode: Molecular Spectroscopy and the Emergence of NMR,” *Ann. Sci.*, 2004, 61:1–32; and George B. Kistiakowsky, “Edgar Bright Wilson, Jr., Theodore William Richards Professor of Chemistry,” *Journal of Physical Chemistry*, 1979, 83:5A–7A. For the beginning of Yost's work on NMR see his annual report to Linus Pauling, 7 July 1950, Yost Papers, Institute Archives, California Institute of Technology, Pasadena, California, folder 10.6; for the grant from Newmont Exploration see Fred Searls, Jr., to Lee A. DuBridge, 14 Sept. 1954, Yost Papers, folder 2.2.4; for Yost's interest in mathematics see his annual report to Linus Pauling, 7 June 1954, Yost Papers, folder 10.6.

At Caltech, for the most part, each instrument was the responsibility of an individual faculty member who was in charge of its operation and saw to its repair; the instruments were available for others to use, however. Roberts already supervised the use of an infrared spectrometer at the division level, and—envisaging the same sort of arrangement for NMR—he convinced some of his faculty colleagues to assign funds from their ongoing research projects to the purchase of the instrument. Roberts collected \$17,500, which was nearly enough for a spectrometer. By highlighting a research problem of interest to Pauling (the borderline of resonance and tautomerism), Roberts finally persuaded the division head to apply for extra funds from the university board of trustees. Surprisingly, the board agreed to fund the full price of the spectrometer, and Roberts was able to spend the money he had raised on additional equipment and its installation.<sup>21</sup>

Roberts's early entrance to NMR was a consequence of his unique position in the discipline of physical organic chemistry and his earlier experience with carbon-14 analysis and infrared spectroscopy. Furthermore, the departmental structure at Caltech fostered the use of advanced physical instrumentation by individual scientists. For Roberts, this proved to be an opportunity to advance his own research program to areas previously unforeseeable, particularly the analysis of interconvertible three-dimensional structures of organic molecules. In 1956–1957 Roberts began to investigate the kind of problems that he later regarded as the most important of his early work in NMR: rotation about single bonds and the effects of molecular asymmetry on the spectra observed.<sup>22</sup> He worked first with fluorine derivatives of relatively simple alkanes, the fluorohaloethanes, mainly because fluorine compounds were easier to observe with NMR than substances that contained just carbon, hydrogen, and oxygen. But fluorine derivatives were difficult to handle, and only when Roberts—through his consultancy at DuPont—heard of an efficient method to introduce two fluorine atoms at one carbon atom did he see the possibility of exploring this area firsthand. The main results of these studies, which Roberts's group continued until the late 1960s, were that the populations of the several possible conformers were not equal and that NMR was shown to be a suitable method for determining both the rates of rotation and the population distributions. Thus Roberts connected NMR to a burgeoning field of research in physical organic chemistry, although doubts arose because of his use of fluorine compounds; some organic chemists questioned the validity of his results for hydrogen-containing substances (the main target for organic chemists).<sup>23</sup>

Even for this early research, Roberts used improved instrumentation. He was the first customer of Varian Associates to purchase the so-called superstabilizer. Thanks to this device, his investigations yielded much more meaningful and reliable results. An important asset of Roberts's research group was its ability to synthesize compounds for innovative

<sup>21</sup> Reinhardt interview with Roberts, 28 Jan. 1999; Roberts, *Right Place at the Right Time*, p. 153; and Prud'homme interview with Roberts, p. 103. See also Carl Niemann to DuBridge, memorandum, 24 Feb. 1955, Roberts Papers (in private possession), folder "Varian Correspondence through 1969." Among Roberts's colleagues, R. M. Badger (physical chemistry), W. Corcoran (chemical engineering), Norman Davidson (chemistry/molecular biology), Verner Schomaker (electron diffraction methods), and Carl Niemann (organic chemistry) expressed interest in the use of NMR.

<sup>22</sup> For a detailed description of this work see Roberts, *Right Place at the Right Time*, pp. 162–167; Prud'homme interview with Roberts, pp. 105–106; and P. Madhavan Nair and John D. Roberts, "Nuclear Magnetic Resonance Spectra: Hindered Rotation and Molecular Asymmetry," *J. Amer. Chem. Soc.*, 1957, 79:4565–4566.

<sup>23</sup> Prud'homme interview with Roberts, p. 106. J. J. Drysdale and William Phillips of the DuPont Experimental Station in Wilmington, Delaware, embarked on very similar studies. See J. J. Drysdale and W. D. Phillips, "Restricted Rotation in Substituted Ethanes as Evidenced by Nuclear Magnetic Resonance," *J. Amer. Chem. Soc.*, 1957, 79:319–322. Drysdale had been a student of Roberts at MIT.

and meaningful research. In this respect, he enjoyed an advantage over physical chemists not versed in the art of chemical synthesis. Moreover, Roberts was carefully considering the complex chemical issues that played a role in the interpretation of the spectra. Because of these advantages, and because he was the first university-based organic chemist to use Varian Associates NMR equipment, he became a preferred customer. This was the beginning of a symbiotic relationship that lasted for more than a decade.

#### VARIAN ASSOCIATES

Varian Associates welcomed this kind of partner in academic chemistry. The company was founded in 1948 by the brothers Russell and Sigurd Varian and—among others—the Stanford physicists William Hansen, Edward Ginzton, and Leonard Schiff; its expertise centered heavily on physics and electronic engineering. In many ways, Varian Associates can be regarded as an offshoot of the physics department at Stanford University. But, as the historians Christophe Lécuyer and Timothy Lenoir have shown, technology transfer between the university and corporate enterprise was not a one-way street leading from the academic to the industrial institution. Varian Associates contributed tremendously to the academic culture at Stanford. Many Stanford physicists wished to escape the constraints of nuclear particle physics, a focus enforced by the military-funded style of research at leading American universities. Varian Associates promised to retain the goal-oriented, but nevertheless creative, research atmosphere that many of its founders had experienced during the war. Essentially, in its first two decades, Varian Associates was a research and development company that relied heavily on orders from the military. With its excellent links to Stanford University, Varian Associates was just the sort of partner Stanford provost Frederick Terman had in mind as he sought to establish close ties between the academic culture of his university and the industrial culture of the companies in its vicinity—what has become known as Silicon Valley.<sup>24</sup>

From the company's point of view, the chemical applications of NMR offered access to a market with the potential to counterbalance the firm's one-sided dependence on military spending. Varian Associates delivered its first NMR spectrometers to petroleum and chemical companies.<sup>25</sup> They could afford the \$25,000 price tag and to support the infrastructure necessary for the machines' operation and maintenance. Moreover, they recognized the possibilities of NMR for analytical use in chemical research, building on their experiences with in-house development of their own instrumentation. Though the market offered by chemical companies was lucrative, the breakthrough of NMR in organic chemistry relied on its uses in academic research and, especially, education. In the early 1950s, academic chemistry departments still had much less funding than their industrial counterparts. More-

<sup>24</sup> Lenoir and Lécuyer, "Instrument Makers and Discipline Builders" (cit. n. 3), p. 287; Stuart W. Leslie and Robert H. Kargon, "Selling Silicon Valley: Frederick Terman's Model for Regional Advantage," *Business History Review*, 1996, 70:435–472; and Rebecca S. Lowen, *Creating the Cold War University: The Transformation of Stanford* (Berkeley: Univ. California Press, 1997), pp. 103–109, *passim*.

<sup>25</sup> The first was either Magnolia Petroleum of Dallas, Texas (Magnolia was a predecessor of Mobil Oil), or Phillips Petroleum, joined in 1953 by Humble Oil in Baytown, Texas (later Exxon), Shell Development Company in Emeryville, California, and the chemical company DuPont of Wilmington, Delaware. See Shannon Mercer, interview with Ralph Kane, Nov. 1989, Varian Associates, Inc., Oral History Project, Department of Special Collections, Stanford University Libraries, Stanford, California, SC M 708, box 1; Don Woessner, "Early Days of NMR at Mobil in Dallas," *TAMU NMR Newsletter*, 1995, 449:33–37, copy in Richard R. Ernst Papers (in private possession); and Raymond C. Ferguson, "William D. Phillips and Nuclear Magnetic Resonance Spectroscopy at DuPont," in *Encyclopedia of Nuclear Magnetic Resonance*, ed. Grant and Harris (cit. n. 4), Vol. 1, pp. 309–313.

over, most organic chemistry departments lacked the organizational capabilities for handling large-scale electronic equipment. This changed with the post-*Sputnik* National Defense Education Act. In contrast to earlier governmental science funding, which had concentrated on research, the National Defense Education Act included support for infrastructure and teaching programs. Until the early to mid 1960s, however, the funders still preferred to support a small number of universities. In the words of one Varian Associates employee, the ensuing distribution of governmental money over a much greater range of educational institutions than ever before allowed “normal market forces to shape the development of NMR.”<sup>26</sup>

In January 1953 Varian Associates opened an applications laboratory, with the Caltech Ph.D. James N. Shoolery as its head. At Caltech Shoolery had been a student of Norman Davidson, a chemist who used physical instrumentation for unraveling problems in molecular biology. Moreover, Shoolery had worked with Don Yost on NMR and microwave spectroscopy and thus was intimately familiar with NMR technology. Fascinated by the prospects of NMR, Shoolery proposed that Varian Associates build up a laboratory for the development and demonstration of its chemical applications. As a chemist with research experience, Shoolery understood the needs of the chemical community. The applications laboratory was essentially a marketing tool, creating and fostering potential applications of the technique and connecting the company to its customers. Shoolery provided badly needed expertise. Because the staff of Varian Associates consisted mainly of physicists and engineers, they were eager for guidance in incorporating parts of the culture of their most important customers, the chemists. The applications laboratory of Varian Associates soon started major marketing efforts. From 1954, a series of advertisements appeared on a monthly schedule on the back cover of the *Journal of the American Chemical Society*. Three years later, Varian Associates began organizing annual workshops, providing training and sales information for a community of academic and industrial researchers.<sup>27</sup> From the mid 1950s to the early 1960s, Shoolery conducted a research program in chemical NMR. Though he was an industrial scientist, he adopted an academic style for research and publication of his results at a time when the community of NMR specialists in academic chemistry was still in its early phase. Thus Shoolery filled a gap and significantly shaped the norms and standards of chemical NMR. In the mid 1960s, when instruments became available for routine use and the NMR community at universities had grown considerably, the Varian Associates Applications Laboratory restricted itself to providing support in analytical tasks. Shoolery himself moved on to a managerial position.

#### USER AND MANUFACTURER INTERTWINED

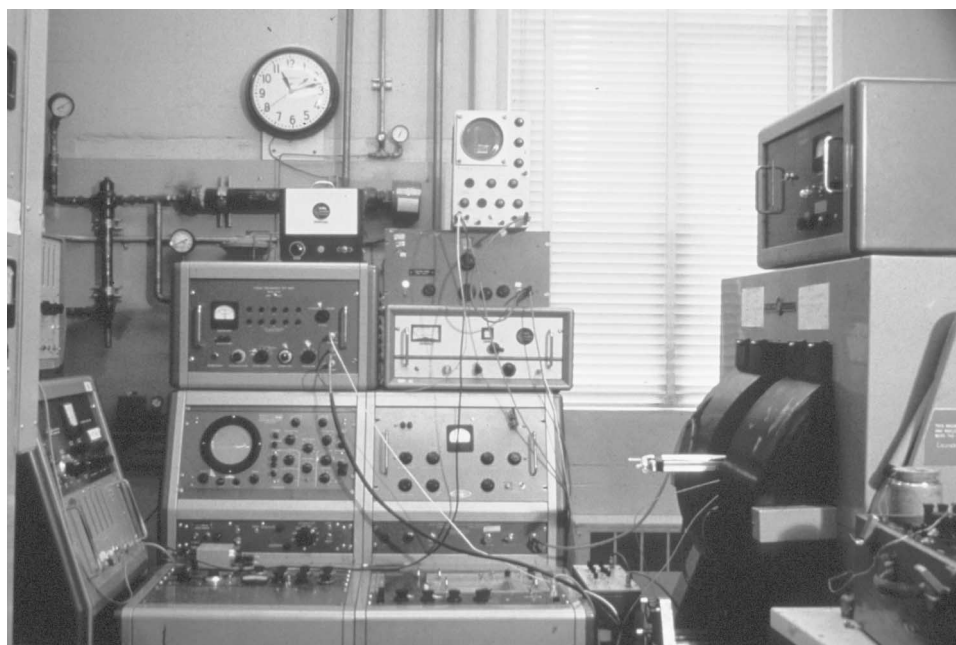
Even in the 1950s the Varian Associates staff developed quite elaborate relationships with the academic world. Management allowed some employees to publish and to participate

<sup>26</sup> Martin Packard, “The Varian Story: As Presented at the 1980 Pittsburgh Conference on Analytical Chemistry,” p. 9, Department of Special Collections, Stanford University Libraries, Stanford, California, SC 345, series Varian Associates, box 4, folder 23. See also Hugh D. Graham and Nancy Diamond, *The Rise of American Research Universities: Elites and Challenges in the Postwar Era* (Baltimore: Johns Hopkins Univ. Press, 1997), Ch. 2: “The Revolution in Federal Science Policy”; and Roger L. Geiger, “Science, Universities, and National Defense,” *Osiris*, 2nd Ser., 1992, 7:26–48.

<sup>27</sup> On Shoolery’s role in promoting NMR see James N. Shoolery, “NMR Spectroscopy in the Beginning,” *Analytical Chemistry*, 1993, 65:731A–741A; and Carsten Reinhardt, interview with James N. Shoolery, 23 Jan. 1999. On Varian’s laboratory and workshops see Lenoir and Lécuyer, “Instrument Makers and Discipline Builders” (cit. n. 3).

in academic affairs and also provided the opportunity for academic workers to join the company for limited periods (although most of them worked in the field of theoretical and practical improvements of instrumental methods, rather than in applications). An extension of this involvement was the support of academic chemists at their own institutions. It seems that no specific policy stipulated this strategy, and it is important to note that this kind of interaction was not formalized. Though some scientists received special treatment, there were no guarantees; and Varian Associates made decisions regarding the development of special instrumentation on a case-by-case basis. The benefits for the scientists came in the form of enhanced scientific productivity, the opening of new and exclusive research fields, and, perhaps, some income created by publications on the novel uses of NMR. For Varian Associates, Roberts proved to be a “stellar salesman,” combining the virtues of an established scientific reputation (in 1954 he won the American Chemical Society award in pure chemistry) and high productivity as a full professor at one of the leading chemistry departments in the country.<sup>28</sup>

Soon after the delivery of his instrument, a Varian V-4300b NMR spectrometer (see Figure 1), in the summer of 1955, Roberts was both excited and dismayed by the fast pace of Varian Associates’ innovation of novel equipment. His own instrument had already been upgraded, improving on the first generation. At the end of 1955 Varian announced



**Figure 1.** Varian Associates V-4300b NMR spectrometer at Caltech, circa 1960. Note the added peripherals that improved the performance of the spectrometer, the origins of Varian Associates’ “Living Instrument” policy of improvements that were compatible with older instrument versions. The superstabilizer is on top of the magnet on the right. Courtesy of John D. Roberts.

<sup>28</sup> Roberts, *Right Place at the Right Time*, p. 170 (“stellar salesman”). On Varian’s relations with the academic world see Sharon Mercer, interview with Martin Packard, Dec. 1989, Varian Associates, Inc., Oral History Project (cit. n. 25), SC M 708, box 1.

the introduction of another upgrade, a control device to stabilize the magnetic field. The quality of the spectra improved substantially, and Roberts had to buy the additional equipment to stay in a competitive position. The relatively high price of the device (ca. \$1,500), and the fact that he was forced to modernize equipment that was less than half a year old, caused both Roberts and the Caltech administration to question the sales policy of Varian Associates. Shoolery felt compelled to defend the pricing and innovation procedure of his employer, emphasizing that they had made great efforts to ensure the compatibility of improvements with older instrumentation. Later, Varian Associates would refer to this system as its “Living Instrument” policy, which enabled users of older instruments to modernize their equipment with prepackaged kits.<sup>29</sup>

Meanwhile, Roberts reassured Shoolery that he would continue to stay in the field of NMR: “I’ll grumble and complain, but after all I am using the equipment and must have it in perfect condition to be able to compete with other researchers in the field.” Before Roberts received the superstabilizer upgrade, Shoolery allowed him to run samples on a prototype at Varian Associates. For Roberts, clearly, this was an opportunity to get sets of improved data before other people could do so—especially one of his closest competitors at that time, Herbert Gutowsky, a physical chemist at the University of Illinois who worked with self-built equipment. Shoolery, on his side, let Roberts know that he would install the improved instrumentation at Caltech as soon as possible. Varian Associates even offered to break from the usual practice of installing updates in the order in which customers had made their initial purchases for the benefit of having a test site at hand.<sup>30</sup>

Roberts devoted himself to improving the instrument. In particular, for some of his studies a device for temperature control would have been desirable, but the Varian V-4300 spectrometer came with a Dewar flask that could be heated or cooled only outside the instrument. Already in his letter of inquiry about the cost of the Varian instrument, Roberts had asked whether it was possible to accommodate more elaborate temperature control. In the months after delivery, Roberts introduced his first improvement of the apparatus. Together with Shoolery, he designed a temperature control device, initially only for heating. Though Roberts coauthored the publication describing this device, his name did not appear on the Varian Associates patent. Roberts’s contribution consisted mainly in the design of suitable glassware.<sup>31</sup>

In addition to improving his own situation, Roberts’s complaints and suggestions addressed concerns that might trouble other potential customers of Varian Associates at universities; he understood that department heads would especially resent the long-run

<sup>29</sup> John D. Roberts to James N. Shoolery, 3 Jan. 1956, and Shoolery to Roberts, 6 Jan. 1956, Roberts Papers (in private possession), folder “Varian Correspondence through 1969”; and Varian Instrument Division, announcement of upgrade possibilities with field/frequency control for the HR-60, DP-60, and HP-100 models, 24 Feb. 1964, Roberts Papers, folder “Varian Correspondence through 1969.” For an in-depth study of the “Living Instrument” policy, with the interesting remark that it referred to both the adding of new hardware and the service provided by the Varian Associates Applications Laboratory, see Jody A. Roberts, “Instruments and Domains of Knowledge: The Case of Nuclear Magnetic Resonance Spectroscopy, 1956–1969” (M.Sc. thesis, Virginia Polytechnic Institute and State University, 2002), p. 45. I thank Roberts for providing me with a copy of his thesis.

<sup>30</sup> Roberts to Shoolery, 11 Jan. 1956; Shoolery to Roberts, 6 Jan. 1956; and W. C. Dersch (Service Manager) to Roberts, 15 Feb. 1956; Roberts Papers, folder “Varian Correspondence through 1969.”

<sup>31</sup> Regarding Roberts’s initial query about temperature control see Emery Rogers to Roberts, 18 Jan. 1955, Roberts Papers, folder “Varian Correspondence through 1969.” The publication that premiered the new device was James N. Shoolery and John D. Roberts, “High Resolution Nuclear Magnetic Resonance Spectroscopy at Elevated Temperatures,” *Review of Scientific Instruments*, 1957, 28:61–62. Roberts describes his contribution in Reinhardt interview with Roberts, 28 Jan. 1999; see also Roberts to Shoolery, 11 Jan. 1956, Roberts Papers, folder “Varian Correspondence through 1969.”

financial obligations that this expensive instrumentation required. Though Roberts gave Varian Associates “superb marks” on its efforts to provide efficient service, he was worried about the fact that the machine did need a lot of detailed attention by qualified personnel:

You can see why the general reaction of a department head is one of “How can we afford it?” The other reaction which follows this one immediately is, “Let’s wait for a few years.” . . . My concern is with respect to some of your future and potential customers, many of whom come to me for advice and all of whom want to know how much it’s going to cost for maintenance and improvements.<sup>32</sup>

In the following years, the relationship between Roberts and Varian Associates went far beyond the customary contacts between user and manufacturer. For example, Shoolery, as a recognized scientific expert, was sent one of Roberts’s first papers on NMR for review before it appeared in the *Journal of the American Chemical Society*. Roberts had previously given him the manuscript for comment, since he was quoting Shoolery’s unpublished observations. The Varian scientist reported favorably on the work of his customer and scientific colleague and suggested only minor revisions, arising from discussions with Weston Anderson, a physicist-colleague at Varian Associates. But in 1956 this friendly coexistence was disturbed—and precisely because of Shoolery’s active scientific role. The problem arose when a friend and colleague of Roberts, Max T. Rogers of Michigan State University, collaborated with Varian Associates on a scientific topic. According to Rogers, the Varian scientists published the results of this investigation without his consent, though he alone had initiated the research. As a result, Rogers pulled out of further cooperation with Varian Associates in another promising field of investigation. Roberts used this example as a warning to Shoolery about the consequences of an aggressive scientific strategy by Varian Associates; he also pondered his own role as a mediator between the company and his fellow-scientists:

I am sure that you must realize that unless you wish to do chemistry yourself and compete on *all* facets of a research problem with the outside world you might get yourself shut out of some very interesting problems if word of this sort gets around. Your function has got to be to help people get started, not to finish their problems, if you want to continue to make sales of your machines and share other people’s ideas for use of n-m-r. I don’t know why I keep getting cast in the role of a hair shirt for Varian. I don’t particularly like the job and sometimes a nice quiet field like dipole moments where no commercial machines are available sounds attractive.<sup>33</sup>

Despite this emerging ill-feeling, the situation was patched up and Rogers and Shoolery continued to cooperate, in 1958 publishing a classical paper on the additivity of chemical shifts in steroids.<sup>34</sup> In the meantime, Shoolery seemed to be more cautious with regard to results that were close to the interests of his customers. For example, in the summer of

<sup>32</sup> Roberts to Shoolery, 11 Jan. 1956, Roberts Papers, folder “Varian Correspondence through 1969.”

<sup>33</sup> Regarding Roberts’s first NMR paper see Roberts to Shoolery, 21 June 1956, 20 July 1956, and Shoolery to Roberts, 6 July 1956, Roberts Papers, folder “Varian Correspondence through 1969.” The paper is J. D. Roberts, “Temperature Effects on Nuclear Magnetic Resonance Absorption of Hydrogens Attached to Nitrogen,” *J. Amer. Chem. Soc.*, 1956, 78:4495. On the incident involving Rogers see Roberts to Shoolery, handwritten letter, 2 Nov. [1956], Roberts Papers, folder “Varian Correspondence through 1969” (emphasis in the original).

<sup>34</sup> J. N. Shoolery and M. T. Rogers, “Nuclear Magnetic Resonance Spectra of Steroids,” *J. Amer. Chem. Soc.*, 1958, 80:5121–5135. See also Norman S. Bhacca and Dudley H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry: Illustrations from the Steroid Field* (San Francisco: Holden-Day, 1964), p. 14; and Becker *et al.*, “Development of NMR” (cit. n. 4), pp. 23–24.

1957 he considered publication of molecular asymmetry effects on the appearance of NMR spectra in the “NMR at Work” advertising series of Varian Associates (see Figure 2). He planned to use results obtained in his own research but—as a referee—he knew that Roberts was publishing a paper on the same subject. Shoolery was anxious to reassure Roberts about the positive effects the advertisement would have: “Although this advertisement may appear about the same time or slightly before your paper, I am sure that it will draw attention to the paper and not detract from it since I have specifically mentioned that you have pointed out the effect in a private communication to be published.”<sup>35</sup>

This episode clearly demonstrates the strong impact of Varian Associates on science. Such situations arose quite often in the course of Varian’s cooperation with outside scientists:

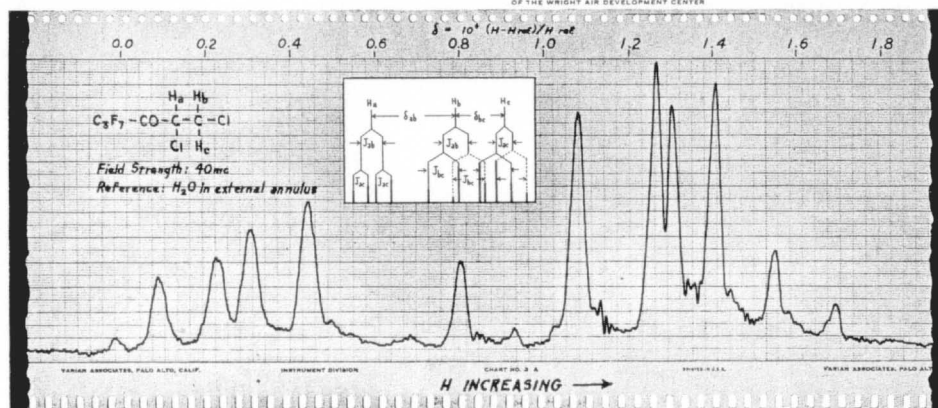
We always had a little bit of a question to settle. That is “OK, we’ve solved your problem. Is it OK that we talk about it in our advertising or do you want us to wait until you’ve published it?” . . . Sometimes our publication preceded the publication in a formal paper. That was a very leading kind of technique. It was very successful at broadening the exposure of this otherwise mysterious kind of thing which seemed like black magic going on in the basement of a physics department.<sup>36</sup>

#### 40 of a series EFFECT OF MOLECULAR ASYMMETRY

**INTERPRETATION.** It has been pointed out by Professor J. D. Roberts<sup>(1)</sup> that in certain cases the chemical shift between like nuclei attached to the same carbon atom is not necessarily averaged out by rapid rotation. In molecules of the type  $\begin{matrix} \text{H} & \text{R}_1 \\ | & | \\ \text{R}_2\text{C}-\text{C}-\text{C}-\text{R}_3 \\ | & | \\ \text{H} & \text{R}_2 \end{matrix}$  in which  $\text{R}_1$ ,  $\text{R}_2$ , and  $\text{R}_3$  are different there may be a chemical shift between the two protons if the residence times of the molecule in the three rotational conformations are not

equal. An example of such a molecule<sup>(2)</sup> is shown below. Its proton spectrum exhibits 12 lines which are assigned in the coupling diagram as arising from 3 non-equivalent protons with coupled spins. The spectrum is independent of temperature over a considerable range which suggests that this model more correctly describes the molecule than one involving a large potential barrier constraining the molecule to one conformation.

(1) PRIVATE COMMUNICATION, TO BE PUBLISHED  
(2) THE SAMPLE WAS FURNISHED THROUGH THE KIND COOPERATION OF THE WRIGHT AIR DEVELOPMENT CENTER



**Figure 2.** Varian Associates advertisement from the “This Is NMR at Work” series, 1957/1958. It shows a new NMR effect, the noncanceling of the chemical shift through rotation of molecular groups, and thus demonstrates that NMR could be used to measure the rotational frequency. Besides the didactic and marketing functions of the advertisement, it also served as an early publication of the method. Note that priority was given to John D. Roberts (see the text). From Varian Associates, Technical Information Bulletin, 1958, 2(2):10. Copy in Roberts Papers, folder “Chemistry 246b.”

<sup>35</sup> Shoolery to Roberts, 18 June 1957, Roberts Papers, folder “Varian Correspondence through 1969.” The paper is Nair and Roberts, “Nuclear Magnetic Resonance Spectra: Hindered Rotation and Molecular Asymmetry” (cit. n. 22).

<sup>36</sup> Reinhardt interview with Shoolery, 23 Jan. 1999.



With its series “This Is NMR at Work,” Varian Associates did more than launch a simple marketing effort. The company set the standards for scientific validity and determined new directions for future work by outside researchers. In the opinion of one of the early users of NMR, Edwin Becker of the National Institutes of Health, scientists awaited the Varian advertisements “as eagerly as they anticipated research articles.” Although publication of the advertisements was the job of the marketing people, Shoolery insisted that the text and design of the scientific part, which showed the spectrum and explained its interpretation, must come under his personal supervision (see Figure 2). He wanted the material to be prepared “exactly as if it had been submitted to a scientific journal” and was aware of the fact that he enjoyed a privilege in “not having to deal with referees” and that the advertisements conveyed a significant advantage in terms of rapid publication. But Varian Associates was involved in many stages of science in the making, not just at the instrument supply side. In the 1950s and early 1960s the “NMR at Work” series appeared on a monthly schedule on the back cover of the most widely read chemical journal in the United States, the *Journal of the American Chemical Society*, and also in the pages of journals such as *Analytical Chemistry* and the *Journal of Organic Chemistry*.<sup>37</sup> Reprinted in the *Varian Technical Information Bulletin*, the series had a tremendous impact on chemical research and teaching. While the first issues of the series were of a largely educational value, real research problems, often tackled in cooperation with academic chemists, soon began to appear.

In addition to this nontraditional—though very effective—manner of publishing, Shoolery also used the ordinary academic pathways to disseminate his views. Between 1953 and 1959 he published thirty-one papers in scientific journals, eleven of them coauthored with university-based chemists and twelve with scientists at governmental and industrial research institutions. For many of these articles, Shoolery undertook only the NMR measurements. But occasionally he was first and quite often second author, an indication of the importance of his contributions. In addition, Shoolery published three reviews and five instrument-related research articles, most of the latter in cooperation with colleagues at Varian Associates. His network of coauthors was large, and with none of them did he write more than three articles. His preferred outlet was the chemical journal with the most general audience, the *Journal of the American Chemical Society*, where he published fifteen articles.<sup>38</sup>

The excellent equipment available to the scientists at Varian Associates provided them a unique opportunity to set new records of achievement. Shoolery, though often in the background, was able to influence the quality standards that counted in the small community of NMR scientists.<sup>39</sup> In the 1958 issue of the *Varian Technical Information Bulletin*, an insert’s green paper mimicked the sports sections in American newspapers. It showed the very best spectrum of acetaldehyde—often used as a standard for gauging the performance of the spectrometer—obtained to that point. Ray Freeman, a postdoc in Paris who

<sup>37</sup> Becker *et al.*, “Development of NMR” (cit. n. 4), p. 23; Shoolery, “NMR Spectroscopy in the Beginning” (cit. n. 27), pp. 734A, 736A; and Reinhardt interview with Shoolery, 23 Jan. 1999. For the appearance of the NMR series in the *Journal of Organic Chemistry* and its role in this community see J. Roberts, “Instruments and Domains of Knowledge” (cit. n. 29).

<sup>38</sup> This paragraph is based on a search done with SciFinder Scholar.

<sup>39</sup> Compare this with the influence that RCA of Camden, New Jersey, a manufacturer of electron microscopes, had on standards in biological electron microscopy. See Nicolas Rasmussen, *Picture Control: The Electron Microscope and the Transformation of Biology in America, 1940–1960* (Stanford, Calif.: Stanford Univ. Press, 1997), Ch. 1.

would later become a world-famous NMR spectroscopist, notes that he regarded Varian's report as a challenge to the rest of the NMR world. He did not have an immediate opportunity to respond to this challenge, as he was using a self-built spectrometer.<sup>40</sup> Later, Freeman joined the staff of Varian Associates. The company became a major player in the scientific field, but it played by different rules than other participants.

So did Roberts. In the mid 1950s the National Science Foundation funded a research program he proposed on the study of small ring compounds and reaction mechanisms. At the same time, a grant from the Office of Naval Research (ONR) supported the beginning of Roberts's NMR projects. In the years to come, Roberts's NSF project rapidly moved into NMR: first in organic chemistry and then with the application of carbon-13 NMR (1966) and nitrogen-15 NMR (1974) to biochemistry and the biological sciences. The National Institutes of Health (NIH) contributed funds for aspects of Roberts's research that promised to be of value for biological and medical purposes. Through NMR, then, Roberts connected physics, chemistry, biology, and medicine. He emphasized the importance of NMR in biological fields in a report to the NIH:

A most significant part of the research effort has been to specify and bring into being NMR instrumentation which, at the time of each production, was not only unique but involved state-of-the-art components. The major elements of the instrumentation so developed are now part of all of the current commercial models of <sup>13</sup>C and <sup>15</sup>N spectrometers. In our view, even if nothing else were accomplished, the conceptualization and commissioning of these instruments has led to a revolution in the use of NMR in biology and biochemistry.<sup>41</sup>

With the spread of the instrument, the scientific community also came to appreciate Roberts's research. But once a certain method was widely used, it lost the appeal of novelty—and exclusivity—for Roberts. Specialists in NMR were always searching for cutting-edge technology to develop new methods. In the mid 1960s, hundreds of chemists used the NMR methods based on the magnetic properties of protons originally developed by Roberts, Gutowsky, Shoolery, and others. In search of a new research project, Roberts decided to continue to focus on NMR. Now, however, he switched to the use of isotopes other than hydrogen, most importantly carbon-13 and nitrogen-15, which were of greatest importance in the biological fields, though very difficult to measure.<sup>42</sup> At about the same time, computers began to appear on the scene, at first used for signal averaging. The use of computers did not by itself solve the problem of obtaining meaningful carbon-13 or

<sup>40</sup> Ray Freeman to Bernard L. Shapiro, 13 Aug. 1990, *TAMU NMR Newsletter*, 1990, 384:15 (special section on Shoolery's retirement), copy in Roberts Papers. See D. Chapman and P. D. Magnus, *Introduction to Practical High Resolution Nuclear Magnetic Resonance Spectroscopy* (London: Academic, 1966), pp. 36–39, where the acetaldehyde spectrum is described as a standard.

<sup>41</sup> John D. Roberts, report of the NIH grant GM 11072-19, "Nitrogen-15 and Carbon-13 NMR Spectroscopy," period 1 May 1981–30 April 1982, Roberts Papers, folder "NSF." See also the summary in John D. Roberts, "Final Project Report," 9 Dec. 1983, NSF CHE81-20508, period 1 May 1979–31 October 1983, Roberts Papers, folder "NSF."

<sup>42</sup> Carbon and nitrogen are, with hydrogen and oxygen, the elements most widely present in organic compounds. While the abundant isotopes of carbon and nitrogen, carbon-12 and nitrogen-14, do not give a signal in NMR experiments, the less abundant isotopes, carbon-13 and nitrogen-15, do. The problem was the low concentration of these isotopes, which led to a dramatic decrease in sensitivity. Though one could work with carbon-13 and nitrogen-15 enriched compounds, this was not an ideal solution to the problem. To be of real use for mainstream organic chemists and biochemists, carbon-13 and nitrogen-15 NMR had to be run at the natural abundance level. This was a considerable challenge in terms of sensitivity. The carbon-12 isotope has a natural abundance of 98.892 percent, carbon-13 an abundance of only 1.108 percent; the ratio of nitrogen-14 (99.635 percent) to nitrogen-15 (0.365 percent) is even worse. For the history of carbon-13 NMR see Becker *et al.*, "Development of NMR" (cit. n. 4), pp. 28–29, 49.

nitrogen-15 NMR spectra. The solution came to Roberts as he was browsing through *Scientific American*: he spotted an advertisement for a frequency synthesizer, manufactured by Hewlett-Packard, with hitherto unheard-of stability. With this kind of frequency synthesizer, gradual sweeping of the radiofrequency field, rather than the magnetic field, became a possibility. Thus Roberts's next proposal involved a major move away from a hardware perspective in the construction of NMR spectrometers. Together with the use of computers for signal averaging, his proposal had the potential to get natural abundance carbon-13 and nitrogen-15 NMR off the ground. After initial hesitations, the Varian Associates management agreed to build a spectrometer according to Roberts's specifications.

In general, Roberts designed the new spectrometer to measure both nitrogen-15 and carbon-13 NMR spectra, but—short of funds—he opted to focus on nitrogen-15 NMR first. It was Varian Associates' wish to develop an instrument for the much broader market of carbon-13 NMR that finally pushed Roberts into the carbon-13 venture. In addition, Roberts agreed to Varian's plan for demonstrating the instrument to potential customers even before delivery, knowing that he could not stem the tide of progress in the field: "I can understand your desire to exhibit it at the Workshop and, although I have pushed for the design and execution of this instrument in hope of starting off at a new tangent to the main stream of n.m.r. research, I guess there is no stopping of progress—hundreds of eager investigators will quickly march in, waving wads of currency to purchase similar instruments for immediate delivery if not sooner." Though the spectrometer did not become a production model, Roberts has observed that Varian Associates included many of its features in later spectrometer types (see Frontispiece).<sup>43</sup>

By joining forces, instrument manufacturers and NMR scientists achieved a major and virtually immediate changeover in the practice of chemical structural analysis. The number of articles published in the *Journal of Organic Chemistry* that included the use of NMR quadrupled between 1960 and 1961 and continued to increase in a near-exponential way to 1966. Articles in the *Journal of the American Chemical Society*, which covered all fields of chemistry, followed a similar, if not so sudden, trend upward, beginning in 1956. In the mid 1960s the quantitative increase leveled off, showing signs of both saturation and, in all likelihood, a certain accommodation to the new technique. The use of NMR was no longer the exception but the rule, and the technique was mentioned in abstracts or indexes only if it constituted a major topic of the article. In any case, as is shown by statistics assembled by chemists themselves, in 1964 the average chemical publication reported the use of at least one of the new physical methods. By the mid 1960s this trend was not restricted to the United States; there were similar effects in Western Europe and Japan. The reasons for this sharp increase were manifold; it is certainly not attributable to the actions of Roberts alone. The boost in the use rate of NMR in organic chemistry during 1961 and 1962 points to a crucial precondition: the availability of a suitable, and affordable, NMR spectrometer. In 1961 the first routine NMR spectrometer, the Varian Associates A-60, appeared on the market. This new instrument enabled organic chemists who were not specialists in NMR to obtain meaningful data by themselves, without help from experts. Between 1960 and 1964, 101 American university chemistry departments reported that

<sup>43</sup> On the initial design for both spectra see Roberts to Forrest Nelson, 19 Jan. 1965, and Roberts to Shooley, 21 July 1965, Roberts Papers, folder "Varian Correspondence through 1969"; and Roberts, *Right Place at the Right Time*, pp. 193–197. On Varian's wish to focus on the carbon-13 NMR market see Shooley to Roberts, 16 July 1965, Roberts Papers, folder "Varian Correspondence through 1969"; for the quotation see Roberts to Shooley, 21 July 1965, Roberts Papers, folder "Varian Correspondence through 1969." On the incorporation of features into later instruments see Roberts, *Right Place at the Right Time*, pp. 194–195.

they acquired eighty A-60 spectrometers, plus twenty-five NMR spectrometers of a more advanced type. Thus, the wide dissemination of instrumentation went hand in hand with the breakthrough of NMR. The immediate commercial success of the A-60 points to the fact that chemists were enormously interested in NMR because they had been alerted to its potential by Shoolery, Roberts, and their colleagues. Furthermore, NMR benefited from the fact that infrared spectroscopy had made deep inroads into chemical practice a decade earlier. Thus chemists were already familiar with the basics of spectroscopy, although the two methods differed considerably in theoretical principle, instrumentation, and range of uses. Infrared and NMR complemented each other, and soon—because of its greater versatility and the wealth of information it rendered obtainable—NMR began to displace the earlier established method.<sup>44</sup>

Before 1960, NMR spectrometers at universities were relatively rare and required delicate handling. Nevertheless, their potential for problem solving in organic chemistry led chemists who did not have access to an instrument to cooperate with NMR specialists. Here, again, Varian Associates played a major role, as the sometimes troubled cooperation of Shoolery with academic chemists illustrates. Roberts also engaged in such cooperation. A typical example is the work of Ernest L. Eliel, one of the most influential experts in stereochemistry and conformational analysis. Since Derek H. R. Barton had pointed to chemical consequences due to different conformational forms of molecules, in 1950, such studies were among the hottest topics in organic chemical research. Conformation describes nonequivalent molecular structures caused by rotation about single bonds. Chemists applied a multitude of methods, including spectroscopy, kinetics, and thermodynamics, to study conformational analysis, and Roberts's own interest in NMR had been stimulated by such work. In 1958 Eliel visited Caltech for a research stay. Although Roberts himself was absent, Eliel had the opportunity to read the galley proofs of his forthcoming textbook on NMR and learned how to use his NMR instrument, supported by some of Roberts's coworkers, including Marjorie Caserio. Thus Eliel added NMR to his armory of instrumentation, although he did not himself become an expert. Soon the method became a standard technique in conformational analysis and, more generally, for reactions that are too fast to be measured by traditional means. In addition, in 1965 organic chemists pointed to the esoteric structures of cubane and bullvalene, recent synthetic triumphs of their art, to underline the capabilities of NMR in structural research. Such advances were not possible with other methods of the time.<sup>45</sup>

<sup>44</sup> In the *Journal of Organic Chemistry* (year/no. of articles): 1956/6, 1957/5, 1958/14, 1959/16, 1960/21, 1961/83, 1962/151, 1963/202, 1964/263, 1965/352, 1966/368, 1967/198, . . . 1976/171. In the *Journal of the American Chemical Society*: 1955/5, 1956/15, 1957/33, 1958/45, 1959/72, 1960/115, 1961/149, 1962/206, 1963/279, 1964/324, . . . 1976/339. The data were acquired by a SciFinder search for publications with the keyword "NMR," restricted to time period and analyzed by journal and year. These figures differ considerably from the numbers published in Lenoir and Lécuyer, "Instrument Makers and Discipline Builders" (cit. n. 3), figs. 4 and 8 (pp. 323, 327). However, they support the main thesis of Lenoir and Lécuyer in attributing significant impact to the A-60 spectrometer in the quantitative breakthrough and their claim that the year 1966 marks the end of the "quantum-leap" of NMR, at least in organic chemistry (see pp. 329–330). For the numbers of instruments in chemistry departments, and for graphs showing the use rate, see National Academy of Sciences, *Chemistry: Opportunities and Needs* (cit. n. 2), pp. 88, 90, 207. Before 1960, not more than twenty-six NMR spectrometers suited for organic chemical research existed in those 101 departments. For more information about the impact of physical methods on organic chemistry and the complementarity of infrared spectroscopy and NMR see Morris and Travis, "Role of Physical Instrumentation in Structural Organic Chemistry" (cit. n. 7); and Rabkin, "Technological Innovation in Science" (cit. n. 3).

<sup>45</sup> Roberts describes his own difficulties in learning to operate the NMR spectrometer and in obtaining reliable results in *Right Place at the Right Time*, pp. 154–159. On Eliel and NMR see Ernest L. Eliel, "Conformational Equilibria by Nuclear Magnetic Resonance Spectroscopy," *Chemistry and Industry*, 1959, p. 568; Eliel *et al.*,

In general, through cooperation with colleagues and instrument manufacturers, organic chemists obtained access to NMR methods before every chemistry department had its own spectrometer. Varian Associates made every effort to acquaint future customers with NMR by arranging workshops that involved practical hands-on experience and through their advertisement series on spectroscopic problems. Roberts also engaged in educational activities, especially when it became clear that the commercial availability and widespread use of NMR spectrometers made the writing of textbooks both a necessary and an attractive endeavor.

#### MAKING NMR TEACHABLE

The teaching of NMR was an integral part of Roberts's research program, since the success of his work depended on the wide use of NMR among organic chemists. Here, his interests and those of Varian Associates complemented each other: the wide diffusion of techniques and instruments was beneficial for both, as long as chemists bought their NMR equipment from Varian Associates and Roberts's research contributions were propagated. Textbook writing was one of the most promising ways to prepare the ground for the dissemination of novel techniques. The first books on NMR for organic chemists appeared in 1959, a decade after the principal usefulness of the technique had been established. Before 1959, organic chemists had to rely on articles and books written for an audience of physical chemists and physicists. Thanks to the new textbooks, chemists could rely on rules of interpretation that were rooted in quantum mechanics, but they were not required completely to understand the physics and mathematics involved. Moreover, the sheer existence of systematic rules enhanced the credibility of NMR in the community of organic chemists, even in cases where these rules were used intuitively rather than formally—or sometimes not applied at all.<sup>46</sup>

Lecturing and teaching also helped Roberts to gain firsthand experience of new techniques. He started to give lectures on NMR at Caltech at a time when he was still at the very beginning of his own research. In 1956 there was only one textbook of any sort on NMR, and this was directed to readers already familiar with the basics of quantum mechanics. Clarification of the technique's principles and demonstrations of its usefulness were badly needed. Accordingly, Roberts designed his "lectures to cover the parts of the basic theory necessary for an organic chemist to use the NMR instrument for practical purposes with reasonable intelligence. No attempt will be made to develop a mathematical basis for resonance absorption—the viewpoint throughout will be qualitative and where desirable much oversimplified (i.e. suitable for electronic morons)."<sup>47</sup>

Beginning with an explanation of the apparatus, the lectures went on to treat its operation, the origins of the signal, and the measurement parameters of greatest use in chemistry, the chemical shift and spin-spin coupling. Applications discussed included the proof of chemical structure (Roberts chose here examples of his own first investigations using NMR), the electronic effects of functional groups, and the study of reaction rates. Roberts

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*Conformational Analysis* (New York: Interscience, 1965), pp. 152–156; and Eliel, *From Cologne to Chapel Hill* (Washington, D.C.: American Chemical Society, 1990), pp. 41–42. The cubane and bullvalene examples are from National Academy of Sciences, *Chemistry: Opportunities and Needs*, p. 94.

<sup>46</sup> This was the case for "Shoolery's rules" on the additivity of the chemical shift. Reinhardt interview with Shoolery, 23 Jan. 1999.

<sup>47</sup> John D. Roberts, "Chemistry 246b—Nuclear Magnetic Resonance," lecture manuscript, undated [1956], p. 1, Roberts Papers.

based his lectures on the available review articles in the field and made use of the *Varian Technical Information Bulletin*.<sup>48</sup> Moreover, he amply illustrated his course with spectra run on his machine, while practical aspects were given prominence through the descriptions of its operation. Roberts taught the calibration of spectra, carefully explained cases where spectral information allowed reliable conclusions for the elucidation of structures, and demonstrated how pitfalls could be avoided. The greatest part of Roberts's lecture course was reserved for explaining the various applications of NMR in organic chemistry. It was aimed at the advanced graduate student with experience in organic chemistry and, preferably, other spectroscopic techniques.

In the following years, Roberts's goal was to make NMR approachable "for the common man" in organic chemistry. He gave approximately forty lectures, based on the Caltech course, at universities and companies all over the United States. A sensational success was a lecture presented at a conference on reaction mechanisms in New York in the fall of 1958. Roberts put great emphasis on the use of self-drawn color illustrations, presented as slides, and he was considering writing a book for organic chemists on the uses of NMR. At the same time, William A. Benjamin, chemistry editor at McGraw-Hill in New York, approached him to discuss a new venture. Benjamin feared that McGraw-Hill was being superseded in organic chemistry by its competitor John Wiley & Sons, and—looking for ways to strengthen his company's position—he set up a series in advanced chemistry that focused on burgeoning subfields. The books were written by acknowledged authorities and covered—among other fields—the two most important new physical techniques in chemistry, NMR and mass spectrometry, with two books each. One was a fundamental and general treatment; the other concentrated on the largest market: organic chemists.<sup>49</sup>

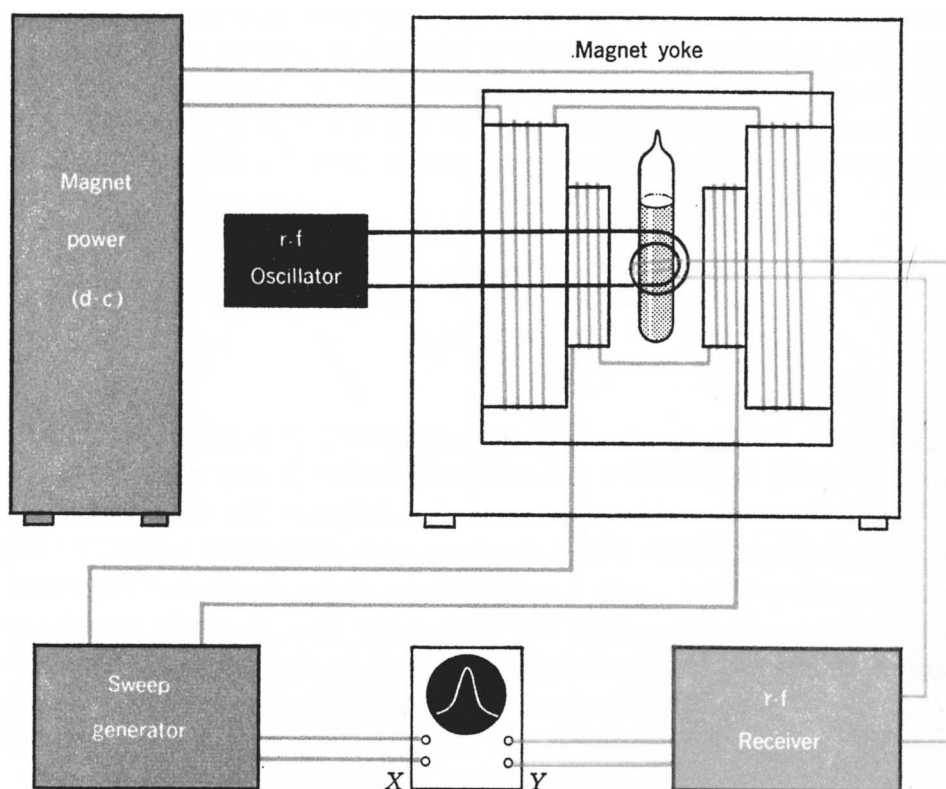
Roberts wrote *Nuclear Magnetic Resonance: Applications to Organic Chemistry*, planned as a sequel to the more advanced treatises available, on lines similar to his Caltech course on NMR. In short, he intended to persuade readers of the usefulness of NMR for chemical studies and to provide them with the necessary practical and theoretical background to engage in studies of their own. In the preface Roberts compared the success story of NMR in chemistry with that of another technique, gas and liquid chromatography. The latter had become ubiquitous in chemistry laboratories in only a decade, and Roberts believed that NMR could be the next technique to enjoy such a spectacular success. The hook for the organic chemist reading the introduction to Roberts's book was that—after a very brief demonstration of the principles of NMR—it offered an NMR spectrum of *N*-ethylethylenimine (modern name 1-ethylaziridine), a compound that Roberts had investigated in his own research. Roberts went on to predict the enormous utility of NMR spectra for the unraveling of various compounds' structures and the rates of rotation and inversion of atomic groups in molecules. Hoping that he had piqued the interest of his readership with this direct statement of the potential of NMR, he then set out to explain its instrumental and physical principles. Color illustrations played a major role in this endeavor; Roberts's

<sup>48</sup> Roberts cited George Pake, "Fundamentals of Nuclear Magnetic Resonance Absorption: I, II," *Amer. J. Phys.*, 1950, 18:438–452, 473–486; John E. Wertz, "Nuclear and Electronic Spin Magnetic Resonance," *Chemical Reviews*, 1955, 55:829–955; and J. A. S. Smith, "Nuclear Magnetic Resonance Absorption," *Quarterly Reviews*, 1953, 7:279–306.

<sup>49</sup> Prud'homme interview with Roberts, p. 77 (quotation); and Roberts, *Right Place at the Right Time*, pp. 169–170 (lectures). The books in the new series were Charles A. MacDowell, ed., *Mass Spectrometry* (New York: McGraw-Hill, 1963); Klaus Biemann, *Mass Spectrometry: Organic Chemical Applications* (New York: McGraw-Hill, 1962); J. A. Pople, W. G. Schneider, and H. J. Bernstein, *High-Resolution Nuclear Magnetic Resonance* (New York: McGraw-Hill, 1959); and John D. Roberts, *Nuclear Magnetic Resonance: Applications to Organic Chemistry* (New York: McGraw-Hill, 1959).

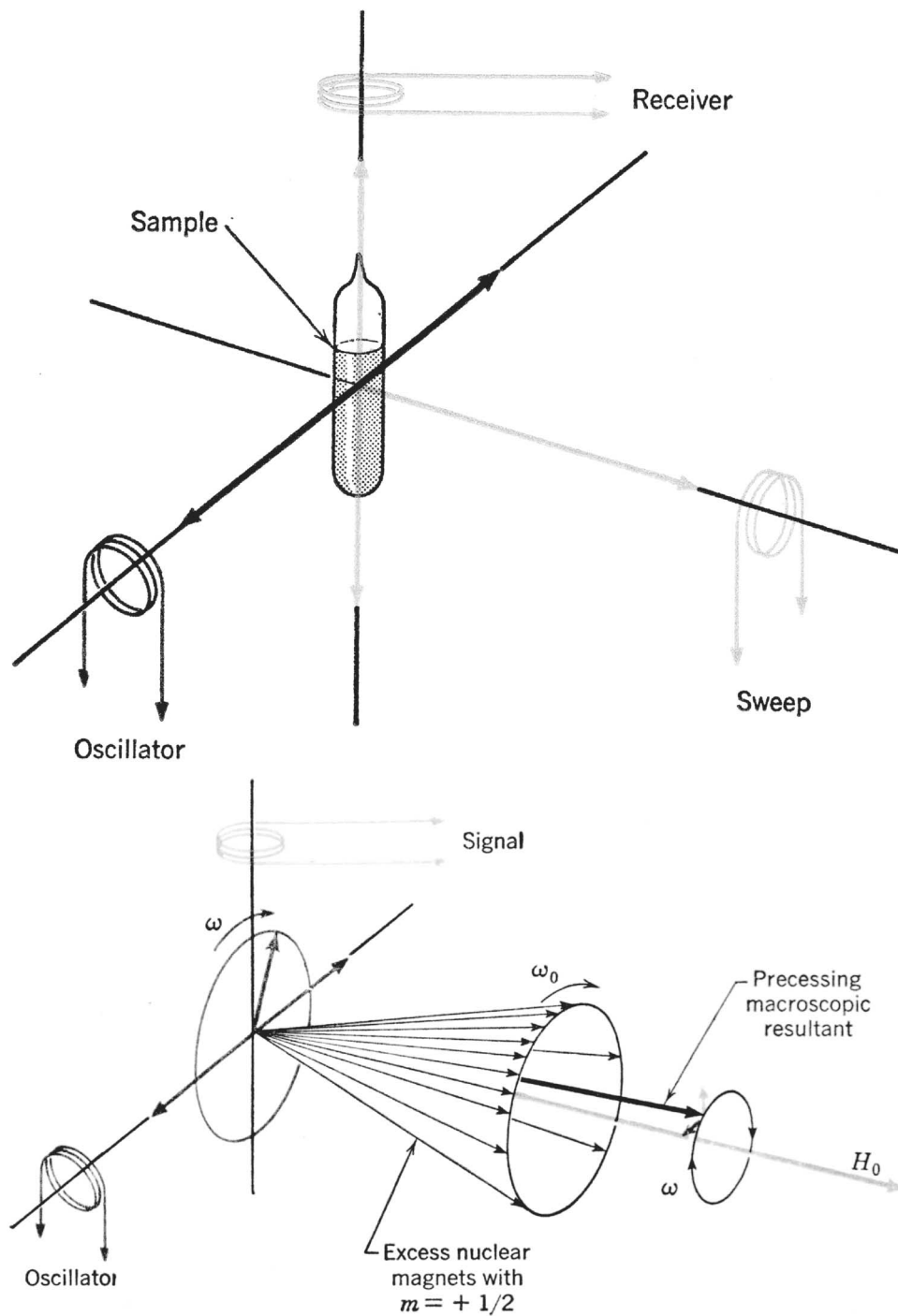
book was the first advanced chemistry text to appear in four-color print. As is shown in the block diagram of an NMR spectrometer (see Figure 4), the colors helped to clarify the interplay of magnetic field, radiofrequency transmitter, and receiver. Here Roberts simplified the instrument in a colorful diagram, hiding the details of the electronic setup. Emphasized and shown in a larger size, out of proportion to its real dimensions, was the test tube containing the sample: the chemical compound was at the core for the chemist approaching NMR.<sup>50</sup>

The connection between physical and chemical detail can be seen in the figure explaining the magnetic forces in an NMR experiment. In the top part of Figure 5, showing the setup before the start of the experiment, the sample is depicted “chemically” in a test tube. In the drawing at the bottom, describing the resonance conditions and the origins of the signal



**Figure 4.** The principal setup of an NMR spectrometer. Note the use of color (visible here as shading) and the sharp difference from earlier block diagrams popular in chemical physics. The latter gave much more detail and were thought to help the viewer to reconstruct the instrument—which would be impossible with the information given here. From John D. Roberts, *Nuclear Magnetic Resonance: Applications to Organic Chemistry* (New York: McGraw-Hill, 1959), page 4. Reproduced with permission of the McGraw-Hill Companies.

<sup>50</sup> Roberts, *Nuclear Magnetic Resonance*, p. 3. In style, Roberts’s figure closely resembles the drawing of a simplified NMR apparatus given by Varian Associates in *Technical Information from the Laboratories of Varian Associates*, 1953, I(1):1—though in the *Bulletin* illustration the dimensions of the test tube and the spectrometer served to emphasize the former even more. Copy in Roberts Papers.



**Figure 5.** The sample in an NMR experiment, illustrating the magnetic forces. In the upper figure, the sample was shown "chemically" in a test tube. The lower figure shows the resonance condition "physically" with a vector. From John D. Roberts, *Nuclear Magnetic Resonance: Applications to Organic Chemistry* (New York: McGraw-Hill, 1959), pages 14, 16.



received, the test tube has disappeared. Instead, a representation of physical forces—here the precession of the magnetic vectors of the nuclei—is given. The transfer of physical explanations to the chemists' view is enhanced by replacing chemical symbols with physical ones, given in a simplified manner as representations of complex effects.

Roberts himself expressed the opinion that this use of color illustrations was important in enabling his book to overcome the possible objection by reviewers that he was not a specialist in physical aspects of NMR.<sup>51</sup> Much of the book dealt systematically with the effects that made the use of NMR in chemistry possible. Though Roberts introduced NMR in nonmathematical terms, an appendix described the Bloch equations for the explanation of the line shapes in nuclear resonance. Roberts hoped thereby to explain the origins of the signals obtained and to clarify the work modes of the spectrometer. A second appendix, presenting problem sets with empirical formulas and spectra of unknown compounds, was meant to initiate the student into the practice of solving structural problems with the help of information obtained by NMR. Varian Associates used a similar approach in its campaign, explaining the features and modes of operation of NMR spectrometers in the *Technical Information Bulletin*. For the purpose of convincing potential customers of the usefulness of NMR, the *Bulletin* included a large selection of spectra and emphasized their application to the unraveling of chemical structures.<sup>52</sup> These spectra were assembled from the "NMR at Work" series.

In many respects, Roberts's *Nuclear Magnetic Resonance: Applications to Organic Chemistry* (1959) resembled Linus Pauling's famous book *The Nature of the Chemical Bond*, published two decades earlier.<sup>53</sup> Both treated the relationship between chemistry and physics, and in both books chemistry came first and physics second. Roberts and Pauling were aware of the possible pitfalls of a complete subordination of chemistry to general physical theory. For example, solvent effects played a critical role in the interpretation of chemical shift data, and Roberts emphasized the chemical expertise that was needed for the correct interpretation of NMR spectra. While Pauling's book concentrated on the principles of chemistry, Roberts's focused on a new experimental technique. Both authors perceived the challenge of communicating the difficulties of physical theory, entrenched in mathematical terms, to an audience of chemists, and both turned to pictorial representations for clarification. Like some early textbooks in quantum chemistry, the early books on NMR sought in their approach to create a certain degree of autonomy for the new field. This required the consolidation of a peculiar language and a body of theoretical and practical knowledge; in this, textbooks for NMR had the same role as textbooks in any new scientific discipline.<sup>54</sup>

For Roberts, the late 1950s and early 1960s were an ideal time for writing textbooks—a period before he knew too much and lost his missionary zeal. Moreover, textbook pub-

<sup>51</sup> Prud'homme interview with Roberts, p. 78. For an example of such a review see Robert I. Walter, "Nuclear Magnetic Resonance," *Journal of Chemical Education*, 1959, 36:531.

<sup>52</sup> See *Technical Information from the Laboratories of Varian Associates*, 1953, 1(1), copy in Roberts Papers.

<sup>53</sup> Linus Pauling, *The Nature of the Chemical Bond and the Structure of Molecules and Crystals* (Ithaca, N.Y.: Cornell Univ. Press, 1939). See Mary Jo Nye, "From Student to Teacher: Linus Pauling and the Reformulation of the Principles of Chemistry in the 1930s," in *Communicating Chemistry: Textbooks and Their Audiences*, ed. Anders Lundgren and Bernadette Bensaude-Vincent (Canton, Mass.: Science History Publications, 2000), pp. 397–414.

<sup>54</sup> Kostas Gavroglu and Ana Simões, "One Face or Many? The Role of Textbooks in Building the New Discipline of Quantum Chemistry," in *Communicating Chemistry*, ed. Lundgren and Bensaude-Vincent, pp. 415–449. See also David Kaiser, ed., *Pedagogy and the Practice of Science: Historical and Contemporary Perspectives* (Cambridge, Mass.: MIT Press, 2005).

lishing was then considered a growth industry, with great potential for future development. William A. Benjamin, who clearly recognized the size of the market for chemistry books, decided to start his own company, W. A. Benjamin, Inc., of New York. In 1960 Roberts became a member of the board, and—together with Benjamin, the Nobel Prize-winning bioorganic chemist Konrad Bloch, and a lawyer—a promoter of the firm. In 1963, when he became chairman of the Caltech chemistry division, Roberts resigned from the board of directors of Benjamin, Inc., but stayed with the company as a consultant. His involvement with Benjamin deeply shaped his later ventures into textbook publishing, most notably *Basic Principles of Organic Chemistry* (1964), written with Marjorie Caserio. Their inclusion of a chapter on spectroscopic methods in a general textbook of organic chemistry was controversial. Though Roberts and Caserio did not insist that this chapter had to be covered in courses on elementary chemistry, they made a strong plea for the early use and teaching of spectroscopy: “Despite the qualms of the older generation in this respect, it really is the proper thing to take spectra before determining the melting point of a new compound—vastly more information can be obtained thereby.”<sup>55</sup>

Roberts’s books had a unique style, aiming at a middle way between a thorough quantum mechanical treatment and a simple setup of rules for the interpretation of spectra. There is no doubt that his first book on NMR was written from the perspective of an organic chemist who wanted to demystify the quantum mechanical foundations of the technique and to apply it rigorously to chemical ends. The question of how much mathematics chemists needed to understand and apply NMR successfully and reliably led to Roberts’s second book on NMR, *An Introduction to the Analysis of Spin-Spin-Splitting*, published in 1961. He believed that chemists could use NMR with a much greater degree of sophistication once they had gained at least a rudimentary knowledge of the quantitative theory and was convinced that this could be achieved quite easily, against all the odds.<sup>56</sup> The formidable task that Roberts had taken on was made easier by the rise of computer programs that reduced the need to understand high-level mathematics, such as group theory. These programs eased calculation and helped in the interpretation of complex spectra. Chemists were able to stick to their familiar strategy of trial and error in the elucidation of chemical structures, as well as establish the correspondence between calculated and experimental spectra. Though it sold several thousand copies, Roberts’s second NMR book was not as successful as its predecessor. Perhaps the advent of computer programs for interpretation prevented the explicit incorporation of more complex quantum mechanics into the community of mainstream organic chemists.<sup>57</sup>

A review of Roberts’s 1959 book applauded the publication as long awaited, noting that the utility of NMR in organic chemistry had already been proven. Some chemists, including Roberts, even considered the widespread use of NMR as being among the most important events in organic chemistry in many decades:

<sup>55</sup> John D. Roberts and Marjorie C. Caserio, *Basic Principles of Organic Chemistry* (New York: Benjamin, 1964), p. ix. An abbreviated version of the book was published three years later: Roberts and Caserio, *Modern Organic Chemistry* (New York: Benjamin, 1967). On the decision to join the Benjamin board see Prud’homme interview with Roberts, p. 79; he also notes (p. 84) that there were financial reasons to relinquish this position.

<sup>56</sup> John D. Roberts, *An Introduction to the Analysis of Spin-Spin-Splitting in High-Resolution Nuclear Magnetic Resonance Spectra* (New York: Benjamin, 1961); on p. 5 he promises to explain the quantitative theory behind NMR in a manner comprehensible to chemists. See also, on this point, Roberts, “Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,” rev. of Lloyd Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* (1959), *J. Amer. Chem. Soc.*, 1960, 82:5767.

<sup>57</sup> Roberts, *Right Place at the Right Time*, p. 174 (on sales); and Becker *et al.*, “Development of NMR” (cit. n. 4), pp. 25–27.

Many organic chemists in this country have recognized the truth of this statement, and anyone who can pretend to any degree of knowledge in this field is asked again and again “Where can I find an intelligible introductory article explaining the principles of NMR and describing its applications to problems in organic chemistry?” Until now, no single satisfactory answer could be given. “Nuclear Magnetic Resonance” was written to fulfill this urgent need.<sup>58</sup>

The great success of Roberts’s first book on NMR and the relative disappointment in the practical impact of his second underline the approach most organic chemists took to NMR. The focus was on learning how to interpret NMR spectra, with as little quantum mechanics as possible. Thus, the spectra “quizzes” that Roberts and Varian Associates adopted in their teaching and advertising served the routine user well. Following the lead of Roberts and Caserio’s 1964 volume, most organic chemistry textbooks included chapters on spectroscopic methods, and soon NMR and other spectroscopic methods were included in undergraduate laboratory teaching. In the early 1970s classical methods based on chemical reactions were boxed as small subsections in introductory texts on laboratory practice—in one case even designated as “more time-consuming methods for structural formula, stereoformula, and conformation.” The “rapid” physical methods had won the day.<sup>59</sup>

While Varian Associates’ and Roberts’s strategies in both designing and improving the DFS-60 spectrometer and teaching new users proved to be compatible, Roberts’s wish in July 1970 to modernize the spectrometer further brought about the break in their fifteen-year cooperative effort.<sup>60</sup> Though the National Science Foundation approved Roberts’s grant application, Varian Associates was not willing to modernize the spectrometer according to his wishes, which included the installation of a Fourier transform unit.<sup>61</sup> At that time, the company was focusing on its high-performance line of spectrometers with high-field superconducting magnets. Such a spectrometer, the HR-220 NMR spectrometer, was the core instrument at the Southern California NMR research facility at Caltech, and Varian Associates proposed to improve this spectrometer rather than the DFS-60.<sup>62</sup> Roberts, however, had only one day of research time at the HR-220 each week; this was inadequate, since his research relied mainly on NMR instrumentation. On his own, then, he decided to modernize the DFS-60 spectrometer with the help of his group, the organic chemists Jean-Yves Lallemand and Bruce Hawkins, and Chris Tanzer, an employee of Bruker-Spectrospin, soon to be a competitor of Varian Associates. This incident marked the final period of Varian Associates’ monopoly in the NMR market of the United States.

<sup>58</sup> Aksel A. Bothner-By, “Nuclear Magnetic Resonance: Applications to Organic Chemistry,” *J. Amer. Chem. Soc.*, 1959, 81:5013–5014, on p. 5013.

<sup>59</sup> Robert B. Bates and John P. Schaefer, *Research Techniques in Organic Chemistry* (Englewood Cliffs, N.J.: Prentice-Hall, 1971), p. 123.

<sup>60</sup> John D. Roberts, Supplemental equipment proposal for support of research by the NSF, “Nuclear Magnetic Resonance Spectroscopy, Structures and Reaction Mechanisms of Organic Compounds,” 1 July 1970, Roberts Papers, folder “NSF.”

<sup>61</sup> Roberts, *Right Place at the Right Time*, pp. 197–198. The basic idea behind Fourier transform (FT) NMR is the excitation of all resonance frequencies in a spectrum at the same time rather than sequentially, as in the “normal” continuous wave techniques, where either the magnetic field or the radiofrequency field was swept through. This traditional mode led to a reduced sensitivity per time unit, because only a narrow frequency band brought about the signal at one time. In FT NMR, the spectrum is excited all at once by a pulsed radiofrequency. Using a mathematical method first developed by Jean Baptiste Fourier in the early nineteenth century, the time-dependent impulse response (called free induction decay, or FID) is transformed to the frequency-domain spectrum—thus, the familiar NMR spectrum. Richard R. Ernst at Varian Associates invented FT NMR in the mid 1960s. Its breakthrough came in the late 1960s and early 1970s with carbon-13 NMR. FT NMR soon became the standard measuring procedure and the basis for subsequent developments.

<sup>62</sup> See Sunney I. Chan, memorandum to the chemistry faculty, research fellows, and graduate students, 21 Aug. 1968, Roberts Papers, folder “Varian Correspondence through 1969.”

In the early 1970s Roberts had to shift gears once again. Carbon-13 NMR had become commonplace among organic chemists and biochemists, and Roberts chose to focus on nitrogen-15 NMR instead. He pushed hard for the development of a nitrogen-15 spectrometer of the “next generation,” using high magnetic field strength and Fourier transform methods. The German-Swiss company Bruker-Spectrospin, with its American subsidiary Bruker Scientific, Inc., of Elmsford, New York, had begun to cater to the U.S. market. When a decision had to be made on the construction of a dedicated nitrogen-15 spectrometer, Bruker’s offer seemed more promising to Roberts than that of Varian Associates. Bruker Magnetics, Inc., of Burlington, Massachusetts, had introduced a line of superconductivity magnets that could be combined with the novel technology of Fourier transform NMR. Bruker was able to beat Varian Associates on nearly every technical aspect and showed a greater willingness to take risks. Roberts’s decision to give the order to Bruker was Caltech’s first break from Varian Associates’ NMR equipment, and it proved to be the beginning of a strong position for Bruker in the United States.<sup>63</sup> In the 1970s Varian Associates decided to focus on the low-end, “analytical” part of the NMR market and thus lost the capacity to compete seriously with Bruker in the high-end segment.

Roberts’s defection from Varian Associates to Bruker demonstrates the importance of the compatibility of scientific and industrial aims. The overlap of functions—most importantly scientific research by the manufacturer and contributions to technological innovation by the user—characterized such cooperation. But if either party overstepped the boundaries of its designated sphere too dramatically friction could result: Roberts and his academic colleagues did not accept independent chemical research activities at Varian Associates, and Roberts tried to avoid involvement in the details of instrument construction. In his opinion, scientists who constructed the instrumentation themselves became so enamored with its design and improvement that their scientific productivity suffered. Cooperation with manufacturers enabled chemists to concentrate on scientific aspects, and this symbiosis worked well if the scientists knew exactly what they wanted and as long as they were able to communicate their concepts and needs to manufacturers that were willing to accommodate them.<sup>64</sup> Both sides needed a carefully balanced scheme for cooperation.

#### CONCLUSION

What makes a successful scientist? The standard view measures scientific performance by means of numbers of citations, amounts of funding, and the prestige associated with awards and prizes. Instruments help scientists to achieve their goals most efficiently if they are successfully adapted to established experimental cultures. Together with instrument manufacturers, John D. Roberts (see Figure 6) came to be a mediator between high-technology instrumentation and chemical research programs. He was a first mover and an innovative player in a scientific market of citations, grants, and accolades who took a prominent role in and full advantage of the marketing of instruments. Even before Roberts started his NMR work he had acquired great prestige in the field of physical organic chemistry. He was able to attach to the instruments a meaning rooted in the traditions of this booming

<sup>63</sup> For a description of the Bruker instrument—the WH-180—see Roberts, *Right Place at the Right Time*, pp. 203–205. On the decision to give the order to Bruker see Roberts to Peter Llewellyn of Varian, 30 Nov. 1972, Roberts Papers, folder “Varian Correspondence, 1970–1972.”

<sup>64</sup> Reinhardt interview with Roberts, 28 Jan. 1999.



**Figure 6.** John D. Roberts in 1967, examining a carbon-13 NMR spectrum taken by Frank J. Weigert with the Varian Associates DFS-60 NMR spectrometer. Courtesy of John D. Roberts.

subfield, and he brought to NMR the social prestige that physical organic chemistry enjoyed in the chemical community of the 1950s. Moreover, many questions in physical organic chemistry could be answered only through the sophisticated use of instrumentation. From the late 1950s, NMR led the way in Roberts's research, and he became a specialist in chemical and biochemical applications of the technique.

In Varian Associates, the first manufacturer of NMR spectrometers, Roberts found an ideal ally for his endeavors. Their mutual interest in the distribution of instruments facilitated a relatively smooth relationship until the end of the 1960s. Strains emerged when Varian Associates' employee James Shoolery acted as a scientific competitor and when the company—conscious of its monopoly—exerted too much influence on the community of NMR users. Though these problems were overcome, the fruitful symbiosis of Varian Associates and Roberts ended when the company's strategy came to favor the low-end side of technology and to concentrate on serving a mass market of users seeking routine, easy-to-use instruments. In the early 1970s, in his zeal for exclusive high-end equipment, Roberts began cooperating with the major competitor of Varian Associates, Bruker-Spectrospin. Lack of innovation and risk taking at Varian Associates caused this change,

as an alliance with an innovative manufacturer of instruments was a crucial requirement of Roberts's research program.

The story presented here is a snapshot, taken at exactly the moment when NMR moved from being a physical to becoming a chemical technique. A decisive issue in this process was the development of modes of investigation that, while still sufficiently attached to the established chemical culture to be recognized as a worthwhile undertaking, yet evoked a new experimental style. The applicability and range of methods determined the success of an instrument in a specific scientific domain. Developing research methods that could be used with soon-to-be commercial equipment became Roberts's specialty. In this, he contributed to the fields of organic chemistry and biochemistry and, finally, to medical applications as well.

Both Roberts and Shoolery can be described as lead users of scientific instruments for their roles in the establishment and development of chemical applications of NMR. Although Shoolery was employed by the instrument manufacturer Varian Associates, he adopted many features of scientific users during the crucial early period of chemical NMR. In this respect, his role went well beyond what might be expected of someone from an industrial applications laboratory. Prompted by his desire to create a market for NMR in chemistry, he contributed to the development of methods and the solution of scientific problems. Roberts came from the academic side with needs that could be fulfilled by a strategy similar to Shoolery's: access to advanced instrumentation and its dissemination in the scientific community. Through their tendency to work both at the limits of existing technology and at the forefront of science, Roberts and Shoolery expanded the range of applications of instruments. In doing so, they acted as mediators between instrument manufacturers and customer-scientists. I judge that such lead users of scientific instruments fulfill their functions best if they are already established scientists; their leadership is consolidated and enhanced by the successful use of instrumentation. In this situation, scientific lead users can contribute to the creation of a market for scientific instruments. Scientific lead users not only experience certain needs earlier than the average fellow scientist; with their paradigmatic solutions they shift future research in a direction that can be tackled with their novel research methods. In this respect, Roberts, as a renowned academic scientist, had crucial advantages over the industrial scientist Shoolery. Furthermore, he enjoyed a neutral position as mediator, while the Varian employee Shoolery did not. When a fully developed academic community of NMR users came into existence in the early 1960s, Shoolery's role as a lead user came to an end. In contrast, Roberts continued and even expanded his activities.

Through dictating specifications for novel custom-built instruments, lead users of NMR supplied the instrument manufacturers with ideas for improvements. This function of lead users must be carefully distinguished from von Hippel's concept of user-dominated innovation. Lead users fed the designers of instruments with specifications of needs and suggested ingenious combinations of existing technology to fulfill those needs. With few exceptions, lead users did not invent novel devices. Roberts, for example, preferred to describe what he needed and let the instrument company devise it. Because the industrial scientist Shoolery was close to the development and manufacturing departments of his firm, his work on improvements certainly was more substantial, but it also remained less visible. However, the aims of the industrial and the academic lead user in this regard differed: Shoolery was most concerned with designing instruments suited to routine use by organic chemists; Roberts, in contrast, never abandoned his aim to open up new fields for applications of NMR and tended to design complex instrumentation at the cutting edges

of science and technology—for example, his carbon-13 and nitrogen-15 NMR spectrometers. A very important part of lead users' activities involved teaching, textbook writing, and, more generally, the provision of an infrastructure that could support the use of NMR. In this category, the main emphasis here has been on Roberts's lecturing and textbook authorship; but Shoolery also contributed, with spectra catalogues, the *Varian Technical Information Bulletin*, and workshops.

For academic chemists, contacts with instrument manufacturers added a new side to long-established forms of cooperation with the chemical industry.<sup>65</sup> Traditionally, the objects of scientific and industrial work—such as substances and reactions—were the units of exchange. Now, however, the relationship became key to the very means that made the scientist's research possible. This created new types of dependency. The ability to maintain at least some influence over design criteria certainly explains a great part of the scientist's motivation in forging alliances of the sort that existed between Roberts and Varian Associates. Moreover, the access a company could afford to cutting-edge research instruments was valuable enough to justify the scientist's investment of his own ideas and time. Characteristically—at least in Roberts's case—financial rewards seem to have played no role. For the industrial scientist, cooperation with academic chemists sometimes resembled a dance on a volcano. If Shoolery did too much in research, he came to be seen as a competitor; not enough, and he might be judged to be unsupportive. As a consequence, the overlap of “typical” industrial and “typical” academic tasks was only partial and time limited.

The cooperation of an academic scientist and an instrument firm involved their respective core activities: the use of research instruments for the former and their construction and marketing for the latter. In this case, the norms of science and the interests of industry converged in a curious and distinct way. Mertonian norms of science dictated free access to results, including the research methods used, for everyone capable of understanding them. In contrast, self-interest led the scientist to cherish exclusivity in his use of advanced instrumentation. As a result, scientists tried to advance the capabilities of their instruments as quickly as possible, so as to stay ahead of their competitors. For this purpose, in particular, the scientist welcomed the support of an instrument manufacturer. Free availability and wide distribution of novel methods suited the business interests of the manufacturer, enhancing sales of instruments; here the norms of science converged with corporate aims. Keeping up the method-innovating pace could be both a successful scientific and a worthwhile business strategy. The lead-user concept directs our focus to the development of research methods as a major scientific activity. Arguably, it affords this perspective precisely because in the case of NMR instrument manufacturers threatened to withhold the chance to participate in such activity from chemists. This threat was in the background of many a quarrel between Roberts and Shoolery at Varian Associates. Nothing less than the methodological autonomy of organic chemists was at stake. In the long run, academic chemists prevailed: most of the methodological advances in NMR tended to be made in an academic environment, while firms designed and built the apparatus.

The levels of scientific practice that I investigated in this essay are those of instrument design, research publication, and teaching. While I do not deny the importance of close-quarter studies of scientists' work in the laboratory or of the intellectual history of theories and rules, I argue that public scientific activities deserve more scrutiny. Publishing, lec-

<sup>65</sup> A recent overview is Carsten Reinhardt and Harm G. Schröter, “Academia and Industry in Chemistry: The Impact of State Intervention and the Effects of Cultural Values,” *Ambix*, 2004, 51:99–106.

turing, and teaching were important components in Roberts's work, and the central role of the instrument expanded their scope. Each instrument based on Roberts's specifications meant that his methods could be used by others and—explicitly or implicitly—had to be cited. Thus, the spread of instruments in the scientific community enhanced the reputation of the scientist who stood behind their design. The instrument became a scientific commodity. While Roberts enjoyed the advantages of applying cutting-edge instrumentation, he had to make sure that the novelties of today would become commonplace tomorrow: the benefits of exclusivity counted only if exclusivity was a transient phenomenon. In pursuit of this goal, lead users worked through formal and informal contacts with the governmental agencies that initiated major funding programs, through public lectures and articles, and through the writing of textbooks that advertised and taught the rules of chemical applications of NMR and other techniques.